COGNITIVE DEFICITS IN CARDIAC REHABILITATION

COGNITIVE DEFICITS IN CARDIAC REHABILITATION: A COMPARISON OF POST-BYPASS SURGERY AND POST-ANGIOPLASTY PATIENTS

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LAY ABSTRACT

Cardiac rehabilitation (CR) is a multifaceted program consisting of exercise and education that is essential to the care of post-coronary revascularization patients. While exercise has shown to improve health outcomes, education has demonstrated inconsistent effects. Since education has imposed cognitive demands, this discrepancy in outcomes may, in part, be due to cognitive deficits present in a proportion of program attendees: the degree of impairment may vary by type of coronary revascularization procedure prior to CR. This study compared cognitive function between two groups of coronary revascularization patients, post-coronary bypass surgery and post-coronary angioplasty, and determined independent variables for cognitive function. Results showed that coronary bypass surgery patients had significantly lower cognitive function than coronary angioplasty patients at program intake. Coronary bypass surgery and accumulated disease burden were weakly associated with decreased cognitive function. Cognitive screening and adapted education for patients with cognitive deficits should be considered to improve CR outcomes.

ABSTRACT

Mild cognitive deficits that negatively impact self-management education-related outcomes may be present in a proportion of cardiac rehabilitation patients and the degree of impairment may vary by the type of coronary revascularization procedure. The purpose of this study was to compare cognitive function, as measured by the Montreal Cognitive Assessment (MoCA), between coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) patients, and to determine independent variables of MoCA score. In a cross-sectional study, 78 cardiac rehabilitation patients (CABG n = 38, PCI n = 40) completed the MoCA. Demographics were collected and disease burden was calculated using the age-adjusted Charlson Comorbidity Index (ACCI). Mild cognitive deficits (MoCA ≤26) were present in 55.3% CABG and 30.0% PCI patients. An independent Student's *t* test showed that MoCA scores were significantly lower among CABG patients (mean = 24.5, SD = 3.3) compared to PCI patients (M = 26.7, SD = 2.7), t (76) = 3.15, $p < 0.01$. Descriptive analyses of cognitive domain scores indicated that deficits in short-term memory and language were present among CABG patients. Using a backward regression, coronary revascularization procedure (CABG vs. PCI) ($p = 0.006$) and disease burden (ACCI) ($p = 0.015$) remained significant, while heart failure diagnosis became non-significant and was removed from the model (F (2, 75) = 8.382, $p < 0.001$). The final model explained 16.1% of the total variance in MoCA score (adjusted $R^2 = 0.161$). Results indicate that cognitive deficits were present in cardiac rehabilitation participants and associated with the type of coronary revascularization procedure, suggesting the need for formal cognitive screening and adaptation of education interventions in cardiac rehabilitation. A future prospective cohort study is required to establish temporality, and to measure education-related outcomes, such as health-related quality of life (HRQOL) and self-management.

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ACRONYMS

ACCI	Age-adjusted Charlson Comorbidity Index
ADL	Activities of daily living
AMI	Acute myocardial infarction
CABG	Coronary artery bypass graft surgery or coronary bypass surgery
CAD	Coronary Artery Disease
HADS	Hospital Anxiety and Depression Scale
HF	Heart failure
HRQOL	Health-related quality of life
MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
NSTEMI	Non-ST-elevation myocardial infarction
PCI	Percutaneous coronary intervention or coronary angioplasty
POCD	Postoperative cognitive dysfunction
STEMI	ST-elevation myocardial infarction

DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis reports the original research that I have conducted under the supervision of Drs. Patricia Strachan, Karen Harkness, Michael McGillion, and Robert McKelvie since September 2014. The supervisory committee members provided their expertise towards: the study design and research methodology, research proposal and protocol, Hamilton Integrated Research Ethics Board application, and all chapters of the thesis dissertation (i.e., introduction and problem statement, literature review and conceptual framework, research methodology, results, and discussion). I completed all components of data collection, including administration of the Montreal Cognitive Assessment and conduction of chart reviews. Statistical analyses were completed by myself with expert consultation and verification of results from Drs. Kathy Fisher, Noori Akhtar-Danesh, and Karen Harkness. Sample size was calculated by Dr. Noori Akhtar-Danesh.

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CHAPTER 1

INTRODUCTION AND PROBLEM STATEMENT

Background

Cardiac rehabilitation is a multifaceted secondary prevention intervention that is integral to the care of patients who have had a coronary revascularization procedure. Typical program components include: (1) supervised exercise and related counseling, (2) self-management education and support, (3) lifestyle counseling and behaviour change, and (4) psychological counseling (Arthur et al., 2010; Cardiac Care Network[CCN], 2014b; Leon et al., 2005; Kwan, & Balady, 2012).

Published evidence has shown that self-management education outcomes in cardiac rehabilitation (as measured by health-related quality of life [HRQOL] and program adherence) may be influenced by individual patient factors, such as cognitive deficits (King, Humen, & Teo, 1999; Karmali et al., 2014; Murray, Craigs, Hill, Honey, & House, 2012; Neubeck et al., 2011). It has been suggested that cognitive deficits may negatively impact HRQOL and adherence to interventions aimed at improving self-management in patients with cardiovascular disease (Caminiti et al., 2012; Cooper, Jackson, Weinman, & Horne, 2002; Feil, Zhu, & Sultzer, 2012; Foster et al., 2011; Heckman et al., 2007; Kakos et al., 2010; Stilley, Bender, Dunbar-Jacob, Sereika, & Ryan, 2010). A large retrospective study of 1245 patients found that patients with cognitive deficits (odds ratio [OR] = 0.26) were associated with a decreased likelihood of cardiac rehabilitation program adherence (King et al., 1999).

While it has been known for nearly two decades that cognitive deficits may impede the success of patients attending self-management education, evidence has suggested that self-management education outcomes in cardiac rehabilitation may still be suboptimal (Anderson &

Taylor, 2014; Brown, Clark, Dalal, Welch, & Taylor, 2011; Janssen, Gucht, Dusseldorp, & Maes, 2012; Kadda et al., 2015; Linden, Phillips, & Leclerc, 2007; Shepherd & While, 2012). In a systematic review, Brown et al. (2011) reported that there was no consistent evidence of improved HRQOL following education interventions (i.e., self-directed vs. group sessions, videotapes, workbook, delivery by health educator, telephone vs. online vs. face-to-face sessions). Poor long-term adherence has continued to be reported among patients attending cardiac rehabilitation programs. A regional analysis of cardiac rehabilitation programs in Alberta showed that less than 50 percent of referred patients completed the program and this is corroborated by studies based in the United States (Daly et al., 2002; Davies et al., 2010; Grace, Bennett, Ardern, & Clark, 2014; Moore, Dolansky, Ruland, Pashkow, & Blackburn, 2003). Cognitive deficits were not considered in contemporary systematic reviews of barriers for and interventions to improve cardiac rehabilitation program adherence despite sustained substandard outcomes (Karmali et al., 2014; Murray et al., 2012; Neubeck et al., 2011).

Mild cognitive deficits are impairments in an individual's processes that influence learning and decision making and may help explain the ineffectiveness of self-management education interventions (Hicks & Holm, 2003; Lippa, Klein, & Shalin, 2008; Naik, Dyer, Kunik, & McCullough, 2010). A systematic review has shown that cognitive deficits are present in some patients with coronary artery disease (CAD) and thus, may be present in a proportion of cardiac rehabilitation patients (Eggermont et al., 2012). Mounting evidence suggests that the type of coronary revascularization procedure that a patient has undergone, (i.e., coronary artery bypass graft surgery [CABG] vs. percutaneous coronary intervention [PCI]), may be positively associated with the degree of cognitive impairment (Djaiani et al., 2012; Farhoudi et al., 2010; Fontes et al., 2013; Kennedy et al., 2013; Knipp et al., 2008; Newman et al., 2001, 2007; Takagi, Tanabashi, Kawai, & Umemoto, 2007; van Dijk et al., 2007; Selnes et al., 2008; Selnes et al., 2012).

Problem Statement

Mild cognitive deficits may contribute to the small and inconsistent effect of education-based cardiac rehabilitation outcomes (HRQOL and program adherence) (Brown et al., 2011; Grace et al., 2014; King et al., 1999). Evidence suggests differential degrees and affected cognitive domains between different types of coronary revascularization procedures, with CABG patients being at increased risk for cognitive deficits (Benvenuti et al., 2013; Djaiani et al., 2012; Eggermont et al., 2012; Farhoudi et al., 2010; Fontes et al., 2013; Kennedy et al., 2013; Knipp et al., 2008; Newman et al., 2001, 2007; Takagi et al., 2007; van Dijk et al., 2007; Selnes et al., 2008; Selnes et al., 2012). The current understanding of cognitive deficits in cardiac rehabilitation is limited despite the deleterious effects that cognitive deficits may have on self-management education and related self-management. Given that the effect of education in cardiac rehabilitation is suboptimal and comparisons of cognitive function by the type of coronary revascularization procedure have not been conducted, further exploration of the cognitive status of cardiac rehabilitation patients who have undergone a coronary revascularization procedure is required.

CHAPTER 2

LITERATURE REVIEW AND CONCEPTUAL FRAMEWORK

Cardiac rehabilitation is an essential component of cardiovascular risk factor management, and includes exercise, lifestyle counseling and behaviour change, self-management education, and psychological counseling components (Arthur et al., 2010; CCN, 2014b). In cardiac rehabilitation programs, exercise-based cardiac rehabilitation interventions have been shown to be more effective than non-exercise interventions in reducing mortality and morbidity and improving HRQOL; other components of cardiac rehabilitation demonstrate small and less consistent effects (Anderson & Taylor, 2014; Brown et al., 2011; Heran et al., 2011; Janssen et al., 2012; Kadda et al., 2015; Lawler, Filion, & Eisenberg, 2011; Linden et al., 2007; Shepherd & While, 2012). Non-exercise components such as self-management education, impose cognitive demands on cardiac rehabilitation participants (Hicks, & Holm, 2003; Lippa et al., 2008; Naik et al., 2010), yet the level of cognitive function of these patients is largely unexplored (King et al., 1999). Acquiring, retaining, and applying knowledge acquired in cardiac rehabilitation that is aimed at learning self-management of a chronic condition requires executive functions, attention, and memory (Naik et al., 2010). It is possible that differences in the effectiveness of exercise and non-exercise components may be due, in part, to cognitive deficits in a proportion of participating patients and further, the degree of this impairment may vary by the type of coronary revascularization procedure that patients have undergone prior to cardiac rehabilitation enrollment. The present study used a conceptual framework that addressed the complexity of chronic disease self-management as the basis for developing further understanding about cognitive function among cardiac rehabilitation patients who had undergone a coronary revascularization procedure.

The Chronic Care Model was the framework used to guide the selection of variables for the present study (Wagner, Austin, & von Korff, 1996). Wagner et al.'s (1996) Chronic Care Model is one of the most widely used conceptual frameworks used in cardiac rehabilitation to address the dynamic relationship between a patient's self-management and self-management support (Arthur et al., 2010; CCN, 2014b). *Self-management* refers to the cognitive skills required to make decisions and engage in healthy behaviours to manage one's chronic disease (Barlow et al., 2002; Russell, 2006). *Self-management support* is defined as the provision of education, counseling, and other interventions by health care providers aimed to help patients gain confidence, knowledge, and skills to manage their chronic disease (Bodenheimer & Wagner, 2002; Epping-Jordan, Pruitt, Bengoa, & Wagner, 2004). The model identifies factors that influence self-management support that guided the selection of variables in this study, such as lifestyle factors (i.e., smoking) and social factors (i.e., education level) (Bodenheimer & Wagner, 2002; Epping-Jordan et al., 2004).

Literature Review

This chapter reviews the evidence surrounding cognitive deficits among cardiac rehabilitation patients, arguing that cognitive deficits pose a potential barrier to effective cardiac rehabilitation participation and associated educational interventions. The chapter begins with a description of the relevant terminology for cardiovascular disease and cognitive function, and is followed by a review of the literature. The evidence is reviewed for cognitive deficits in cardiovascular patients whether or not they are enrolled in cardiac rehabilitation, including CABG, PCI, heart failure (HF), post-myocardial infarction (post-MI), and CAD patients.
There was incomplete reporting of statistical tests for some studies; where possible, test statistics were provided for reviewed studies. First, the effectiveness of exercise-based cardiac

rehabilitation and self-management support are reviewed in relation to mortality, morbidity and HRQOL, proposing that there are potential cognitive barriers to effective cardiac rehabilitation outcomes. Second, the relevance of cognitive deficits to cardiac rehabilitation participation and educational interventions and related self-management is discussed. Third, the etiology and nature of cognitive deficits in cardiac rehabilitation are reviewed, supporting the need to examine cognitive deficits among different types of coronary revascularization procedures. Evidence is reviewed in relation to (1) classifications, pathophysiological mechanisms and risk factors for cognitive deficits related to cardiac interventions, specifically CABG and PCI, and (2) the types of cognitive deficits that may be observed in cardiac rehabilitation. The limitations of cognitive screening instruments used in existing studies of cardiac patients are discussed, arguing for the necessity of using a cognitive screening instrument that is sensitive for subtle cognitive deficits that have been reported in cardiac populations. A summary of the conclusions follows the review of the literature. The chapter concludes with the conceptual framework developed from Wagner et al.'s (1996) Chronic Care Model (1996) that guided the selection of variables in this study.

Definition of Terms.

The following section describes the key terms and concepts regarding cardiac disease and cognitive function in this thesis dissertation (See Table 1).

Table 1: Concepts and Definitions for Cardiovascular Disease and Cognitive Function

Cardiovascular Disease Concepts and Definitions	
Term	**Description**
Coronary Artery Disease (CAD)	CAD is the most common form of cardiovascular disease and refers to the progressive narrowing of one or more arteries that supply blood to the myocardium (Menees & Bates, 2010). CAD begins when cholesterol is deposited as plaques into the coronary arteries; plaques narrow the arteries and result in the formation of clots that further obstruct blood flow.

	Obstruction of blood flow, also known as *ischemia*, produces typical signs and symptoms of CAD, such as *angina* or *acute myocardial infarction* (*AMI*).
Cardiovascular Risk Factors	A number of modifiable and non-modifiable factors may increase an individual's risk for developing CAD. *Modifiable risk factors* include: hypertension, smoking tobacco, diabetes mellitus, physical inactivity, unhealthy diet, dyslipidemia, and obesity (Goff et al., 2014). *Non-modifiable risk factors* include: age, sex, and family history.
CAD Management	The management of CAD consists of *pharmacological* and *non-pharmacological* therapies: *Pharmacological management* is further subdivided into antianginal therapies (i.e., beta blockers, calcium channel blockers, and nitrates), antiplatelet therapies (e.g., P2Y12 inhibitors [clopidogrel] and aspirin), angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers, and statins (Mancini et al., 2014). *Non-pharmacological management* of CAD consists of coronary revascularization procedures and cardiac rehabilitation programs.
Coronary Revascularization	Coronary revascularization is the restoration of blood flow to an ischemic area of the myocardium. The two types of coronary revascularization procedures are: (1) Coronary artery bypass graft surgery (CABG), and (2) Percutaneous coronary intervention (PCI).
Coronary Artery Bypass Graft Surgery (CABG)	CABG is a type of surgical procedure in which a section of a blood vessel, usually an internal mammary artery or saphenous vein, is grafted from the aorta to a site on a coronary artery beyond an occlusion (Weintraub et al., 2012). Indications for CABG include, but are not limited to: (1) Greater than 50% occlusion of the left main coronary artery, (2) Greater than 70% occlusion of the proximal left anterior descending and proximal circumflex arteries, and (3) Three-vessel disease (Hillis et al., 2011). CABG is performed either *on-pump* or *off-pump*. (1) *On-pump* CABG is performed while the heart is stopped using a cardiopulmonary bypass machine (heart-lung machine or pump) for artificial circulation.

	(2) *Off-pump* CABG is performed while the heart is still beating.
Percutaneous Coronary Intervention (PCI)	PCI is a non-surgical procedure in which a balloon catheter is used to dilate a narrowed coronary artery followed by the insert of a stent (Boden et al., 2008). Patients who have undergone PCI represent a significant portion of the non-CABG population who attend cardiac rehabilitation. In the CCN annual report (2014a), there were 24,573 Ontarians who underwent PCI, 78 percent of which were done immediately following diagnostic angiography. Post-PCI patients have similar cardiovascular risk factors compared to post-CABG patients according to recent Ontario data. A comparison of clinical characteristics adapted from the CCN is summarized in Table 2 (CCN, 2014a). Indications for PCI include, but are not limited to: (1) ST-elevation myocardial infarction (STEMI), (2) Non-ST-elevation myocardial infarction (NSTEMI), and (3) Stable angina (Levine et al., 2016). Stents are either bare metal stents or drug-eluting stents.
Cardiac Rehabilitation	Participation in cardiac rehabilitation is recommended for most patients with CAD as a risk reduction intervention (Anderson & Taylor, 2014; Heran et al., 2011; Janssen et al., 2012; Kadda et al., 2015; Lawler et al., 2011; Linden et al., 2007; Shepherd & While, 2012). Cardiac rehabilitation programs are comprehensive and multidisciplinary health interventions aimed at reducing cardiovascular risk factors through therapeutic exercise, health education, and counseling. Cardiac rehabilitation typically begins 4 to 6 weeks following a coronary revascularization procedure with a patient intake assessment and identification of cardiovascular risk factors. The patient engages in components of the programs aimed at reducing his or her modifiable risk factors. Indications for cardiac rehabilitation include: (1) Acute coronary syndromes (STEMI, NSTEMI, unstable angina), (2) Chronic stable angina, (3) Congestive HF, (4) Post-PCI, (5) Post-CABG, and (6) Post-valve surgery (CCN, 2014b).
Self-Management	Self-Management is defined as having sufficient knowledge about a chronic condition and its relevant therapies, and having the cognitive ability to apply it towards making decisions and adhering to behaviours

	that maintain health (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002; Russell, 2006).

Cognition Concepts and Definitions

Term	**Description**
Cognition	Cognition encompasses all intellectual functions that allow individuals to process and interact with the environment through thoughts, feelings, and emotions (Fayers et al., 2005). Cognitive domains include: executive functions, memory, language, visuospatial skills, and behaviour (McLennan, Mathias, Brenna, & Stewart, 2011). Cognition in aging individuals is considered a spectrum that ranges from normal cognitive aging to levels of cognitive impairment.
Normal Cognitive Aging	Normal cognitive aging refers to the expected changes in cognitive function as an individual advances in age. Older adults require increased time to complete cognitive tasks, especially those that require significant working memory, processing speed, and complex problem solving (Anstey & Low, 2004).
Cognitive Deficits	A cognitive deficit is a general term used to describe an impairment in an individual's intellectual processes. Relevant cognitive deficits among individuals with CAD are: (1) Postoperative delirium, (2) Post-operative cognitive dysfunction (POCD) related to cardiac surgery (i.e., CABG), and (3) Mild cognitive impairment (MCI).
Postoperative Delirium	Postoperative delirium is a transient and reversible state of confusion that may occur following CABG or other major surgery. The American Psychological Association's Diagnostic and Statistical Manual, 5th edition (DSM-5) primarily identifies delirium as a disturbance in attention or the ability to direct focus that fluctuates over time (American Psychological Association [APA], 2013). Inattention is often accompanied by memory deficits, disorientation to time and/or place, language deficits, or visual-spatial impairment.
Postoperative Cognitive Dysfunction (POCD)	POCD is a temporary, but persistent, state of relative cognitive decline that presents following CABG (Evered, Silbert, & Scott, 2016; Newman et al., 2001, 2007; Sauër, Kalkman, & van Dijk, 2009; Tan & Amoako, 2013).

	Unlike delirium, POCD may last several months before it is resolved. It is typically measured by a battery of 8 to 10 neuropsychological tests and is defined by a set number of standard deviations (SD), which varies between studies, away from preoperative cognitive function (Evered et al., 2016; Tan & Amoako, 2013). The definition of POCD is distinct from other types of cognitive deficits in that there is no functional assessment or subjective interpretation of decline in cognitive function (Evered et al., 2016; Tan & Amoako, 2013).
Mild Cognitive Impairment (MCI)	MCI is a slight, but measurable, chronic decline in cognitive function (Chertkow et al., 2007). Unlike POCD, MCI is defined by a decline in the ability to perform *instrumental activities of daily living (IADLs)*, such as managing finances and organizing medications, but sustained ability to perform *basic activities of daily living (ADLs)*, such as bathing and toileting. Diagnosis of MCI also requires decline in at least one cognitive domain on a neuropsychological test (Chertkow et al., 2007). MCI is known as an intermediate stage between normal cognitive aging and *dementia*, a severe and progressive type of cognitive deficit; most individuals with MCI will progress to dementia (Chertkow et al., 2007).

Table 2: Cardiovascular Risk Factors of PCI and CABG Patients in Ontario (CCN, 2014a)

Variable	**PCI** (n = 24, 575)	**CABG** (n = 11,442)
Age (years) (mean)	65.2	65.9
Hypertension (%)	64	69
Diabetes (%)	29	33
History of Smoking (%)	49.7	51.1
Cerebrovascular Disease (%)	5.9	8.7
Peripheral Vascular Disease (%)	5.9	8.9
Heart Failure (HF) (%)	6.1	14.4
Hyperlipidemia (%)	61.5	63.8

Effectiveness of Cardiac Rehabilitation Programs.

Cardiac rehabilitation is a specialized and multidisciplinary component of cardiovascular risk factor management. This review discussed the effectiveness of components of cardiac rehabilitation as they pertain to exercise- (i.e., supervised exercise) and non-exercise-based (i.e., self-management support, nutritional counseling, smoking cessation, psychological counseling, medication optimization and adherence) interventions. Although cardiac rehabilitation is widely supported by both national and international guidelines, there are discrepancies in effectiveness between exercise and non-exercise interventions (Arthur et al., 2010; CCN, 2014b; Armstrong et al., 2004; Grace et al., 2011). While these discrepancies may exist as a result of a number of factors (i.e., implementation or delivery of self-management education), this review solely examined cognitive deficits. A limited number of studies include cognitive function as an outcome of exercise-based cardiac rehabilitation, which are discussed later in this review. No known studies directly examined the relationship between educational interventions in cardiac rehabilitation and cognitive function. However, cardiac rehabilitation interventions are associated with improved HRQOL, a common outcome of self-management education interventions, and the presence of cognitive deficits have been shown to decrease HRQOL (Pressler et al., 2010). Therefore, this literature review focuses on the effect of HRQOL and other outcomes related to self-management support, such as cardiovascular risk profiles.

Exercise-Based Cardiac Rehabilitation.

Numerous studies have shown that exercise is the most demonstrably effective component of cardiac rehabilitation that is associated with improvements in mortality, morbidity, and HRQOL (Anderson & Taylor, 2014; Heran et al., 2011; Lawler et al., 2011). A meta-analysis of 47 RCTs (n = 10,794, median age = 55.0) reported that participation in exercise-based cardiac rehabilitation was associated with a reduction in all-cause mortality (relative risk [RR] 0.87, 95% CI 0.75, 0.99), cardiovascular related mortality (RR 0.69, 95% CI 0.51, 0.93), and hospital admissions (RR 0.69, 95% CI 0.51, 0.93) (Heran et al., 2011). Ten studies examined

HRQOL, and the studies included in this systematic review did not show a consistent effect in improving HRQOL (Heran et al., 2011). Due to the use of different HRQOL instruments across studies, a meta-analysis could not be conducted. Seven of these 10 RCTs reported that cardiac rehabilitation increased HRQOL. Exercise-based cardiac rehabilitation programs varied considerably in duration (1 to 12 months), frequency (1 to 7 sessions per week), and session length (20 to 90 minutes) (Heran et al., 2011). HRQOL was measured using a number of different validated instruments, such as the Medical Outcomes Study Short Form-36 (SF-36), Nottingham Health Profile (NHP), and the Sickness Impact Profile (Heran et al., 2011). Exercise-based cardiac rehabilitation has also been shown to improve the cardiovascular risk profiles of cardiac patients. The results of a systematic review of 34 RCTs (n = 6,111) indicated that patients participating in a structured, exercise-based program had improved cardiovascular risk profiles when compared to a control group, including decreased smoking, blood pressure, and body weight, and improved lipid profile (Lawler et al., 2011). The cognitive status of participants was not measured in the studies included in the systematic review and the presence of cognitive deficits was not considered directly as part of the selection criteria. This evidence suggests that delivery of exercise and exercise counseling interventions in cardiac rehabilitation may not be optimal in improving HRQOL and supports the need to explore potential intervening factors.

Self-Management Education and Support.

The inconsistent effects of self-management education and support have been documented in a number of quantitative studies of cardiac rehabilitation. A meta-analysis of 13 RCTs by Brown et al. (2011) (n = 68,556, mean age = 62; post-MI, post-PCI, and HF patients) reported that there were no statistically significant improvements in all-cause mortality (RR 0.79, 95% CI 0.55, 1.13), recurrent AMI (RR 0.63, 95% CI 0.26, 1.48), CABG (RR 0.58, 95% CI 0.19, 1.71), and hospitalization (RR 0.83, 95% CI 0.65, 1.07). A pooled estimate could not be provided for HRQOL since several different HRQOL instruments were used across the included studies. No consistent differences in total or domain scores for HRQOL were reported between the intervention and control groups. Five studies individually demonstrated statistically significant differences in favour of the intervention, and no studies favoured the control group. Intervention content included cardiovascular risk factor management, education regarding pathophysiology, behaviour change and adherence strategies, and cardiac medications. Education dose (mode of delivery or intensity) varied and ranged from a total of two clinic visits to a four-week residential stay with an 11-month follow-up. HRQOL was measured using generic (SF-36, NHP, Sickness Impact Profile) and disease-specific (Seattle Angina Questionnaire, Angina Pectoris-Quality of Life Questionnaire) instruments.

In summary, the evidence is clear that exercise-based cardiac rehabilitation is effective in reducing mortality and morbidity, however the results for HRQOL are considerably more variable. Furthermore, the effect of self-management education and support on HRQOL is inconsistent. While some studies indicated that educational interventions improved HRQOL, the variability in the results limited generalizability. The inconsistency of the study results suggests that there may be barriers to effective cardiac rehabilitation that have not yet been examined. One known barrier for effective self-management education in other chronic disease populations is the presence of cognitive deficits (Hicks & Holmes, 2003; Lippa et al., 2008).

Cognitive Deficits as a Barrier for Cardiac Rehabilitation.

Cognitive deficits are a well-known contributor to decreased HRQOL and functional impairment and have implications for cardiac rehabilitation effectiveness, self-management education and related self-management, and participation in cardiac rehabilitation (Gunstad et al., 2005). Evidence from four observational studies suggests that poor cognitive function may negatively impact cardiac rehabilitation outcomes. An observational study by Kakos et al. (2010) (n = 44; mean age = 67.6 years, SD = 9.3) reported that executive dysfunction was weakly associated with lower cardiovascular fitness as measured by metabolic equivalents (METs) ($r = -0.27$, $p < 0.05$) upon program completion after adjusting for age, reading ability and HRQOL. Executive dysfunction was also negatively associated with decreased HRQOL as measured by the mental component of the SF-36 ($r = -0.25$, $p < 0.05$) upon program completion. HRQOL was assessed using the SF-36 and cognitive function was measured with the Trail-Making Test B, a test commonly incorporated in many cardiac-sensitive cognitive screening instruments and test batteries (McLennan et al., 2011). A subsequent quantitative study of older adults with HF examined the negative impact of cognitive deficits on cardiovascular fitness (Garcia et al., 2013). Garcia et al. (2013) (n = 41; mean age = 68.34, SD = 8.41) reported the results of partial correlation analyses, showing that decreased executive function (Trail-Making Test B) ($r = 0.40$, $p < 0.02$) and attention (Trail-Making Test A) ($r = 0.34$, $p < 0.047$) were associated with poorer cardiovascular fitness (2-minute step test [2MST]).

Foster et al. (2011) (n = 27) reported similar findings in a sample of HF patients. The presence of executive dysfunction (Dysexecutive Questionnaire), and depressive symptoms (Center for Epidemiological Studies Depression Scale) were negatively associated with cardiac rehabilitation participation, accounting for 35% of the variance in cardiac rehabilitation participation (Activity Card Sort) ($r^2 = 0.35$, F [2, 20] = 6.68, $p < 0.01$) in community-dwelling patients. Burkauskas, Brozaitiene, & Bunevicius (2013) (n = 539; mean age = 58 years, SD = 9) also reported in a multivariate regression analysis that cognitive function, measured by backward digit recall, was negatively associated with fatigue ($\beta = -0.089$, $p < 0.05$) and decreased motivation ($\beta = -0.116$, $p < 0.01$). These studies underscore the negative impact that cognitive deficits appear to have on participation in outpatient cardiac rehabilitation and its subsequent health outcomes (i.e., cardiovascular fitness, HRQOL). In summary, the available quantitative studies suggest that there is considerable cognitive demand placed on people engaged in self-management education and self-management activities, and that cognitive deficits may play a pivotal role in the context of negative cardiac rehabilitation-related outcomes.

Education and Related Self-Management.

Although evidence about the necessary cognitive function prerequisites for effective cardiac rehabilitation is limited, evidence from other chronic disease populations suggest that self-management education is demanding cognitively. Lippa et al. (2008) interviewed 18 patients with diabetes to examine the relationships between cognitive processes and self-management behaviours. Results from the Kruskal-Wallis *H* test suggested that a patient's ability to detect problems was associated with improved self-management (i.e., glycemic control) ($H = 9.93$, $p < 0.05$). Being able to verbally articulate relationships involved in self-management behaviours ($H = 6.085$, $p < 0.05$) and being able to articulate problem solving strategies ($H = 6.70$, $p < 0.05$) were associated with improved treatment adherence (Lippa et al., 2008). While the study did not include patients with cardiac disease and the sample size was small, it emphasized that self-management required that patients could describe tasks involved in self-management and apply subsequently the knowledge as self-management actions.

The negative impact of cognitive deficits on self-management education and self-management, such as memory impairment or executive dysfunction on self-management education and self-management, were reported in several quantitative studies (Hayes, Alosco &

Forman, 2014; Heckman et al., 2007; Rudolph et al., 2010; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007). A prospective cohort study (n = 8,698; mean age = 73.1, SD 7.0) examining community-based older adults found that decreased self-management behaviour (Self-Neglect Scale) was independently associated with poorer global cognitive function, after controlling for socio-demographic characteristics and comorbidity covariates, accounting for almost 32% of the variability in global cognition ($R^2 = 0.317$, $\beta = -0.363$, standard error [SE] = 0.026, $p < 0.001$) (Dong, Truong, Towle, Kerins, & Chaudhry, 2009). Studies of cognitive deficits in cardiac disease have primarily examined patients with HF (Alosco et al., 2014; Heckman et al., 2007; Harkness et al., 2014; Hjelm, Broström, Riegel, Årestedt, & Strömberg, 2015; Pressler et al. 2010).

Associations related to decreased HRQOL, reduced medication adherence, missed appointments, and poor adherence to health behaviours have been established in HF and CABG patients (Harkness et al., 2014; Heckman et al., 2007; La Pier, 2007; Phillips-Bute et al., 2006; Vogels et al., 2007). An observational study by Pressler et al. (2010) (n = 249; mean age = 62.9 years, SD 14.6, HF) showed that age, depressive symptoms, HF severity, and total recall memory were negatively associated with HRQOL, explaining 55 percent of the variance in HRQOL (R^2=55%).

Harkness et al. (2014) (n = 100; mean age = 72, SD 10 years) reported similar results using the Montreal Cognitive Assessment (MoCA) to measure cognitive function and the Self-Care Heart Failure Index (SCHFI) to measure self-management. The presence of cognitive deficits (low MoCA score) predicted poor self-management in a backward regression model (R^2=18.03%, $p = 0.001$). In another cross-sectional study, Hjelm et al. (2015) (n = 105; mean age = 72, IQR 65-79, HF patients) found that impairments in psychomotor speed and executive function (Trail Making Test A) explained 12% of the variance in self-management in a multivariate linear regression when controlled for age, education and New York Heart Association class ($R^2 = 0.12$, $F [5, 99] = 2.74$, $p < 0.023$). These data suggest that in community-dwelling adults, cognitive problems that affect behaviour are apparent, and that self-management education that does not consider cognitive function may not be sufficient to improve health outcomes.

The results of an observational study by Alosco et al. (2014) (n = 197; mean age = 68.07 years, SD 8.94) supported the assertion that cognitive deficits negatively impacted cardiac rehabilitation outcomes. Community-dwelling patients with HF completed a neuropsychological battery of tests (Trail-Making Tests A and B, Digit Symbol Coding, Letter Number Sequencing, California Verbal Learning Test-Second Edition), physical fitness test (2MST) and total activities of daily living (ADL) capacity score (composite score of ADLs and IADLs). Although the total ADL capacity was a composite score, patients frequently reported challenges with IADLs, including laundry (38.8%), housekeeping (36.6%), and food preparation (31.5%). The addition of cognitive function to the model diminished the relationship between physical fitness and functional capacity so that it became non-significant. The structural pathways of the model indicated that decreased fitness was associated with decreased cognitive function and decreased cognitive function was associated with decreased total ADL capacity ($\beta = 0.35$, $p < 0.05$). The mediating effect of cognitive function was supported with further statistical testing (Sobel test), which showed that fitness indirectly affected functional capacity through the effects of cognitive function ($p < 0.05$). The results indicated that cognitive deficits may reduce the benefits of physical and functional outcomes of cardiac rehabilitation and may create challenges with self-management. Thus, cognitive deficits may reduce the effectiveness of cardiac rehabilitation outcomes.

Two observational studies examined the impact of cognitive deficits among post-CABG patients. Phillips-Bute et al. (2006) (n = 551; mean age = 62.32, SD 11.0, post-CABG) found that cognitive deficits, measured using a validated battery of five tests at 6-weeks and 1-year post-CABG, were associated with reduced improvements in HRQOL after the first postoperative year. Thirty-six percent of post-CABG patients had detectable cognitive deficits (Phillips-Bute et al., 2006). When covariates were controlled (preoperative cognitive function, baseline quality of life, sex, race, age, and Charlson Comorbidity Index [CCI]), a multivariate linear regression model revealed the cognitive deficits (change in cognitive function after 1 year) were negatively associated with the following HRQOL outcome measures: (1) IADL performance from the Duke Activity Index ($\beta = -3.66$, 95% confidence interval [CI] -4.77 to -2.54, $p < 0.0001$); (2) the presence of symptoms that limited daily activities ($\beta = -3.33$, 95% CI -5.03 to -1.63, $p < 0.0001$); (3) perceived problems with daily cognitive processes ($\beta = -18.98$, 95% CI -27.74 to -10.21, $p < 0.0001$); and (4) depressive symptoms measured by the CES-D ($\beta = -7.65$, 95% CI -10.95 to -4.35, $p < 0.0001$) (Phillips-Bute et al., 2006). Cognitive deficits were positively associated with HRQOL as measured by General Health Perception ($\beta = 0.72$, 95% CI -1.08 to -0.36, $p = 0.0001$) (Phillips-Bute et al., 2006). The results reveal that short- and long-term declines in cognitive function were also associated with declines in HRQOL at 1-year following CABG surgery (Phillips-Bute et al., 2006).

Fontes et al. (2013) (n = 229; mean age = 67.6, SD = 10.3 in cognitively impaired patients) reported similar results with a retrospective study of post-CABG patients, suggesting that patients who have underwent CABG may have experienced greater cognitive impairment compared to other cardiac populations. The results showed greater years of education (OR 0.987 [0.976, 0.998], $p = 0.02$), greater performance in daily activities (OR 0.891 [1.014, 1.075], $p = 0.02$), and less decline in cognitive function at the sixth postoperative week (OR = 1.044 [1.014, 1.075], $p = 0.004$) were significant predictors of successful cognitive recovery following CABG. Therefore, evidence suggests that cognitive deficits may be problematic for both exercise and self-management education/support components of cardiac rehabilitation, and that CABG patients may be more likely to experience cognitive problems compared to other cardiac rehabilitation attendees. Studies comparing post-CABG cognitive deficits with other types of coronary revascularization procedures have not been conducted (Fink et al., 2014).

Cardiac Rehabilitation Participation and Adherence.

With only 15 to 30 percent eligible patients enrolling in cardiac rehabilitation and under 50 percent of attendees adhering to behaviours long-term, it is well-established that cardiac rehabilitation programs are underutilized (Daly et al., 2002; Grace et al., 2014; Moore et al., 2003; Neubeck et al., 2011). Three systematic reviews summarized the barriers and facilitators that influenced cardiac rehabilitation program adherence. Karmali et al. (2014) (n = 2505, mean age range = 52 to 68 years) reviewed 18 RCTs of interventions aimed at increasing adherence to cardiac rehabilitation. The patient samples consisted of patients with HF, stable angina, post-MI, and post-PCI who attended cardiac rehabilitation. Seven studies focused on improving adherence to exercise, and one study focused on lifestyle counseling or education components (Karmali et al., 2014). The interventions included a variety of approaches including goal setting, self-monitoring, coping strategies, written and oral commitment, and formalized counseling led by a nurse or therapist (Karmali et al., 2014). Three of the eight RCTs (n = 486) reported improvements in adherence to cardiac rehabilitation, but there was no evidence on the effect of adherence interventions at 12 months, and no studies reported any significant differences in HRQOL (Karmali et al., 2014). No studies found any differences in mortality, although one study reported an increase in revascularization rates among patients in the intervention group. A meta-analysis could not be conducted due to the use of multiple HRQOL instruments across included studies. Therefore, although some interventions were shown to improve cardiac rehabilitation adherence, there were no statistically significant improvements to HRQOL and no interventions addressed cognitive function or deficits.

Murray et al. (2012) conducted a systematic review that included 11 observational studies examining 121 factors that influenced cardiac rehabilitation program completion. Barriers for cardiac rehabilitation program completion were organized into the following categories: (1) emotional (increased anxiety, depression, greater neuroticism); (2) psychological and spiritual (greater personal control and less treatment control); (3) information and communication (less education); (4) family and friend support (not married or living alone); (5) transport and related costs (unemployment or retirement); (6) physical wellbeing (increased body weight or body mass index, poor physical functioning), (7) cultural and demographic (Caucasian ethnicity, female); and (8) attitudes to exercise and personal choice (less regular exercise, current smoking). There was insufficient literature regarding the effect of social support, cardiac rehabilitation attitudes, and integration of lifestyle changes into daily life. Murray et al. (2012) reported 3 studies that examined social support, 4 studies that examined attitudes to rehabilitation and exercise, and one study that examined the effect of balancing and integrating behaviour change with daily activities on cardiac rehabilitation program completion. Cognitive deficits were not examined in any of the included studies.

Neubeck et al. (2011) (n = 1,213) identified similar barriers to cardiac rehabilitation participation in a meta-synthesis of 34 studies, including personal, physical and instrumental barriers. Although many factors affecting cardiac rehabilitation participation were examined, the systematic reviews discussed in this literature review of cardiac rehabilitation adherence did not explore the impact of cognitive deficits in cardiac rehabilitation (Murray et al., 2012; Neubeck et al., 2011). Furthermore, the level of cognitive function was not collected in studies included in these aforementioned systematic reviews.

In summary, components of cardiac rehabilitation such as self-management education, have cognitive function requirements that influence the effectiveness of patient engagement in self-management behaviours and related cardiac rehabilitation outcomes. Evidence suggests that cognitive deficits may not only negatively impact adherence to cardiac rehabilitation, but may also negatively impact post-program physical fitness levels and overall and domain-specific HRQOL. Research on cognitive deficits in the context of cardiac disease has focused mostly focused on HF populations but some studies have also examined cognitive deficits in CABG patients. Studies included in three systematic reviews identified potential barriers to cardiac rehabilitation adherence and interventions to address these barriers. However, few studies focused on improving adherence to education and counseling interventions (Karmali et al., 2014; Murray et al., 2012; Neubeck et al., 2011). It is possible that the presence of cognitive deficits may help to explain why interventions to promote adherence have shown only modest improvements and insignificant changes in HRQOL. Some evidence suggests that cognitive deficits, notably among CABG patients, are of concern for cardiac rehabilitation programs. To inform cardiac rehabilitation programming, a more robust understanding about the presence and effect of cognitive deficits among patients who have undergone coronary revascularization procedures is required. Comparisons about the level of cognitive function between patients who have had coronary revascularization procedures are also needed.

Classification, Etiology and Pathophysiology of Cognitive Deficits.

The term *cognitive deficits* is used to describe several types of cognitive impairments. Cognitive deficits in CAD are complex, not well understood and vary in the duration of symptoms, severity, and clinical manifestations (Eggermont et al., 2012). Several terms have been used to describe cognitive deficits and some are not consistently defined. *Mild cognitive impairment (MCI)* in CAD is chronic, irreversible, and non-amnestic in nature, and is defined as subtle cognitive deficits affecting primarily executive function and attention. *Postoperative cognitive dysfunction (POCD)* refers to transient but persistent cognitive deficits that can occur following CABG (Evered et al., 2016; Selnes et al., 2012). *Postoperative delirium* can occur in the acute phase following surgery, affects 46 percent of post-CABG patients, and typically resolves upon hospital discharge (Saczynski et al., 2012).

The following section focuses on POCD and cognitive deficits reported in general cardiac populations, emphasizing the necessity of further examination about the differences in cognitive function between cardiac rehabilitation participants who have undergone cardiovascular revascularization procedures.

Postoperative Cognitive Dysfunction.

The most common clinical presentation of POCD is memory impairment; this is distinct from the non-amnestic MCI observed in general cardiac patients (Eggermont et al., 2012). Symptoms onset in the immediate postoperative period and typically resolve in 1 to 3 months, although duration may vary significantly. The etiology of POCD is multifactorial and not fully clear; proposed mechanisms of pathogenesis for cognitive deficits among post-CABG patients include inflammation from the surgical procedure or anaesthesia, intra-operative hypotension and associated hypo-perfusion, and micro-embolic brain injury resulting in cerebral ischemia (Ghafari et al., 2012; Selnes et al., 2012). Human studies examining the pathological mechanisms of cognitive deficits among CABG patients are limited; evidence from animal experiments suggests that inflammation plays an important role in the pathogenesis of POCD. Terrando et al. (2011) reported the activation of tumour necrosis factor alpha (TNF-α) and nuclear factor kappa beta (NF-κβ) signal cascades following peripheral surgical procedures in mice. The release of pro-inflammatory cytokines led to impaired integrity and increased permeability of the blood-brain barrier, resulting in macrophage migration to the hippocampus and subsequent memory impairment. Further animal experimentation also indicated that anti-inflammatory cholinergic cascade activation prevented the development POCD in mice (Terrando et al., 2011). Although evidence has shown that extensive surgical procedures under general anesthesia and secondary surgery increase the risk of POCD, it remains inconclusive whether anesthesia itself directly leads to POCD and there is no documented difference of severity of cognitive deficit between general and regional anesthesia (Rundshagen, 2014).

The results from a longitudinal study by Kline et al. (2012) (surgical cohort n = 41; non-surgical cohort n = 123; age 55 to 90) supported the findings from Terrando et al.'s (2011) animal studies. Structural magnetic resonance imaging (MRI) revealed decreased cerebral gray matter volume, hippocampal atrophy and increased lateral ventricle size 5 to 9 months following extensive surgery. More severe cognitive impairment was observed in patients with prior MCI and accelerated atrophy was observed in older adults. POCD was measured using a Z score change greater than 2 SD on 2 or more of five cognitive tests (digit symbol substitution test, digits span forward and backward, Trail-Making Tests A and B).

Risk factors for POCD can be divided into patient-, operative-, and anesthesia-related factors. Patient-related risk factors for POCD include: advanced age; lower education level; cerebrovascular, cardiac, or vascular disease; preoperative MCI; and history of alcohol abuse (Boodhwani et al., 2006; Ernest et al., 2007; Evered et al., 2016; Rundshagen, 2014; Selnes et al., 2012; Sendelbach, Lindquist, Watanuki, & Savik, 2006; Trubnikova, Tarasova, Artamonova, Syrova, & Barbarash, 2013). Operative risk factors include: extensive surgical procedures, intra- or postoperative complications, and secondary surgery (Evered et al., 2016; Rundshagen, 2014). Anesthesia-related factors include: long-acting anesthetics, organ ischemia from hypoxia and hypo-perfusion (Rundshagen et al., 2014). In addition to the inflammatory cascade hypothesis, psychological factors, such as anxiety, depression, and ineffective coping have also been suggested (Selnes et al., 2012).

Some evidence suggests that disease burden may be a risk factor for cognitive decline following cardiac surgery. Lahariya et al. (2013) (cardiac ICU patients with delirium: n = 81, mean age = 61.69, SD = 13.46) reported in a binary logistic regression that disease burden measured by the Charlson Comorbidity Index (CCI) was independently associated with cognitive function measured by the Confusion Assessment Method for Intensive Care Unit (CAM-ICU) (OR 3.30, 95% CI 2.14 to 5.09, $p < 0.001$).

Several cardiovascular risk factors were found to also be risk factors for POCD. Arntzen, Schirmer, Wilsgaard, & Mathiesen (2011) (n = 5033) found significant associations with various cardiovascular risk factors and cognitive function in an observational study. Physical inactivity (OR 1.28, 95% CI 1.01, 1.63 for men) and diabetes (OR 2.98, 95% CI 1.56, 5.68 for men) were associated with an increased risk of poor verbal memory performance among men and women (Arntzen et al., 2011). Smoking was also associated with poor verbal memory (OR 1.40, 95% CI

1.09, 1.81 in men), inattention (OR 1.56, 95% CI 1.20, 2.03 in men), and decreased psychomotor speed (OR 1.58, 95% CI 1.23, 2.03 in men) (Arntzen et al., 2011). These cardiovascular risk factors are also consistent with risk factors for MCI (Ganguli, Fu, Snitz, Hughes, & Chang, 2013; Zou et al., 2014).

Low ejection fraction (EF) and low blood pressure are also associated with poor short-term and long-term cognitive performance (Athilingham et al., 2011; Ernest et al., 2007; Kennedy et al., 2013; Takagi et al., 2007). Gottesman et al. (2009) (n = 234) reported that low EF ($p = 0.04$) and low mean arterial pressure ($p = 0.03$) were significant predictors of global cognitive function among CAD patients. A significant proportion of patients with low EF as a risk factor for cognitive deficits were post-CABG patients (Gottesman et al., 2009). Of the 234 included participants with CAD, 66.7% of those with moderately reduced EF (EF 33-55%) had undergone on-pump CABG, while 16.7% had undergone off-pump CABG. Sixty-five per cent of participants who had a markedly reduced EF (EF<35%) had undergone on-pump CABG and 30.0% had undergone off-pump CABG.

Although previously considered a POCD risk factor, the use of cardiopulmonary bypass has been shown to not independently influence cognitive function (Fontes et al., 2014; Kennedy et al., 2013). A meta-analysis by Kennedy et al. (2013) reviewed a total of 13 randomized control trials (RCTs) (n = 2,405) and reported that there were little to no significant differences in cognitive function between patients who had undergone on- and off-pump CABG in the early (≤3 months) and late (6 to 12 months) postoperative periods. Six of the seven neurocognitive tests used in the meta-analysis failed to show significant heterogeneity. Only preoperative scores from the Stroop colour test reported heterogeneity (I^2=55%, $p = 0.04$) in favour of off-pump CABG procedures. These results support that although postoperative cognitive deficits may be present among CABG patients, it may not be due to differences in cognitive function between on- and off-pump CABG.

Evidence has suggested that POCD may persist long-term. An observational study by Habib et al. (2014) (n = 134, mean age = 53.7 years, 8.36 SD) identified that 44.8% of CABG patients showed signs of POCD in the early postoperative period and this proportion increased to 54.5% upon discharge as indicated by the MMSE. Although there was some improvement in cognitive function among some post-CABG patients, 39.7% continued to experience cognitive deficits at 6 months into the postoperative period. Benvenuti, Patron, Zanatta, Polesel, & Palomba (2014) (n = 79; mean age = 63.8 years, 11.0 SD) also reported that approximately 28 percent of post-CABG patients continued to experience cognitive deficits at 3-months post-discharge ($p = 0.003$). The results regarding cognitive deficits of patients who had undergone on-pump and off-pump CABG were comparatively less conclusive (Jensen, Hughes, Rasmussen, Pedersen, & Steinbrüchel, 2006; Farhoudi et al., 2010; Kennedy et al., 2013; Takagi et al., 2007; van Dijk et al., 2007). In a study by Farhoudi et al. (2010) (n = 201, mean age = 57.17), patients who had undergone on-pump versus off-pump CABG experienced no significant differences in cognitive function when evaluated using a neurocognitive test battery.

The reported trajectory of CABG-related cognitive deficits is varied however some studies have shown they persist beyond the first postoperative year. Longitudinal studies substantiate that although some CABG patients may experience short-term improvements or preservation in cognitive function, this is usually not sustained after one year (Bruce, Yelland, Smith, & Robinson, 2013; Djaiani et al., 2012; Knipp et al., 2008; Newman et al., 2001, 2007; Selnes et al., 2008). The previously discussed retrospective study by Fontes et al. (2013) revealed that after an initial period of cognitive decline within the first 6 weeks post-CABG, approximately 55% of patients did not experience recovery in cognitive function. Additionally, a population-based cohort study by Lyketsos et al. (2006) (n = 5,092) reported that post-CABG patients experienced a greater decline in cognitive function 5 years postoperatively compared to patients who had not undergone CABG. Despite the incongruous literature, there is some evidence that cognitive decline is present in post-CABG patients beyond the first year of recovery. Thus, POCD poses a definite risk for post-CABG patients, especially in connection with their future successful participation in cardiac rehabilitation programs.

POCD is distinct from MCI in that it is an entirely objective measure that does not involve an assessment of function. It differs from postoperative delirium in that symptoms do not fluctuate over time and it may persist long after the patient is discharged post-surgery (Evered et al., 2016). In a systematic review of 62 studies, Rudolph et al. (2010) identified that POCD following cardiac surgery was measured using non-recommended neuropsychological tests in more than half of the included studies. Most studies used neuropsychological test batteries, few studies used the MMSE, and no studies used the Montreal Cognitive Assessment (MoCA). Studies of POCD have used percent decline and standard deviation decline measurement methodologies and often employed more than one methodology. POCD was inconsistently defined across studies however most studies measured POCD as a specified number of SDs (1 to 2 SDs) from the patient's preoperative neuropsychological test battery score (Sauër et al., 2009; Rudolph et al., 2010). Therefore, it is difficult to make comparisons of POCD between studies (Newman et al., 2001, 2007; Sauër et al., 2009).

In summary, the pathogenesis of POCD is multifactorial and an inflammatory cytokine cascade mechanism is likely involved. Risk factors for POCD include, but are not limited to older age, lower education, cardiovascular and cerebrovascular risk factors, preoperative MCI, psychological factors (i.e., depression), and decreased EF. POCD typically onsets in the immediate postoperative period, but evidence suggests that symptoms may persist beyond the first postoperative year. Challenges exist in comparing studies involving POCD due to variations in how POCD is defined and diagnosed. Although it is clear that cognitive deficits are present in CAD patients and potentially more so among CABG patients, the proportion of these patients enrolling in cardiac rehabilitation is not known. Therefore, it is necessary to determine the proportion of CABG patients with cognitive deficits that are present in cardiac rehabilitation. In considering the examination of POCD among CABG patients, it is important to use standardized cognitive screening instruments to allow for comparison between studies.

Mild Cognitive Impairment.

The most common subtype of MCI in general cardiac populations is non-amnestic MCI. Cardiac patients with non-amnestic MCI typically experience domain-specific problems (i.e., executive dysfunction) or global cognitive deficits with preserved memory (Eggermont et al., 2012; Maekawa, Baba, Otomo, Morishita, & Tamura, 2014). Symptoms are chronic, irreversible, and may progress to non-Alzheimer's disease forms of dementia, such as vascular dementia (Mufson et al., 2012). While not studied specifically among CABG and PCI patients, it is reasonable to infer that there could be differences in the clinical presentation of cognitive deficits between the two types of coronary revascularization procedures. Evidence has shown an association between non-amnestic MCI and CAD, so it is reasonable to expect that PCI patients would tend to experience symptoms similar to that of non-amnestic MCI compared to symptoms of POCD (Eggermont et al., 2012; Roberts et al., 2010). Similar to POCD, the pathogenesis of non-amnestic MCI is also poorly understood and likely multifactorial. Risk factors for non-amnestic MCI are similar to risk factors of POCD, including age, education level, and risk factors for cardiovascular and cerebrovascular disease (Eggermont et al., 2012; Mufson et al., 2012). Non-amnestic MCI is less common than amnestic MCI, and thus has not been a focus of rigorous study.

In general, MCI does not follow the plaque and tangle pathogenesis mechanism of Alzheimer's disease. Non-amnestic MCI, in particular, may not show any similar pathology to Alzheimer's disease and cannot typically be identified by changes in brain structure. Comparisons of gross morphology show similar cortical gyral and sulcal patterns between brains with non-amnesiac MCI and no cognitive impairment. Macroscopic cerebral infarcts are expectedly more commonly seen in patients with non-amnestic MCI (18.6%) compared to amnestic MCI (18.6%) (Mufson et al., 2012).

Although it is known that MCI is present in cardiac rehabilitation participants, it has not been a major focus of study (King et al., 1999; Intzandt et al., 2015). Studies of MCI in cardiac disease have primarily examined patients with chronic HF (Athilingham et al., 2011, 2013; Cameron, Worrall-Carter, Page, Stewart, & Ski, 2013; Davis et al., 2015; Dodson et al., 2013; Harkness, Demers, Heckman, & McKelvie, 2011; Harkness et al., 2014; Hjelm et al., 2012). However, recent evidence suggests that MCI is a concern for patients with CAD (Almeida et al., 2012; Eggermont et al., 2012). A 2-year longitudinal study by Almeida et al. (2012) (n = 77; mean age = 68.4 years, SD = 10.2) reported no significant differences in Cambridge Cognitive Examination of the Elderly (CAMCOG) scores between patients with CAD (mean score 93.7, SD 5.8) and HF (mean score 92.2, SD=6.3). Individuals with CAD and HF CAMCOG scores have demonstrated similar declines in cognitive function when compared to a group of healthy individuals without CAD (mean score 95.1, SD 5.1). Studies further examining whether or not cognitive impairment lies on a continuum from CAD to HF have yet to be conducted.

In summary, non-amnestic MCI commonly presents among patients with CAD, and it can be inferred that patients following PCI are at risk for MCI. MCI in cardiac disease is subtle and difficult to identify by gross anatomy and cognitive screening tests. It is reasonable to expect that there are differences in the presence and severity of cognitive deficits between different groups of cardiac patients following revascularization (CABG and PCI) however, comparative studies have not been conducted. Given the potential implications that such deficits may have for clinical practice, it is necessary to examine the between-group differences in cognitive function between patients who enrol in cardiac rehabilitation following a coronary revascularization procedure.

Instruments for Measuring Cognitive Function.

Evidence shows that cognitive deficits are present among cardiac patients and suggests that these impairments may create challenges in cardiac rehabilitation (Benvenuti et al., 2013; Djaiani et al., 2012; Eggermont et al., 2012; Farhoudi et al., 2010; Fontes et al., 2013; Kennedy et al., 2013; Knipp et al., 2008; Newman et al., 2001, 2007; Takagi et al., 2007; van Dijk et al., 2007; Selnes et al., 2008; Selnes et al., 2012). However, current studies have examined cognitive function using a number of cognitive screening instruments, some of which are not sensitive to subtle cognitive deficits in cardiac populations, and cognitive test batteries that are not feasible to use at the point-of-care (McLennan et al., 2011). Prior to conducting the present study, it was necessary to select a cognitive screening tool that would best detect the presence and magnitude of cognitive impairment in cardiac rehabilitation. The MMSE and MoCA are both 30-point cognitive screening questionnaires. In particular, the MMSE has been used in a greater number of studies regarding cognitive function (Fontes et al., 2013; Foster et al., 2011; Habib et al., 2014; Lyketsos et al., 2008; Selnes et al., 2008). A notable difference between the MMSE and MoCA is that the MMSE does not have a cognitive test for executive function (Fink et al., 2014).

Emerging evidence suggests that the MMSE may not accurately detect subtle cognitive deficits, and that the MoCA is a more valid cognitive screening tool for cardiac populations. A validity study by McLennan et al. (2011) (n = 110; mean age = 67.9 years, SD = 11.7) examined MoCA scores among community-dwelling cardiac patients, using the Neuropsychological Assessment Battery Screening Module to determine the presence of MCI using a cut-off of <24. The MoCA had a sensitivity of 100 percent for detecting amnestic MCI and 83.3 percent sensitivity for detecting multiple-domain MCI; specificity for amnestic and multiple-domain MCI were 50 percent and 52 percent respectively (McLennan et al., 2011). The results indicated that the MoCA has a relatively high sensitivity for detecting MCI and is supported in previous studies of patients with HF (Athilingham, D'Aoust, Miller, & Chen, 2013; Harkness et al., 2014). While not specifically examining cognitive screening of MCI among cardiovascular patients, the initial MoCA validity study (n = 94; MCI group: mean age = 75.19, SD = 6.27) found that the MoCA was more sensitive in detecting MCI compared to the MMSE (90.0 vs. 18.0, MoCA cut-off score ≤26) with comparable specificity (87.0 vs. 78.0) (See Table 3) (Nasreddine et al., 2005).

Evidence supports the use of the MoCA over the MMSE in cerebrovascular populations. Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell (2010) (n = 494) reported that 70 percent of post-ischemic stroke patients who had a MoCA score of less than 26 also had a MMSE score of greater than or equal to 27. Furthermore, the MoCA is also recommended in the Canadian Stroke Network guidelines for vascular patients (Dong et al., 2009). The MoCA remains greatly underutilized in cardiovascular populations despite evidence supporting its use. Rudolph et al.

(2010) reported that there were no studies that used the MoCA to measure cognitive function following cardiac surgery. In addition, Fink et al. (2014) reported in a systematic review that only 3 of 21 (14.3%) included studies (17 RCTs and 4 prospective cohort studies) (n = 7,802, weighted mean age = 68 years) measured cognitive function with the MoCA. See Table 3 for a comparison of domain-specific test items between the MoCA and MMSE.

The differences in instrumentation were a barrier in comparing cognitive function between studies. Screening tools vs. partial or full neuropsychological test batteries are scored differently and contain different test components. For example, a fundamental difference in the MoCA and MMSE is that the MMSE does not evaluate executive function. The variance in cognitive domain coverage creates a significant challenge in comparing scores despite both screening tools being 30 items in length. Neuropsychological test batteries are rarely identical and so challenges exist for making comparisons as well. For example, Newman et al. (2001) measured cognitive function using a battery of 5 tests and Knipp et al. (2008) used a battery of 11 tests. The Weschler Memory Scale-Revised Digit Span Test for short-term and working memory was the only test that both studies used. Thus, pooled estimates of cognitive function were not possible. Kennedy et al. (2013) was the only meta-analyses found in the review of the literature that examined cognitive function of coronary revascularization patients, namely on- and off-pump CABG. No other meta-analyses of CAD patients were found due to heterogeneity of cognitive test measures (Eggermont et al., 2012).

Table 3: Cognitive Assessment Test Items by Domain on the Montreal Cognitive Assessment and Mini-Mental Status Examination

Cognitive Domain / Test Characteristic	MoCA Items (Maximum Score)	MMSE Items (Maximum Score)
Visuospatial	Cube-Drawing Task (1) Clock-Drawing Test (3)	Interlocking Pentagon Drawing Test (1)
Executive	Trail Making Test B (1) Phonemic Fluency Task (1) Two-Word Verbal Abstraction (2)	None
Attention, Concentration, and Working Memory	Digits Forward and Backward (2) Serial Subtraction (Serial 7) (3) Target Detection using Tapping (Letter A Task) (1)	Serial Subtraction (Serial 7) (5) Registration of Three Words (3)
Language	3-Item Animal Naming (3) Sentence Repetition (2) Phonemic Fluency Task (1)	Naming a pencil and a watch (2) Phrase Repetition (1) Three-Stage Verbal Command (3) Written Command (1) Sentence Writing (1)
Short-Term Memory	Delayed Recall Task (5)	Object Recall (3)
Orientation	Orientation (Time and Place) (6)	Orientation to Time (5) Orientation to Place (5)
Impairment Threshold	Score < 26	Score < 24
Sensitivity for MCI*	90.0	18.0
Specificity for MCI*	87.0	78.0
Total Score	30	30

*Validity study data from Nasreddine et al. (2005)

Summary of Literature Review.

Despite widespread recommendation in literature and clinical practice guidelines, self-management education and support interventions in cardiac rehabilitation have not been effective in improving HRQOL (Brown et al., 2011). Self-management education and support components of cardiac rehabilitation have cognitive demands, and evidence suggests that the presence of cognitive deficits may negatively impact cardiac rehabilitation outcomes and treatment adherence. Intervention studies to improvement cardiac rehabilitation adherence do not significantly improve HRQOL, nor do they consider the impact of cognitive deficits (Karmali et al., 2014; Murray et al., 2012; Neubeck et al., 2011). However, evidence suggests that cognitive deficits may be present in those undergoing cardiac rehabilitation, and the severity of impairment may differ based on coronary revascularization procedure prior to enrolment.

Cognitive deficits in cardiac rehabilitation are complex. Pathological mechanisms for both POCD and MCI are multifactorial. POCD occurs frequently among CABG patients and likely involves a pro-inflammatory cytokine cascade mechanism (Evered et al., 2016; Selnes et al., 2012; Terrando et al., 2011). Risk factors include age, cardiovascular and cerebrovascular risk factors, and preoperative MCI. Symptoms are transient, resolving typically in 1 to 3 months, and often manifests as subtle short-term memory impairment. Non-amnestic MCI typically occurs in the general cardiac population, and by extension, PCI patients (Eggermont et al., 2012). MCI is difficult to identify by gross anatomy, and proposed mechanisms relate to macroscopic cerebral infarcts (Mufson et al., 2012).

Few studies have examined POCD and MCI in the context of cardiac rehabilitation, and comparisons have not been made between different patient groups attending cardiac rehabilitation, such as CABG and PCI. Methodological challenges exist in exploring the impact of cognitive deficits in cardiac rehabilitation. The literature included in this review had limited generalizability; relevant studies were largely exploratory/ descriptive in nature, had small sample sizes, and were primarily correlation studies (Benvenuti et al., 2013; Djaiani et al., 2012; Eggermont et al., 2012; Farhoudi et al., 2010; Fontes et al., 2013; Kennedy et al., 2013; Knipp et al., 2008; Newman et al., 2001, 2007; Takagi et al., 2007; van Dijk et al., 2007; Selnes et al., 2008; Selnes et al., 2012). The limited external validity of the current literature supports the need for further investigation and comparison of cardiac rehabilitation patients with cognitive deficits. Different definitions for various types of cognitive deficits create challenges with making comparisons between studies (Rudolph et al., 2010). In addition, existing studies have used cognitive screening tools that are impractical to implement at the point-of-care (i.e., neuropsychological test batteries), and are not sensitive to subtle or mild cognitive deficits (Cameron et al., 2013). An observational study is needed to explore the relationships between cognitive function and various demographic and clinical factors in cardiac rehabilitation.

Conceptual Framework

The primary dependent variable for this cross-sectional study was cognitive function. Independent variables included age, education level, language, and number of co-morbidities. Wagner et al.'s Chronic Care Model (1996) guided the selection of these variables.

Wagner et al.'s Chronic Care Model.

Wagner et al.'s Chronic Care Model (1996) focuses on the care provision over a continuum of care and describes changes to the health care system that will improve health outcomes among patients with chronic disease. Current cardiac rehabilitation standards in Ontario reflect the Chronic Care Model (Arthur et al., 2010; CCN, 2014b). A central focus of the model and the present study is the relationship between self-management support and self-management. *Self-management* is defined as the cognitive skills required to make decisions and engage in behaviours related to the management of chronic disease (Barlow et al., 2002; Russell, 2006; Wagner et al., 1996). *Self-management support* is the education and counseling provided by health care professionals to promote effective patient self-management (Bodenheimer & Wagner, 2002; Epping-Jordan et al., 2004). The model consists of six interrelated, evidence-based health system components: (1) health care organizations, (2) delivery system design, (3) decision support, (4) clinical information systems, (5) self-management support, and (6) community resources (Bodenheimer & Wagner, 2002; Epping-Jordan et al., 2004). Table 4 summarizes recommendations for cardiac rehabilitation programs by the Canadian Heart Health Strategy and Action Plan in the context of the Chronic Care Model (Arthur et al., 2010; Wagner et al., 1996).

Table 4: Components of the Chronic Care Model

Component	**Description**
Health care organization	Chronic disease management is a focus in the structure, goals, and values of an organization. Cardiac rehabilitation is an accessible, funded, insured service that is part of the chronic cardiac care continuum. Currently, these recommendations have not been achieved in Canada.
Delivery system design	Care is restructured to incorporate a multidisciplinary practice team comprised of health professionals with clearly defined roles (i.e., cardiologists, nurses, kinesiologists, dietitians). Care is shared between the patient's primary care physician, cardiologist, and cardiac rehabilitation team.
Decision support	Evidence-based clinical practice guidelines should be reinforced and integrated into regular practice.
Clinical information systems	Computerized systems have accessible registry data to facilitate care planning at the individual and population levels.
Self-management support	Health care providers work collaboratively with patients to ensure that they acquire the skills and confidence to engage in self-management behaviours (i.e., organizing medications, exercise, diet, smoking cessation, blood pressure or bloodwork monitoring). Patients are encouraged to be informed and take an active role in their care.
Community Resources and Policies	Provider organizations are linked to community programs (i.e., outpatient, hospital-based cardiac rehabilitation programs partnered with family physician). Public support for cardiac rehabilitation and cardiovascular health promotion is important.

The model promotes a multidisciplinary approach to the care of patients with chronic disease, suggesting that improved transitions between chronic (i.e., primary and outpatient) and acute care settings (i.e., hospital) through planned, ongoing patient and team interactions will result in better health outcomes.

Application of Wagner et al.'s Chronic Care Model.

The interaction between self-management support and self-management served as the conceptual basis for this study (Bodenheimer & Wagner, 2002; Epping-Jordan et al., 2004). It was purported that cognitive function could affect the relationship between self-management support and self-management. Cognitive function was operationalized and measured using the MoCA, a validated cognitive screening tool for cardiac populations (McLennan et al., 2011). Independent variables that may influence cognitive function were selected. Socio-demographic variables such as advanced age and multiple co-morbidities are known predictors of cognitive deficits (Selnes et al., 2012).

In summary, Wagner et al.'s Chronic Care Model (1996) is the theoretical framework that guided the selection of variables in the present study. Prior application of the Chronic Care Model in cardiac rehabilitation served to provide an understanding of the nature of self-management support and self-management in chronic cardiac care, suggesting an interactive relationship (Bodenheimer & Wagner, 2002). Cognitive function was considered a potential mediating factor between the dynamic relationship between self-management support and self-management, and was operationalized as the primary dependent variable by the MoCA. Variables that may influence cognitive function were selected as independent variables in the present study.

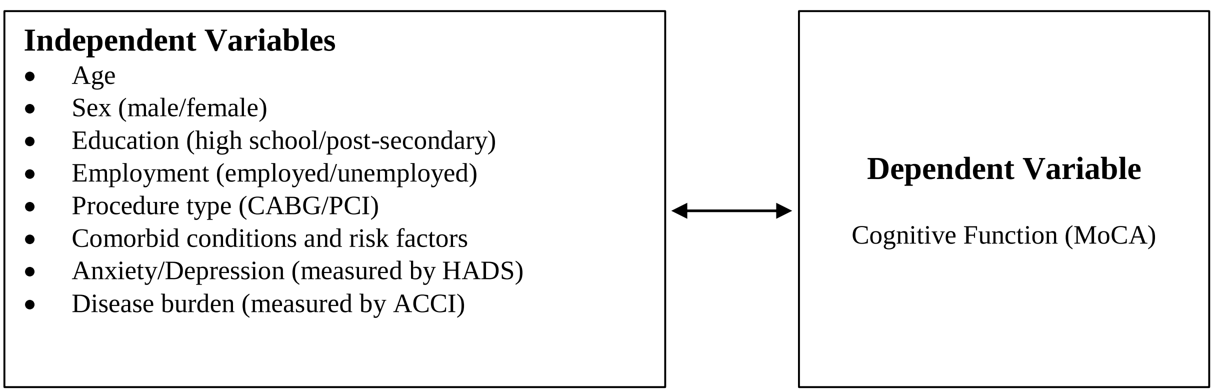
CHAPTER 3

METHODOLOGY

Purpose

This study compared the difference in cognitive function between CABG and PCI patients entering cardiac rehabilitation and determined variables that were independently associated with cognitive function in the study sample. A cross-sectional design was utilized for this study (See Figure 1). Cross-sectional studies are appropriate for preliminary investigations of association due to the low demand on participants, short duration of data collection, and low relative cost compared to other study designs (Levin, 2006).

Figure 1: Cross-Sectional Study Design



CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; HADS = Hospital Anxiety and Depression Score; ACCI = Age-adjusted Charlson Comorbidity Index; MoCA = Montreal Cognitive Assessment

Study Questions

Primary Research Question.

Among patients who are enrolled in cardiac rehabilitation, is there a difference in cognitive function in patients who have undergone CABG compared to patients who have undergone PCI?

Secondary Research Question.

Among patients who are enrolled in cardiac rehabilitation, what variables are independently associated with cognitive function?

Description of Setting

Participants were recruited from the Cardiac Health and Rehabilitation Centre (CHRC) at Hamilton Health Sciences. The CHRC is an outpatient program in Hamilton, Ontario, that primarily provides multidisciplinary rehabilitation services for patients recovering from cardiac events. The CHRC multidisciplinary team consists of cardiologists, nurses, kinesiologists, dietitians, and social workers. Available programs include nutritional counseling, supervised exercise and exercise counseling, stress management, weight management, smoking cessation, and cardiac health teaching.

Patients recovering from a cardiac event are referred by a physician to the CHRC, and must attend an intake appointment prior to participation in the program. CABG and PCI patients attend their intake appointment for cardiac rehabilitation at a mean duration of 7.7 weeks (SD = 1.5) and 6.4 weeks (SD = 2.8) respectively following their coronary revascularization procedure. Intake appointments consist of an education session about the cardiac rehabilitation program followed by an intake (initial) assessment of the patient by a nurse. Intake appointments are held two days per week (Tuesdays and Wednesdays). After an education session, participants decide whether or not they wish to enroll in the program. Routine patient information collected from the intake assessment includes demographic information and social determinants of health (e.g., education and employment); cardiovascular risk factors, medical history, and a physical exam. Patients who enroll in the program must then complete an exercise test and relevant blood work prior to starting cardiac rehabilitation. Program duration is specific to the individual, but typically lasts up to 6 months.

Selection Criteria

Inclusion Criteria.

The inclusion criteria were: ≥18 years of age; post-procedure from CABG surgery or PCI only; and enrolled in cardiac rehabilitation following the initial intake assessment.

Exclusion Criteria.

Patients meeting any of the following criteria were excluded from participation in the study: non-English speaking, documented moderate or severe cognitive impairment; diagnosis of major depression; history of stroke; major surgery within the last 6 months aside from CABG; and known alcohol abuse or drug addiction. Patients who had previously undergone emergency CABG surgery or who are being treated with only medical management were also excluded.

Sampling Strategy

Sample Size Calculation.

The estimated sample size needed to answer the primary and secondary research questions was 78 participants with approximately 39 participants for each cohort (post-CABG and post-PCI). Sample size was calculated with a significance level (α) of 0.05, a standard deviation of 3.1 points on the MoCA, and a power (β) of 0.80. Standard deviation was estimated by taking the average of three samples: a normal cognitive function sample (mean MoCA score 28.4, SD 2.2) (Nasreddine et al., 2005), a sample with MCI (mean MoCA 22.1, SD 3.1) (Nasreddine et al., 2005), and a sample with HF (mean MoCA 22, SD 4.5) (Harkness et al., 2014). Based on a previous study, a minimal clinically important difference (MCID) of 2 points on the MoCA was used (Peters et al., 2012).

Recruitment and Feasibility.

Convenience sampling was employed for participant recruitment. Consecutive patients were screened for eligibility by a CHRC nurse.

Approximately 48 new patients attend an intake appointment at the CHRC each week. It was anticipated that an average of 8 participants per week, or 4 participants per intake appointment day, would be recruited for the study. The estimated duration of recruitment was 8 to 10 weeks based on reported patient volumes from the CHRC and the required sample size.

The MoCA was administered to a total of 78 participants (38 post-CABG and 40 post-PCI) who enrolled in cardiac rehabilitation at the CHRC. Recruitment occurred between May and September 2016, and all participants completed informed consent, the MoCA and the case report form in a 15- to 20-minute data collection session with the investigator. Five of the 83 eligible patients declined to participate due to time constraints or disinterest.

Variables

The included variables for data collection in this study were: (1) cognitive function, (2) socio-demographic variables, and (3) clinical variables and disease burden. MoCA score was considered the primary dependent variable, and all socio-demographic and clinical characteristics were considered independent variables. The following section will describe each of the aforementioned instruments.

Montreal Cognitive Assessment (MoCA).

Cognitive function was the primary dependent variable of interest and was measured as a continuous variable using the MoCA. The MoCA is a short, cognitive screening tool that is validated and feasible, in terms of time, to administer at the point-of-care. Level of cognitive function is represented as both a composite and domain-specific sub-scores. The MoCA has a higher diagnostic accuracy for MCI among HF and stroke patients, and has been validated for the detection of subtle changes in cognitive function compared to the MMSE among cardiac patients (Cameron et al., 2013; McLennan et al., 2011). The internal consistency of the test was low (Cronbach's $\alpha = 0.55$), but may be attributed to the broad test content (McLennan et al., 2011). Although the MoCA has been found to have 83.3% sensitivity, it only has been found to have 52% specificity (McLennan et al., 2011). The following cognitive domains are examined in the MoCA: visuospatial abilities, memory recall, executive function, language, attention, orientation, conceptual thinking, and calculations. Scoring is from 0 to 30 points, and a score below 26 suggests MCI. One additional point is given to participants with an education level $\leq$12 years; three participants from the CABG group had less than a 12 years of formal education, and MoCA scores were adjusted accordingly. Test administration is approximately 10 minutes in duration. See Appendix B for a blank template of the MoCA.

Socio-Demographic Characteristics.

Socio-demographic characteristics were collected by the investigator from the participant and verified by the participant's intake assessment form. Categorical independent variables included: sex, level of education, employment, and primary spoken language (Ernest et al., 2007; Selnes et al., 2012; Trubnikova et al., 2013). Age was collected as a continuous variable. All socio-demographic characteristics were recorded onto a study-designed case report form (see Appendix C).

Clinical Characteristics and Disease Burden.

Clinical characteristics were also collected by the investigator from the participant and verified by the participant's intake assessment form. Categorical independent variables consisted of cardiac history, cardiovascular risk factors, and comorbid conditions obtained from the medical history. Cardiac history included: hypertension, history of AMI, atrial fibrillation, HF, left ventricular ejection fraction (LVEF), and type of coronary revascularization procedure (Athilingham et al., 2011; Arntzen et al., 2011; Ernest et al., 2007). Cardiovascular risk factors included: smoking history, diabetes mellitus, obesity (body mass index >30), and dyslipidemia (Ernest et al., 2007). Comorbid conditions included: peripheral vascular disease, chronic obstructive pulmonary disease (COPD), arthritis, osteoporosis, peptic ulcer disease, gastroesophageal reflux disease, liver disease (i.e., chronic hepatitis, cirrhosis), and cancer. All clinical characteristics were recorded onto a study-designed case report form (see Appendix C).

Coronary Revascularization Procedure.

Type of coronary revascularization procedure (CABG versus PCI) was the primary comparison in this study. CABG patients were identified as those who had undergone his or her first CABG surgery, and who may or may not have had a prior PCI procedure. PCI patients were identified as patients who have undergone PCI and who have not had a prior CABG surgery.

Hospital Anxiety and Depression Score.

Symptoms of anxiety and depression were assessed from the Hospital Anxiety and Depression Score (HADS), which was administered by clinic staff as a part of CHRC routine care (see Appendix D) (Baune et al., 2009). HADS scores were used to assess for the presence of subclinical depressive symptoms that may influence cognition. The HADS is a validated screening tool for anxiety and depression in cardiovascular populations (Haworth, Moniz-Cook, Clark, Wang, & Cleland, 2007; Stafford, Berk, & Jackson, 2007). It is a 14-item self-reported questionnaire reporting ordinal categorical data. Seven items relate to anxiety and the remaining seven relate to depression. Each item in the questionnaire is scored between 0 and 3. An individual can score between 0 and 21 for either anxiety or depression. A HADS score of 0 to 7 for either anxiety or depression is interpreted as normal, whereas 8 to 10 suggests mild symptoms, and 11 to 21 suggests moderate to severe symptoms of anxiety or depression accordingly (Haworth et al., 2007). The internal consistency or reliability of the HADS was relatively high for screening depression in CAD patients (Cronbach's $\alpha = 0.81$) (Stafford et al., 2007). The sensitivity and specificity for detecting any depressive disorder were 77.8% and 80.6% respectively using a cut-off score ≥5 points on the HADS (Stafford et al., 2007).

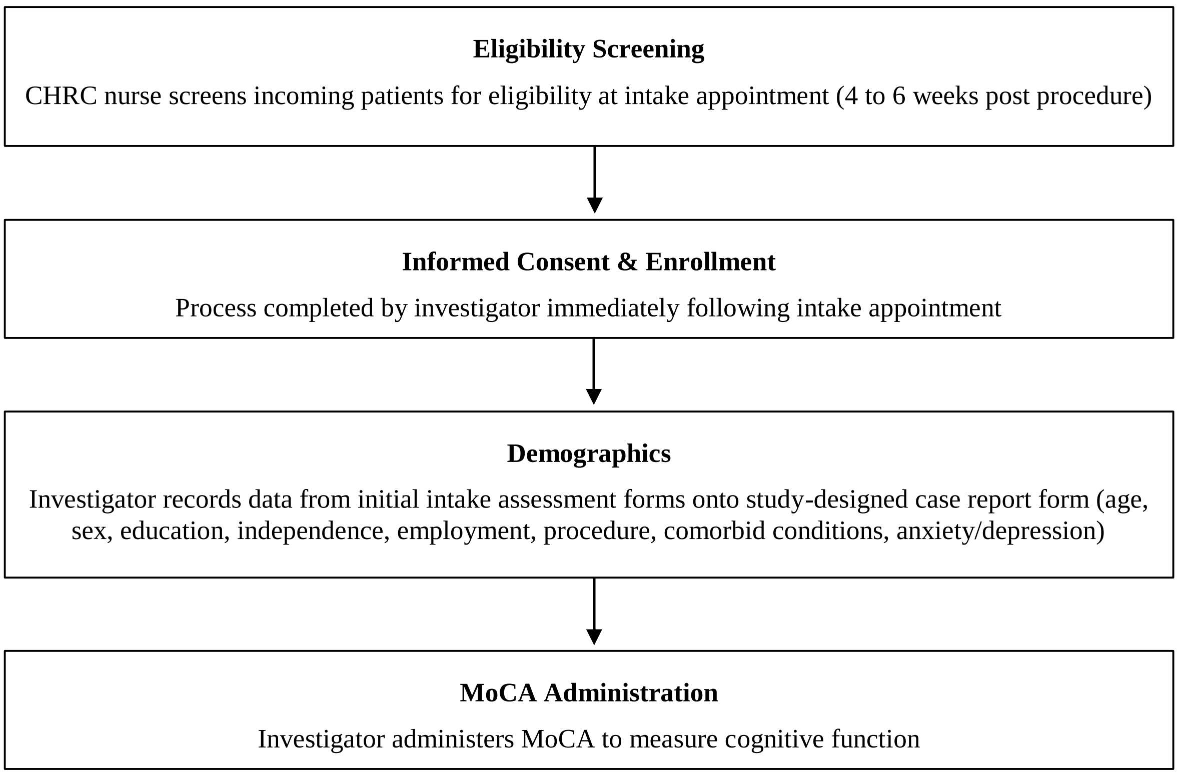
Age-Adjusted Charlson Comorbidity Index (ACCI).

Disease burden was measured by the ACCI (see Appendix E). The CCI is a well-known tool to measure comorbidities in cardiovascular clinical research (Afonso et al., 2010; Charlson, Pompei, Ales, & MacKenzie, 1987; Charlson, Szatrowski, Peterson, & Gold, 1994; de Groot, Beckerman, Lankhorst, & Bouter, 2003). Comorbid conditions are assigned a weight (1, 2, 3, or 6) and are then added together to make a summative score. The investigator completed the age-adjusted CCI (ACCI) based upon review of the patient's health record. In the ACCI, age is added as a comorbidity and is assigned a weight; one point is added for each decade beyond 40 years of age (e.g. 50-59 years = 1 point, 60-69 years = 2 points; 70-79 years = 3 points; 80-89 years = 4 points) (Charlson et al., 1994). These age-related points are added to the CCI to create a combined age-comorbidity index or ACCI. The ACCI has been shown to be a significant predictor of mortality among cardiovascular surgical patients in a proportional hazards model: the estimated RR for each combined age-comorbidity unit was 1.45 (99% CI, 1.25 – 1.68) (Charlson et al., 1994).

Data Collection

The process of data collection proceeded in the following steps: (1) eligibility screening by a CHRC nurse, (2) written and informed consent process, (3) brief chart review for socio-demographic and clinical characteristics, and (4) MoCA administration. The study protocol is summarized below in Figure 2.

Figure 2: Study Protocol



Screening for Eligibility.

Patients attending their intake appointment and who choose to enroll in the cardiac rehabilitation program were screened for eligibility by the CHRC nursing staff. CHRC nurses approached potential study participants who met inclusion criteria and did not meet any exclusion criteria. The investigator remained onsite during the two intake appointment days each week, and completed the informed consent process to all eligible interested patients.

Written and Informed Consent.

The investigator provided potential study participants with a brief description of the study purpose, protocol and potential risks of study participation (See Appendix F). Interested patients were informed that they would be asked to complete a short cognitive screening test (MoCA).

They were also informed that the investigator would perform a brief chart review of the participant's CHRC health records for socio-demographic and clinical characteristics. Each participant was presented with the opportunity to ask questions about the study and their role as a participant. They were advised that participation in the study would not affect their care at the CHRC, and that they may withdraw from the study at any time. Lastly, before providing written consent, potential participants were assured that their participation would be confidential, and that all data would be de-identified and stored separately from their signed consent forms.

Socio-Demographic and Clinical Characteristics.

Socio-demographic data and clinical characteristics were collected by the investigator using a study-designed case report form (see Appendix B). After written and informed consent was obtained by the investigator, the investigator completed the case report form electronically, and sought clarification from the patient if needed.

MoCA Administration.

The investigator was trained to administer the MoCA. Training involved reading the MoCA administration and scoring manual, watching a 10-minute video on proper test administration and scoring, and practicing administration of the test on simulated participants (Nasreddine et al., 2005). The MoCA was administered immediately following completion of the case report form. Participants were informed that there were no correct answers and to complete the test to the best of their ability. The MoCA was administered solely by the investigator in order to reduce inter-rater variability.

Data Management.

Collection of socio-demographic and clinical characteristics from the participant's health records from the CHRC were shared with the investigator solely for descriptive and inferential statistical purposes. Personal information, such as the participant's name, was removed from the data and replaced with a participant identification number to maintain confidentiality. All data were de-identified prior to statistical analyses and were stored separately from the consent forms and participant tracking sheet. Consent forms were kept in a locked cabinet in a locked room at the CHRC. The participant tracking sheet was recorded in a password-protected Excel document and stored on a secure hard drive, which was stored in a locked cabinet at the CHRC. The participant tracking sheet was destroyed upon completion of the study, and de-identified data were stored in the office of Dr. Patricia Strachan at McMaster University. Physical de-identified data will be destroyed in three years, and electronically recorded, de-identified data will be stored electronically with Dr. Strachan after this time period.

Data Analyses

Descriptive Statistics.

Categorical data were expressed by frequencies and percentages. Continuous data were expressed by means and standard deviations. Non-parametric tests were used if data were not normally distributed. Total MoCA scores and cognitive domain scores were reported as mean (SD) if normally distributed, and median (interquartile range) if not normally distributed. The proportion of participants scoring above and below the cut-off of 26 was also reported.

Inferential Statistics.

Approach for Primary Research Question.

Independent Student's *t* (parametric) and Wilcoxon signed rank tests (non-parametric) were used in the data analyses for the primary hypothesis (Norman & Streiner, 2008). For this study, the two groups that were compared were: (1) post-CABG with or without PCI, and (2) post-PCI without CABG. Cognitive function, as measured by the MoCA, was treated as the dependent variable, and was analyzed as both a total score and domain-specific sub-scores. Assumptions for Student's *t* test were assessed using Shapiro-Wilk test for normality and Levene's test for equality of variances (Norman & Streiner, 2008).

Effect size was used to estimate the clinical significance of the statistically significant result in differences in total MoCA score between groups. Upon completion of the study, Cohen's *d* formula was used to calculate effect size: $d = \frac{\mathrm{M}_1 - \mathrm{M}_2}{\sigma_{\mathrm{pooled}}}$, where *d* is defined as the difference between group means divided by the pooled variance (Norman & Streiner, 2008). The pooled variance was calculated as follows: $\sigma_{\mathrm{pooled}} = \sqrt{\frac{\sigma_1^2 + \sigma_2^2}{2}}$, where σ_{pooled} is defined as the square root of average standard deviation of both groups (Norman & Streiner, 2008). Effect sizes were defined as follows: 0.2 to 0.3 was small, 0.5 was medium, and ≥0.8 was large (Cohen, 1992).

Approach for Secondary Research Question.

Bivariate correlation analyses were used to examine associations between categorical and continuous independent variables and MoCA score (dependent variable) (Norman & Streiner, 2008). Statistically significant variables from the bivariate analyses were selected to be included in a backward linear regression analysis. Independent variables included in the model were selected based on statistical significance from the bivariate analyses and clinical importance due to sample limitations. An adjusted regression model was constructed using 3 to 4 putative factors associated with MoCA score as indicated from the bivariate correlation analyses.

The assumption of little to no multicollinearity for the regression analysis was assessed using chi-square and bivariate correlation analyses, and variance inflation factors (VIF) (Norman & Streiner, 2008). Chi square analyses were conducted to determine associations between the type of coronary revascularization procedure and categorical demographic variables. Bivariate correlation analyses were conducted to determine associations between the type of coronary revascularization procedure and continuous demographic variables. All statistical analyses were conducted using SPSS v23.0 software. A p value <0.05 was considered statistically significant. Results were verified by a biostatistician.

Ethical Considerations

Health Risks and Concerns.

This was a non-invasive study. All participant data were de-identified and confidentiality was maintained. The potential benefits for this study outweigh its potential risks. There was the potential that some of the questions from the MoCA may make participants upset, frustrated or anxious. The investigator emphasized to participants that they may choose to withdraw or not answer a question at any time if they were distressed. Since the HADS is part of routine care, there is an existing and standardized pathway of care for patients who demonstrate severe depressive symptoms. Although the issue did not arise, it had been arranged that the investigator would inform the CHRC medical director or the CHRC Clinical Nurse Specialist, to discuss the participant's answers and MoCA results if a participant's scores were indicative of a severe cognitive deficit.

Benefits.

Participants did not have any direct benefit for participating in the study. Patients were made aware of potential societal benefits as a result of this research, such as helping to understand cognitive deficits in CABG and PCI, and to promote the development of future education and counseling interventions in outpatient cardiac rehabilitation programs that target persons with cognitive deficits. Participants were offered a one-time use hospital parking voucher in appreciation of the addition time required to participate in the study. These incentives were minimal so as to not be coercive.

Research Ethics Board Approval.

The study protocol was approved by the Hamilton Integrated Research Ethics Boards (HiREB, Project Number 0935), and has adhered to the Tri-Council Policy Statement (TCPS) Ethical Conduct for Research Involving Humans and the Declaration of Helsinki. Study purpose, protocol, and potential risks were discussed with potential participants prior to participation. Interested patients were then asked to read the study information sheet, written at a grade 8 reading level, and sign a written consent form (See Appendix F).

CHAPTER 4

RESULTS

The results of the data analysis for these CABG and PCI patients are reported in this chapter. First, the sample is described according to socio-demographic and clinical characteristics. Second, a descriptive analysis of MoCA cognitive domains between CABG and PCI groups was conducted. Third, the results of the primary research question are presented, including verification of statistical test assumptions, a comparison of total MoCA scores between CABG and PCI, frequency of cognitive deficits in each group, and effect size. Fourth, the results of the secondary research question are presented, including variable selection, verification of statistical test assumptions, and final regression model.

Characteristics of the Sample

The mean ages for CABG and PCI patients were 64.6 years (SD = 8.7) and 59.6 years (SD = 9.8) respectively. Both groups were primarily male and over half of participants had post-secondary education (Table 5). A greater proportion of CABG vs. PCI patients were unemployed or retired and spoke English as a second language.

The mean number of pre-existing chronic conditions among CABG and PCI patients were 3.5 (SD = 1.5) and 3.2 (SD = 1.3) respectively; the most common being CABG patients were: hypertension (73.7%), diabetes (42.1%), arthritis (39.5%), gastroesophageal reflux disease (GERD) (28.9%), and HF (13.2%). In the PCI group, hypertension (70.0%), GERD (32.4%), arthritis (27.5%), diabetes (20.0%), and obstructive sleep apnea (12.5%) were most commonly reported. Approximately 65% of CABG patients and 48.6% of PCI patients had an EF that was 50% or greater. ACCI scores were slightly higher in the CABG vs. PCI cohort while both groups had comparable anxiety, depression, and composite HADS scores (see Table 5).

Table 5: Socio-Demographic and Clinical Characteristics by Procedure Type

Variable	CABG (N = 38)		PCI (N = 40)	
	n (%)	**Mean (SD)**	**n (%)**	**Mean (SD)**
Procedure to Intake (weeks)	–	7.7 (1.5)	–	6.4 (2.8)
Sex (Male)	32 (84.2)	–	32 (80)	–
Age (years)	–	64.6 (8.7)	–	59.6 (9.8)
Education				
High School or Less	17 (44.7)	–	19 (47.5)	–
Post-Secondary	21 (55.3)	–	21 (52.5)	–
Employment				
Employed	18 (47.4)	–	28 (70)	–
Unemployed or Retired	20 (52.6)	–	12 (30)	–
English Second Language	10 (26.3)	–	5 (12.5)	–
EF <50% (4 CABG, 3 PCI missing)	12 (35.3)	–	19 (51.4)	–
History of AMI	17 (44.7)	–	36 (90.0)	–
Chronic Conditions				
Arthritis	15 (39.5)	–	11 (27.5)	–
Atrial Fibrillation	3 (7.9)	–	1 (2.5)	–
Benign Prostate Hyperplasia	3 (7.9)	–	0 (0.0)	–
Cancer	1 (2.6)	–	1 (2.5)	–
Chronic Kidney Disease	1 (2.6)	–	0 (0.0)	–
Diabetes Mellitus	16 (42.1)	–	8 (20.0)	–
Gastroesophageal Reflux Disease	11 (28.9)	–	13 (32.5)	–
Heart Failure	5 (13.2)	–	1 (2.5)	–
Hypertension	28 (73.7)	–	28 (70.0)	–
Irritable Bowel Syndrome	1 (2.6)	–	1 (2.5)	–
Liver Disease	1 (2.6)	–	2 (5.0)	–
Obstructive Sleep Apnea	2 (5.3)	–	5 (12.5)	–
Osteoporosis	2 (5.3)	–	4 (10.0)	–
Peripheral Vascular Disease	2 (5.3)	–	2 (5.0)	–
ACCI	–	4.42 (2.0)	–	3.87 (1.5)
HADS Scores				
Anxiety (HADS-A)	–	4.6 (4.0)	–	6.1 (4.4)
Depression (HADS-D)	–	3.9 (4.0)	–	4.7 (4.1)
Total	–	8.5 (7.4)	–	10.9 (7.5)

ACCI = Age-Adjusted Charlson Comorbidity Index; AMI = Acute myocardial infarction; CABG = Coronary artery bypass graft surgery; EF = Ejection Fraction; HADS = Hospital Anxiety and Depression Score; PCI = Percutaneous coronary intervention

Descriptive Analysis of MoCA Cognitive Domain Scores

A descriptive comparison of the differences between MoCA cognitive domain scores observed between CABG and PCI groups was conducted. CABG patients enrolled in cardiac rehabilitation scored lower on short-memory (CABG mean sub-score = 2.6, SD = 1.4; PCI mean sub-score = 3.7, SD = 1.2), and language (CABG mean sub-score = 4.7, SD = 1.2; PCI mean sub-score = 5.2, SD = 1.1) compared to PCI patients. Short-term memory scores translate to forgetting 2 to 3 out of 5 words on the delayed recall task. Cognitive domain scores for visuospatial function, executive function, attention, and orientation were comparable between groups (see Table 6).

Table 6: Montreal Cognitive Assessment Cognitive Domain Mean Scores by Procedure Type

Cognitive Domain	MoCA Items	Total Possible Score	CABG (n = 38)		PCI (n = 40)	
			Mean Score (SD)	Median Score (IQR)	Mean Score (SD)	Median Score (IQR)
Short-term memory	Delayed recall	5	2.6 (1.4)	3.0 (2.0)	3.7 (1.2)	4.0 (2.0)
Visuospatial function	Draw clock, copy cube	4	3.5 (0.6)	4.0 (1.0)	3.6 (0.6)	4.0 (1.0)
Executive function	Trails, fluency, abstraction	4	3.2 (1.1)	3.5 (1.0)	3.4 (0.8)	4.0 (1.0)
Attention, concentration, working memory	Digit, serial 7, letter A	6	5.3 (0.9)	6.0 (1.0)	5.5 (1.0)	6.0 (1.0)
Language	Naming, sentence repetition, fluency	6	4.7 (1.2)	5.0 (2.0)	5.2 (1.1)	5.0 (1.0)
Orientation	Orientation	6	5.9 (0.3)	6.0 (0.0)	6.0 (0.0)	6.0 (0.0)
Total MoCA Score		30	24.5 (3.3)	25.0 (3.0)	26.7 (2.7)	27.0 (4.0)

Primary Research Question

An analysis was conducted to answer the primary research question, “Among patients who are enrolled in cardiac rehabilitation, is there a difference in cognitive function in patients who have undergone CABG compared to patients who have undergone PCI?”

Student’s *t* Test Assumptions.

The assumptions for conducting a Student’s *t* test for independent samples were verified. First, CABG and PCI groups were mutually exclusive, and this was verified during completion of the case report forms. Second, data were also tested for departures from normality as well as for homogeneity of variance. The results of the Shapiro-Wilk test for normality for CABG (W = 0.927, p = 0.016) and PCI (W = 0.892, p = 0.001) indicated that both groups were not normally distributed. The skewness of the data was also calculated to assess normality (Norman & Streiner, 2008). MoCA scores in both groups were negatively skewed, particularly for the PCI group (CABG skewness = -0.96, standard error = 0.38; PCI skewness = -1.35, standard error = 0.37). Although a negative skew suggests that the data do not follow a normal distribution, a negative skew in the data was expected as participants were more likely to have normal cognitive function (MoCA score $\geq$ 26) versus a lower MoCA score. Third, data were tested for homogeneity of variances. The results from Levene’s test were not significant, indicating that CABG and PCI groups had equal variances. Since the assumptions for normally distributed samples were not met, both parametric (Student’s *t* test) and non-parametric (Wilcoxon signed rank test) statistical tests were conducted.

Comparison of Cognitive Function Between CABG and PCI Patients.

The results of Student's *t* test indicated that there was a statistically significant difference in MoCA scores between patients with CABG and PCI. MoCA scores were significantly lower among CABG patients (mean = 24.5, SD = 3.3) than PCI patients (mean = 26.7, SD = 2.7), t (76) = 3.15, $p < 0.01$. The mean difference in MoCA score for the CABG vs. PCI groups was 2.12 points (95% CI 0.78 to 3.47). The interpretation is that cognitive function is significantly lower in the CABG group compared to the PCI. There were 21 out of 38 CABG patients (55.3%) and 12 of 40 PCI patients (30.0%) that scored below the MoCA threshold for MCI (Nasreddine et al., 2005).

Median MoCA scores for CABG and PCI were 25 (interquartile range [IQR] = 3.0) and 27 (IQR = 4.0) respectively. The results of the Wilcoxon signed rank test corroborated the results of Student's *t* test, indicating that there was a statistically significant difference in the median MoCA scores for CABG and PCI, with MoCA scores being lower in the CABG group (W = 1180.50, $p < 0.001$). Using Cohen's *d* formula, the calculated effect size for MoCA score in this study was 0.73, indicating a medium effect size.

Secondary Research Question

An analysis was conducted to answer the secondary research question, "Among patients who are enrolled in cardiac rehabilitation, what variables are independently associated with cognitive function?"

Selection of Variables.

Bivariate correlation analyses were conducted to identify independent variables that were significantly associated with total MoCA score (see Table 7). Weak correlations were identified between the following independent variables and MoCA score: coronary revascularization procedure type ($r = 0.339$, $p = 0.002$), age (r = -0.2148, $p = 0.028$), employment ($r = -0.330$, $p = 0.003$), history of AMI ($r = 0.308$, $p = 0.006$), HF diagnosis ($r = -0.306$, $p = 0.007$), and ACCI ($r = -0.309$, $p = 0.006$). A moderate negative correlation was identified between primary spoken language and total MoCA score ($r = -0.412$, $p < 0.001$).

Independent variables of interest to be included in the regression model were the type of coronary revascularization procedure, ACCI, and the presence of HF. Other variables were considered for inclusion in the regression analysis, but were ultimately not included in the model. Sex, education level, and level of independence were not significantly associated with MoCA score in the bivariate analysis, and thus were not included. Language and employment were significantly associated but were not included due to collinearity. Language was correlated with coronary revascularization procedure and employment was correlated with age. Age was not included because ACCI remained in the final model with a greater R-squared value compared to the model with age and CCI as separate variables (Data not shown).

Table 7: Bivariate Analyses of Significant Correlations (Pearson r) and Level of Significance (p value) Between Independent Variables and MoCA Score (n = 78)

Independent Variable	Associated with low MoCA	Pearson *r*	*p* Value
Coronary revascularization procedure type (CABG = 1, PCI = 2)	CABG	0.339	0.002
Age	Increased age	-0.248	0.028
ACCI	Increased ACCI	-0.309	0.006
HF diagnosis	HF	-0.306	0.007

ACCI = Age-adjusted Charlson Comorbidity Index; HF = Heart failure

Assumptions for Regression Analysis.

The assumptions for a linear regression analysis were verified. In addition to assumptions that were verified in prior to conducting Student's *t* test, variables that were included in a regression analysis require little to no evidence of multicollinearity. Potential multicollinearity was assessed with Chi-square tests and bivariate correlation analyses, and was further confirmed using variance inflation factor (VIF) (Norman & Streiner, 2008).

First, Chi-square tests were performed on categorical demographic variables and coronary revascularization procedure type to determine potential collinearity for the regression model. Statistically significant associations were found with employment (X^2 (1) = 4.12, p = 0.04) and diagnosis of diabetes (X^2 (1) = 4.47, p = 0.08). Fisher's exact test indicated that history of acute myocardial infarction was significantly associated with coronary revascularization procedure type ($p < 0.001$). Bivariate correlation analyses were performed on continuous demographic variables. There was a weak negative correlation between age and coronary revascularization procedure type (r (78) = -0.26, p = 0.02). Moderate correlations were found between age and employment (r = 0.595, p <0.001), and the type of coronary revascularization procedure and history of AMI (r = 0.485, p < 0.001), indicating potential collinearity. No significant associations were found between ACCI and coronary revascularization procedure type.

Second, multicollinearity was assessed using VIF and collinearity was assumed if VIF was greater than 10 (Norman & Streiner, 2008). VIFs for all significant variables of interest to be included in the regression model that were statistically significantly associated with MoCA score were less than 1.25, indicating no significant collinearity.

Independent Variables Associated with Total MoCA Score.

A backward stepwise linear regression was conducted for MoCA score. Three independent variables were selected based on relevance to the present study and a statistical significance threshold of p <0.05. The following independent variables were included: coronary revascularization procedure type, ACCI, and HF diagnosis. The final adjusted model was significant (F (2, 75) = 8.382, p < 0.001), accounting for 16.1% of the total variance in total MoCA score (R^2 = 0.183, adjusted R^2 = 0.161). The type of coronary revascularization and ACCI remained in the model (See Table 8).

Table 8: Regression Analysis for Montreal Cognitive Assessment Score (n = 78)

Variable	B	SEB	95% confidence interval		*p* value
			Lower	Upper	
Constant	24.722	1.389	21.954	27.389	<0.001
ACCI	-0.472	0.183	-0.831	-0.092	0.015
Coronary revascularization procedure	1.870	0.661	0.555	3.186	0.006

R^2 = 0.183, Adjusted R^2 = 0.161, F (2, 75) = 8.382, p < 0.001
ACCI = Age-adjusted Charlson Comorbidity Index; B: Beta Coefficient; SEB: Standard Error of Beta Coefficient

Summary of Results

In this study, approximately half of CABG patients who enrolled in cardiac rehabilitation had underlying cognitive deficits (MoCA < 26) compared to a third of PCI patients. The results of Student's *t* test and the Wilcoxon signed rank test indicated that CABG patients scored significantly lower on the total MoCA (2 points) compared to PCI patients upon intake to cardiac rehabilitation. These results suggest that there is a potentially clinically significant difference in the cognitive function of CABG vs. PCI patients. CABG patients scored lower than PCI patients in short-term memory and language domains on the MoCA, but scored similarly within other cognitive domains. Results of the regression analysis indicated that CABG procedure, speaking English as a second language, unemployment or retirement, and HF diagnosis were significantly and independently associated with lower total MoCA scores. The adjusted linear regression model accounted for 16.1% of the total variance in cognitive function as measured by the total MoCA score. Bivariate correlation analyses also indicated that age, language, employment, and AMI were significantly associated with MoCA score, but were not included in the model due to collinearity and limitations imposed by sample size.

CHAPTER 5

DISCUSSION AND CONCLUSION

This chapter is divided into six sections. The first section discusses the results of the study for the primary research question as they pertain to mean differences of cognitive function for CABG vs. PCI patients, MCID, effect size, frequency of cognitive deficits, and previous studies. The second section discusses the results of the study for the secondary research question, detailing the significant independent variables in the linear regression model and comparing them to the results of previous observational studies examining cognitive function in CAD, cardiac surgery, and cardiac rehabilitation. The third section discusses the contributions that this study makes in examining the cognitive function of patients who have undergone a coronary revascularization procedure. The fourth section addresses the strengths and limitations of the present study. The fifth section discusses the clinical significance of all statistically significant results, and the potential implications of the results for clinical practice and future research. The sixth section summarizes this thesis dissertation and the conclusions from the discussion of the results.

Primary Question: Comparison of Cognitive Deficits

The primary research question sought to compare the level of cognitive function between CABG and PCI patients enrolled in cardiac rehabilitation at the initial intake assessment. The MoCA measured several domains of cognitive function.

Education and Self-Management Implications of Total MoCA Scores.

The clinical significance of the results was determined by comparing the mean difference in MoCA score between CABG and PCI groups to the MCID used in the sample size calculation. The mean difference in MoCA score for CABG vs. PCI groups was 2.12 (mean difference = 26.7

– 24.5). A MCID of two points was used as the comparator since no studies were found that reported a MCID for MoCA scores among patients with cardiovascular diseases. In addition, this difference in MoCA score represents a shift of a patient from the normal range of cognitive function to MCI. This MCID value has also previously been used in a study of cognitively impaired patients with Parkinson's disease (Peters et al., 2012). These data show that the difference in MoCA score for CABG vs. PCI is approximately at the threshold to detect a clinically significant difference in cognitive function. On average, CABG patients scored approximately two points lower on the MoCA compared to PCI patients, indicating that post-CABG patients have MoCA scores that are indicative of MCI (MoCA $\leq$ 26). This is a novel comparison of patients who have undergone different coronary revascularization procedures, which suggests that CABG patients with cognitive deficits may have greater difficulty engaging effectively in education and self-management components of cardiac rehabilitation programs in contrast to PCI patients. Future research is required to establish this relationship.

Self-management education is a complex process that requires tailoring of the format, duration, and dose of education to the individual (Lambrinou, Protopapas, & Kalogirou, 2014). Cognitive deficits are one of many factors that increase a patient's risk for poor health outcomes (HRQOL, physical fitness, and functional outcomes) and non-adherence with self-management education, treatment and care recommendations (Alosco et al., 2014; Burkauskas et al., 2013; Fontes et al., 2013; Foster et al., 2011; Harkness et al., 2014; Kakos et al., 2010; King et al., 1999; Lambrinou et al., 2014; Lippa et al., 2008; Phillips-Bute et al., 2006). Moreover, the presence of cognitive deficits may negatively impact a patient's ability to understand, recall, and apply disease-specific information to manage one's chronic illness (Lambrinou et al., 2014). Some evidence in non-cardiac older adults and HF patients confirms the deleterious effect of mild cognitive deficits on self-management education and treatment adherence. In a sample of 8,698 community-dwelling older adults (mean age = 73.1, SD = 7.0), Dong et al. (2009) identified that neglect in tending to daily activities and health care needs (Self-Neglect Scale) was negatively associated with the level of cognitive function measured by the MMSE, explaining 31.7% of the variance in cognitive function in a multivariate linear regression model (R^2 = 0.317, β = -0.363, standard error [SE] = 0.026, p < 0.001).

In addition, two cross-sectional studies of HF patients reported results that support the negative effect of mild cognitive deficits on self-management behaviour. Harkness et al. (2014) (n = 100; mean age = 72, SD 10 years) reported that cognitive function as measured by the MoCA was independently associated with self-management (SCHFI), explaining 18.03% of the variance in self-management in a linear regression model controlled for age and sex (R^2 = 0.1803, F (3,96) = 7.04, p = 0.001). Hjelm et al. (2015) found in a study of 105 HF patients (mean age = 72, IQR 65-72) that decreased psychomotor processing and executive dysfunction measured by the Trail Making Test A was independently associated with self-management (Heart Failure Self-Care Behaviour Scale), explaining 12% of the variance in self-management in a multivariate linear regression when controlled for age, education level, and New York Heart Association class (R^2 = 0.12, F [5, 99] = 2.74, p < 0.023). However, no studies were found that directly examined the cognitive status of coronary revascularization patients and self-management.

Results which are in contrast to those reported in the present study were reported in a prospective observational study by Selnes et al. (2008), designed to examine 6-year cognitive outcomes of patients who underwent CABG or medical therapy. Selnes et al. (2008) employed the MMSE to measure global cognition, which has a low sensitivity for detecting mild cognitive deficits. Although POCD was observed in CABG patients, there were no significant differences in cognitive decline in the 72-month postoperative period between CABG patients and the medically managed control group. In addition, both CABG patients and controls showed similar degrees of cognitive deficits that are typically observed in all patients with CAD, including worse visual memory, visuoconstruction, executive function, and global cognition (Selnes et al., 2008). The findings from the present study were based on the MoCA since it is more sensitive than the MMSE in detecting amnestic mild cognitive deficits that are commonly found in CABG patients (sensitivity = 100.0%) (McLennan et al., 2011). Thus, it is likely that the MoCA scores from this study more accurately reflect the cognitive status of patients who underwent a coronary revascularization procedure compared to cognitive test scores of previous studies.

The mean MoCA score of PCI patients (26.7, SD = 2.7) was above the threshold for MCI (MoCA ≥26) (Nasreddine et al., 2005). In this study, with the exception of short-term memory and language, the cognitive domain profiles of the PCI group were similar to the CABG group. Higher MoCA scores in PCI patients may be due to a slightly young PCI compared to CABG cohort (PCI: mean age = 59.6, SD = 9.8; CABG: mean age = 64.6, SD = 8.7). Differences in comorbidity burden may also contribute the higher MoCA score among PCI patients. A prospective study of 309 cardiac ICU patients (mean age of patients with cognitive deficits = 61.69, SD = 13.46) supported the impact of comorbidity burden on cognitive function (Lahariya et al., 2013). Comorbidity burden measured by the CCI was independently associated with cognitive function (CAM-ICU) (OR 3.30, 95% CI 2.14 to 5.09, $p < 0.001$). In the present study, PCI patients had slightly less combined age-comorbidity burden (ACCI mean = 3.87, SD = 1.5) compared to CABG patients (ACCI mean = 4.42, SD = 2.0).

The CI of the mean difference was relatively large due to the small sample size; the true mean difference of the sample is likely to lie within the interval 0.78 and 3.47 points on the MoCA for 95% of the time. It is possible that the true mean difference may lie at the lower bound of the CI where the mean difference in MoCA between CABG and PCI groups may not be large enough to detect a clinically significant difference in cognitive function. In contrast, the upper bound of the CI surpasses the MCID and thus, it is expected that a clinically significant difference in cognitive function would be detected between CABG and PCI patients should the true mean difference lie closer to the upper limit of the 95% CI. This may mean that CABG patients may not experience challenges with education and related self-management behaviour at the lower bound of the 95% CI. A larger sample size is needed to be confident that the mean difference in MoCA score between CABG and PCI patients represents the true mean MoCA scores in this population.

Clinical Significance and Effect Size.

There was a medium effect size for the mean MoCA scores between CABG and PCI groups (Cohen's $d = 0.73$). This effect size is comparable to previous studies of cognitive screening instruments for the detection of MCI. Larner (2014) compared the effect sizes for the diagnosis of MCI versus no dementia for different cognitive screening instruments (MMSE, MoCA, Mini-Mental Parkinson, Six-Item Cognitive Impairment Test, and Test Your Memory Test) and found that the MoCA had the largest effect size, ranging from medium to large (range 0.48 – 1.45). A similar effect size (0.75) was calculated in an observational study of patients with systolic and diastolic HF (Athilingham et al., 2013). Thus, the medium effect size estimate for MoCA score in this study is deemed clinically significant, suggesting a detectable difference may exist in clinical practice in the level of cognitive function between CABG and PCI patients.

This may translate into challenges with effectively engaging in various aspects of a cardiac rehabilitation program.

Education and Self-Management Implications of Cognitive Domain Scores.

Marked differences were observed in the cognitive domain profiles of CABG and PCI patients. The results of the present study identified that CABG patients scored lower than PCI patients for the MoCA language domain (3-Item Animal Naming, Sentence Repetition, and Phonemic Fluency Task). Only one known study has documented language deficits in cardiac rehabilitation patients, and these deficits were not exclusive to CABG patients (Moser et al., 1999). In this study, a greater proportion of CABG patients spoke English as a second language and significant associations were found between first spoken language and the type of coronary revascularization procedure. The language deficits among CABG patients in this study are therefore likely to be related to the higher proportion of patients who did not learn English as their first language and not attributed to the CABG procedure (See Table 5 in Chapter 5).

Cognitive deficits are known to interfere with a number of self-management behaviours related to the domains of attention, memory, executive function, and speech (Lambrinou et al., 2014). Notably, CABG patients predominantly showed impairment in short-term memory (Delayed Recall task). Memory impairment may result in patient unresponsiveness to self-management education. Patients with mild cognitive deficits may have difficulties with recalling content from educational sessions, attending to self-management behaviours (e.g. medication administration, diet restrictions, regular exercise), and recognizing symptoms related to health status changes (Lambrinou et al., 2014).

The domain-specific difference between CABG and PCI patients was corroborated in several previous studies of POCD (Eggermont et al., 2012; Knipp et al., 2008; Phillips-Bute et al., 2006). A systematic review of studies evaluating cognitive function in CAD patients that CABG patients showed significant impairment in verbal memory, while all CAD patients showed declines in motor speed, psychomotor speed, and global cognitive function (Eggermont et al., 2012). Pooled estimates for cognitive function could not be calculated due to heterogeneity of the test measures. A longitudinal study (n = 551; mean age = 62.32, SD 11.0) also reported that approximately 12 percent of patients had deficits in verbal memory and language (Randt Memory Test) that persisted one year following CABG (Phillips-Bute et al., 2006).

A three year prospective cohort study of 39 patients who had undergone on-pump CABG (mean age = 67.0, SD = 9.8) showed similar results (Knipp et al., 2008). Knipp et al. reported that verbal memory (Delayed Recognition Test) was significantly lower 3 years following CABG than before the surgery (preoperative: mean score = 5.88, SD = 1.79; 3 years postoperative: mean score = 4.75, SD = 1.78; $p = 0.011$). A univariate logistic regression analysis also revealed that decline in verbal memory upon hospital discharge predicted further decline at 3-years post-CABG (OR = 0.422, 95% CI 0.182 to 0.971, $p = 0.043$) (Knipp et al., 2008). The domain-specific results of the present study are consistent with the literature and support future research on the effect of mild memory impairment among CABG patients in cardiac rehabilitation. Short-term memory deficits in CABG patients may predict challenges with education and self-management throughout the entire cardiac rehabilitation program (approximately 6 months), and may extend to challenges with self-management long after program completion.

Frequency of Cognitive Deficits Following Coronary Revascularization.

Over half of CABG patients scored below the MoCA threshold, whereas under one-third of PCI patients had MoCA scores that were indicative of mild cognitive deficits. Findings suggest that although cognitive deficits commonly present among patients who have undergone CABG, they are not exclusive to CABG. A comparison of CABG and PCI groups to a group of CAD patients that were medically managed and had no prior coronary revascularization would strengthen these results. However, in this study it was not possible to recruit a medically managed CAD group as these patients are not frequently referred to cardiac rehabilitation. The results of the present study reflect previous studies of general cardiac patients (e.g., patients with CAD) (Eggermont et al., 2012; Maekawa et al., 2014; Mufson et al., 2012). Noteworthy is that cognitive deficits present differently between CABG and PCI patients. These differences may have implications in clinical cardiac rehabilitation practice, such as learning, self-management education outcomes, and related self-management outcomes. Due to the small sample size in this study, an estimation of prevalence was not possible. Future research should consider a third medically managed CAD group and examine differences in cardiac rehabilitation outcomes between memory deficits related to POCD in CABG and amnestic MCI related to PCI.

No known studies have reported specifically cognitive deficits in PCI patients. In the present study, approximately one-third (12 out of 40) of PCI patients scored below the cut-off for MCI (MoCA $\leq$ 26). This proportion is comparable to proportions reported from previous studies of CABG patients at greater than one-year post-CABG. The proportion of CABG patients who had cognitive deficits persisting beyond one year ranged from 19 to 30 percent (Djaiani et al., 2006; Knipp et al., 2008; Selnes et al., 2008). These data suggest that PCI patients may not differ from other CAD patients in cognitive status, but further comparisons with medically managed CAD patients are required.

The reported proportion of post-CABG cognitive deficits is broad. Several studies have reported frequencies of POCD that range from 19 to 59 percent at varying postoperative time points (Boodwhani et al., 2006; Djaiani et al., 2012; Lyksetsos et al., 2006; Knipp et al., 2008; Newman et al., 2001, 2007; Phillips-Bute et al., 2006; Selnes et al., 2008). At nearly eight weeks following coronary revascularization (mean = 7.7 weeks, SD = 1.5), the CABG group showed a similar proportion of cognitive deficit to CABG patients three previous studies (Knipp et al., 2008; Newman et al., 2001). Knipp et al. (2008) reported that a proportion of 56 percent (22 of 39) of CABG patients had POCD (neuropsychological battery of 11 tests) at hospital discharge. Newman et al. (2001) reported similar results: 53 percent of CABG patients (138 out of 261) had POCD (neuropsychological battery of 5 tests) at hospital discharge. Lastly, a study by Boodhwani et al. (2006) reported that cognitive deficits persisted among 59 percent of CABG patients (265 out of 448) at 3 months, which were similar to the present findings. In contrast, these previous studies reported significantly lower proportions of POCD (23 to 36 percent) during the 6-week to 3-month postoperative period (Knipp et al., 2008; Newman et al., 2001). The results from the present study suggest that cognitive deficits may be underreported at the 8-week post-CABG time period, but further research is needed into order to establish prevalence.

Secondary Question: Independent Variables of Cognitive Deficits

The secondary research question sought to determine independent variables that were associated with cognitive function (MoCA score) by developing a linear regression model. The backward linear regression resulted in type of coronary revascularization procedure (CABG versus PCI) and disease burden (age-adjusted CCI) remaining in the model as independent variables for cognitive function (MoCA score). The overall adjusted model did not strongly predict MoCA score (r^2 = 0.161).

This is the first study to use the type of coronary revascularization procedure (CABG versus PCI) as an independent variable for cognitive function. One other study that was previously discussed compared CABG patients with medically managed controls using the MMSE to measure cognitive function and found no significant between-group differences (Selnes et al., 2008).

Disease burden, as measured by the ACCI, was independently associated with MoCA score. No known studies have compared CCI and MoCA score among cardiac patients, although one study of cardiac ICU patients measured disease burden using the CCI and cognitive function using the CAM-ICU (Lahariya et al., 2014). Another study found that cognitive impairment, measured by the MMSE, was associated with CCI among HF patients (Ghanbari et al., 2013). Results from the regression analysis of the present study suggest that high ACCI is negatively associated with cognitive deficits. It can be inferred that patients with accumulated disease burden may have subsequent challenges with education and self-management.

Other independent variables associated with cognitive function among cardiac patients in other studies include: advanced age, lower education level, pre-existing MCI, cardiovascular/ cerebrovascular/ peripheral vascular disease, history of alcohol abuse, depression, physical inactivity, diabetes, smoking, and low EF (Arntzen et al., 2011; Boodhwani et al., 2006; Ernest et al., 2007; Evered et al., 2016; Gottesmann et al., 2009; Rundshagen, 2014; Selnes et al., 2012; Sendelbach et al., 2006; Trubnikova et al., 2013). Many of the risk factors in this study were controlled for in exclusion criteria or were not significant. For example, patients with pre-existing cognitive impairment, a history of alcohol abuse or who were diagnosed with depression were excluded from this study. Education, low EF, cerebrovascular and peripheral vascular disease were not significant in the bivariate analyses and were subsequently not included in the regression model. Future research should recruit a larger sample in order to control for more covariates in the linear regression model.

Contributions to Knowledge About Cognitive Function and Coronary Revascularization.

This study contributes to the knowledge about cognitive function and coronary revascularization in three ways. This is the first study to investigate the cognitive function of post-coronary revascularization patients immediately prior to their entry into cardiac rehabilitation. Previous studies did not examine the magnitude of cognitive deficits in cardiac rehabilitation (Intzandt et al., 2015; Fink et al., 2014; Kakos et al., 2010). Intzandt et al. (2015) surveyed 72 cardiac rehabilitation programs in Canada (Response rate = 50 percent) and determined that 61.1% of cardiac rehabilitation programs treated patients with known MCI. However, the proportion of cognitively impaired patients in each program was not determined nor was the demographic profile of the patients (i.e., type of coronary revascularization procedure, comorbidities, etc.). While the present study has focused on post-coronary revascularization patients, results of this study support that further investigation is required to determine the prevalence of cognitive deficits for all patients entering cardiac rehabilitation.

Second, this is the first study to directly compare the cognitive function of patients who underwent different coronary revascularization procedures (i.e., CABG vs. PCI). A systematic review of 21 studies (n = 7,802, weighted mean age = 68 years) concluded that there were no known RCTs or controlled clinical trials that compared cognitive outcomes of different types of coronary revascularization procedures (Fink et al., 2014). Comparisons have not been made between medically managed CAD patients and post-coronary revascularization patients, which leaves a gap for future research (Fink et al., 2014).

Third, this is one of a few studies that used a cognitive screening tool (MoCA) that is sensitive for detecting mild cognitive deficits in cardiovascular populations. Fink et al. (2014) reported that only 3 out of 21 (14.3%) of studies examining cognitive outcomes of coronary revascularization procedures used the MoCA. McLennan et al. (2011) (n = 110; mean age = 67.9 years, SD = 11.7) validated the MoCA for detection of amnestic MCI (sensitivity = 100.0%, specificity = 50%) and multiple-domain MCI (sensitivity = 83.3%, specificity = 52.0%), suggesting that the MoCA is an effective screening tool for detecting mild cognitive deficits in both CABG and PCI patients. A key manifestation of cognitive deficits in CABG patients is memory impairment whereas PCI patients are likely to show global cognitive deficits, but not memory deficits (Eggermont et al., 2012).

Study Strengths and Limitations

The present study employed a number of study design and statistical methods to reduce systematic biases and random error. To reduce the probability of confounding variables, patients with known risk factors for cognitive deficits were excluded, such as pre-existing cognitive deficits, diagnosis of anxiety or depression and history of cerebrovascular disease. The duration of time from coronary revascularization procedure was documented to reduce the influence of cognitive recovery on the study results. A strength of the present study is that the MoCA was used to determine cognitive function. The MoCA is a validated cognitive screening tool in cardiovascular populations and its use in this study addresses a major conceptual weakness in previous studies of cognitive deficits among patients with cardiac disease (Cameron et al., 2013; Habib et al., 2014; Lyketsos et al., 2006; Selnes et al., 2012). The MoCA was administered solely by the investigator in order to promote consistency and limit inter-rater variability.

Statistical methods were employed to reduce potential random error in the primary and secondary research questions. For the primary question, both parametric (Student's *t* test) and non-parametric tests (Wilcoxon Signed Rank test) were conducted, since the MoCA scores were not normally distributed. For the secondary question, an adjusted R-squared was calculated to account for the number of terms in the model.

There were potential sources of bias that may have influenced the study results. Since the study employed a cross-sectional design, there may be error from using a single measurement of cognitive function. Cognitive function prior to and immediately following the coronary revascularization procedure was not collected, limiting temporal association and causal inference from this study. The study design is vulnerable to sampling error due to the use of non-probability sampling. Convenience sampling from a single tertiary clinical setting may have led to misrepresentation of each cohort sample, and thus, may limit the generalizability of the study results. Due to the cross-sectional study design and the rolling basis of cardiac rehabilitation enrollment, the total sampling frame was not known and it was not possible to use more robust methods of probability sampling. To minimize selection bias, a systematic approach was employed, and eligibility was assessed by two independent assessors, first by a clinic nurse and second by the investigator, prior to enrollment in the study. The study demographics were susceptible to social desirability and recall bias, such as forgetting to list certain chronic conditions, over-reporting education level or under-reporting smoking frequency, from self-reporting of socio-demographic and clinical characteristics. Social desirability and recall biases related to collection of self-reported demographic data, and recall bias and potential coding errors collected from the chart review were minimized by corroborating responses from both data sources.

Study results were also limited by the sample size and data collection from a single site. Although the sample size provided adequate power to minimize the probability of Type II error for the parametric and non-parametric tests conducted in the primary research question, it was too small to include more than four independent variables in the regression model, restricting the robustness of the final model. Small sample size also limits the possibility of calculating the prevalence of cognitive deficits in cardiac rehabilitation; however, the presence of cognitive deficits was determined. Lastly, data collection from a single site may also reduce external validity of the study results. However, a comparison of sample demographics to CCN data for Ontario indicates that both CABG and PCI cohorts had similar characteristics to the general cardiac rehabilitation population. Age was the only demographic variable that was different between in the PCI cohort and CCN data of PCI patients (59.6 vs. 65.9) (See Table 2) (CCN, 2014a).

Future Directions

Since this was a small sample cross-sectional study, generalizability of the results to clinical practice and health policy is limited. Implications for future research pertain to power, prospective examination of cognitive deficits, comparator groups, and the effect of cognitive effects on self-management education-based health outcomes.

This study lacked the adequate power to estimate prevalence and construct a robust multivariate regression model. Incidence could not be calculated due to the cross-sectional design. Subsequent studies should calculate appropriate sample sizes and employ a prospective cohort design to estimate the prevalence and incidence of cognitive deficits following CABG and PCI. Future research should also estimate sample size to ensure adequate power to account for more than four categorical variables, and for nominal and ordinal variables that have more than two levels.

The primary investigator conducted the present study at a single site. Although the protocol was standardized and a single MoCA administrator (primary investigator) was used to minimize interrater variability, conduction of a multi-site study will strengthen the external validity of the results.

While low-level evidence does not recommend cognitive screening for asymptomatic older adults in the general population (Canadian Task Force on Preventive Health Care, 2016), patients attending cardiac rehabilitation constitute a specialized population with inherent risk factors for cognitive deficits (i.e., cardiovascular risk factors, type of coronary revascularization procedure). Moreover, the purpose of cognitive screening in cardiac rehabilitation, unlike in the general population, would not be to improve cognitive function but to improve the delivery of self-management education (format, dose, and duration). Results from the study support the need for a prospective cohort study to establish temporality of cognitive deficits. Alterations in cognitive function may be due to unreported pre-existing cognitive deficits that would not be accounted for in a cross-sectional study. Future longitudinal studies should examine cognitive function prior to coronary revascularization and follow a cohort of patients through to completion of a cardiac rehabilitation program. A prospective cohort study would establish a temporal relationship between the type of coronary revascularization procedure and cognitive function, as well as determine the duration/trajectory of POCD. Importantly, cognitive function could then be evaluated in relation to self-management and HRQOL outcomes.

This study only compared patients who had undergone CABG and PCI. Although CABG and PCI patients represent a significant proportion, they do not account for all cardiac rehabilitation attendees. For example, patients with CAD who do not require revascularization or patients with valvular heart disease were not included in the present study, and should be considered in future research when estimating prevalence of cognitive deficits in cardiac rehabilitation participants.

Since definitions of POCD do not consider the effects of cognitive deficits on functional abilities, future research should establish an association between cognitive function and self-management education outcomes such as HRQOL and self-management (Evered et al., 2016). Examples of general HRQOL measures validated in cardiovascular populations include the SF-36, Sickness Impact Profile, Nottingham Health Profile, and the European Quality of Life-5D (Failde, Medina, Ramirez, & Arana, 2010; Failde & Ramos, 2000; Tully, 2013; Whynes & TOMBOLA Group, 2008). Validated CAD-specific HRQOL instruments that should be considered for examination with cognitive function include the Duke Activity Status Index, MacNew Heart Disease Quality-of-Life Measure, and the Seattle Angina Questionnaire (Dixon, Lim, & Oldridge, 2002; Hlatky et al., 1989; Spertus et al., 1995).

The goal of education in cardiac rehabilitation is to promote chronic disease self-management. While there is some evidence to show that cognitive deficits may hinder self-management and program adherence among patients attending cardiac rehabilitation (King et al., 1999), these relationships have been explored in greater detail in patients with HF and diabetes (Hicks & Holm 2003; Lippa et al., 2008). Thus, future research should examine the relationship between cognitive deficits, self-management, and program adherence in cardiac rehabilitation. Two validated disease-specific self-management tools that may be used in future studies are the Cardiac Knowledge Assessment Tool and Heart Disease Facts Questionnaire (Rosneck et al., 2014; Wagner, Lacey, Chyun, & Abbott, 2005).

The potential clinical implications of this study include (1) adapting existing self-management education interventions to better address cognitive deficits and (2) incorporating formal cognitive screening into cardiac rehabilitation to identify those at-risk for having challenges in education-based interventions. Although there is a lack of supporting evidence, Lambrinou et al. (2014) summarized strategies that have been used in providing education for community-based HF patients with cognitive deficits: (1) reinforcement of new information using short and clear instructions; (2) implementation of patient-specific learning goals and priorities; (3) use of written and illustrated patient education materials to supplement education sessions; (4) maintenance of a diary of self-management activities; and (5) involvement of family or caregivers in the educational process.

Engagement in education-based interventions and subsequent self-management behaviours is a complex process that requires patients to have the cognitive skills for symptom recognition and self-management decision making. Self-management education must incorporate concepts of pathophysiology and pharmacotherapy that are essential to chronic cardiac care (Brown et al., 2011). In addition, self-management education is influenced by a number of personal factors, one of which being cognitive deficits (King et al., 1999; Murray et al., 2012; Neubeck et al., 2011). Thus, specific tailoring of self-management education should be considered for each patient. Future research should focus on the adaptation and development of educational interventions that are appropriate for patients with cognitive deficits who enroll in cardiac rehabilitation (See Table 9 for a summary of recommendations for future clinical research). Cardiac rehabilitation staff should be aware of and consider cognitive deficits in their daily practice.

Table 9: Summary of Research Recommendations

Summary of Research Recommendations
1. Study Design: • Prospective Cohort 2. Data Collection and Recruitment: • Multiple sites of recruitment • Larger sample size • Comparisons between CABG, PCI and medically managed CAD patients • Include other non-coronary revascularization patients that attend cardiac rehabilitation (e.g., medically managed CAD patients, valve surgical patients, HF patients who have not undergone coronary revascularization) • Examination of short-term, intermediate and long-term cognitive status 3. Primary outcome: • Cognitive function measured by the MoCA 4. Secondary outcomes: • Self-management and other outcomes related to education • Functional status measures • HRQOL using general and CAD-specific measures 5. Analysis • Analysis of Variance (ANOVA) to account for additional groups (i.e., medically managed patients) • Linear regression model with more than four independent variables • Prevalence and incidence 6. Future Intervention Studies • Interventions that provide tailored education for patients with cognitive deficits (e.g., supplemental written and illustrated patient education material, family involvement in educational process, modification of education dose [high frequency, short sessions)

Conclusion

Cognitive deficits have not been a focus of national and international standards of practice and clinical practice guidelines for cardiac rehabilitation programs (British Association for Cardiovascular Prevention and Rehabilitation, 2012; CCN, 2014b; Leon et al., 2005). Although the pathophysiological mechanisms are poorly understood, evidence from observational studies suggests that cognitive deficits are present in patients with cardiac disease and that the degree of deficit is also associated with the coronary revascularization procedures

(Benvenuti et al., 2013; Djaiani et al., 2012; Farhoudi et al., 2010; Fontes et al., 2013; Kennedy et al., 2013; Kline et al., 2012; Knipp et al., 2008; Newman et al., 2001, 2007; Takagi et al., 2007; van Dijk et al., 2007; Selnes et al., 2008, 2012; Terrando et al., 2011). Cognitive deficits have the potential to interfere with education-based cardiac rehabilitation, affecting health outcomes such as HRQOL and self-management practice (Alosco et al., 2014; Burkauskas et al., 2013; Garcia et al., 2013; Ghafari et al., 2012; Kakos et al., 2010; Fontes et al., 2013; Foster et al., 2011; Harkness et al., 2014; Hicks & Holm, 2003; Lippa et al., 2008). However, previous studies have methodological problems, such as the use of cognitive screening tests that are not sensitive to mild cognitive deficits. The cognitive status of patients attending cardiac rehabilitation was not previously known and comparisons between CABG and PCI patients have not been made (Fink et al., 2014; Kakos et al., 2010; Intzandt et al., 2015).

The purpose of this cross-sectional study was to compare cognitive function using the MoCA between CABG and PCI coronary revascularization patients who have just enrolled in cardiac rehabilitation. Guided by Wagner et al.'s Chronic Care Model (1996), demographic variables that may affect cognitive function were selected. CABG patients were found to score significantly lower on the MoCA compared to PCI patients upon cardiac rehabilitation intake. The type of coronary revascularization procedure and disease burden (age-adjusted CCI) were independently associated to cognitive function measured (MoCA). Results of the study have implications for improving education-based cardiac rehabilitation interventions and cognitive screening in cardiac rehabilitation. A large sample prospective cohort study is required to determine temporality and prevalence of cognitive deficits, and to determine associations between cognitive deficits and self-management education-related health outcomes.

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APPENDICES

Appendix A: Literature Review Search Strategy

Research Question.

Do CABG vs. PCI patients differ in level of cognitive function upon intake to cardiac rehabilitation?

Primary Search Strategy.

A search of the observational literature was conducted in the following databases: Embase, Medline, PsychINFO, and CINAHL. A Google Scholar search was also conducted to find any relevant grey literature. The search was restricted to English, observational, human studies and reviews conducted between 2005 and 2015. The focus of the literature search was to find evidence for the presence of the cognitive function of patients who underwent CABG and of patients attending cardiac rehabilitation. Studies that examined associations with serum values or brain imaging, pediatric cardiac populations or cognitive function in non-cardiac disease were excluded. Studies that exclusively studied postoperative delirium were also excluded.

Terminology Used in the Search Strategy.

The table below summarizes the key terms and Boolean search operators used in the literature search:

1) Cognition OR Cognitive OR Cognitive Deficits OR Mild cognitive impairment OR Postoperative cognitive dysfunction

AND

2) Coronary artery disease OR Ischemic heart disease OR Cardiac surgery OR Heart surgery OR Coronary artery bypass graft OR Cardiac rehabilitation OR Heart rehabilitation

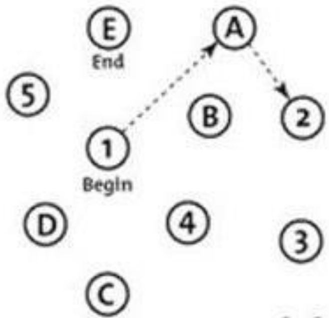
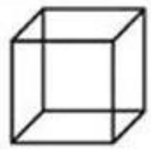
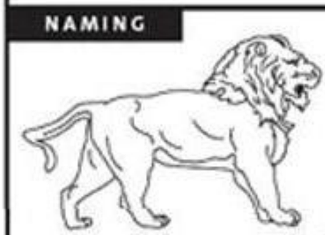
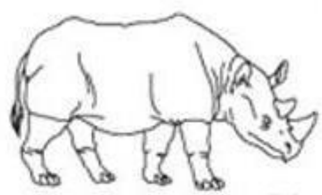
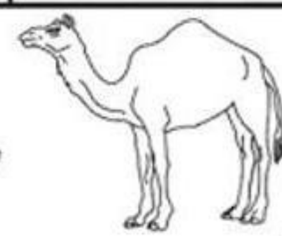
AND

3) Observational study OR Cross-sectional study OR Prevalence OR Prospective study OR Cohort analysis OR Retrospective study OR Longitudinal study OR Systematic Review

Appendix B: Montreal Cognitive Assessment (MoCA)

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

		POINTS
VISUOSPATIAL / EXECUTIVE	 [ ]  Copy cube [ ] Draw CLOCK (Ten past eleven) (3 points) [ ] Contour [ ] Numbers [ ] Hands	__/5
NAMING	 [ ]  [ ]  [ ]	__/3

MEMORY	Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	No points
		1st trial						
		2nd trial						

ATTENTION	Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4 Subject has to repeat them in the backward order [ ] 7 4 2	__/2
	Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] FBACMNAAJKLBAFAKDEAAAJAMOFAAB	__/1
	Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65 4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**	__/3
LANGUAGE	Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]	__/2
	Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)	__/1
ABSTRACTION	Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler	__/2

DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	__/5
Optional	Category cue							
	Multiple choice cue							

ORIENTATION	[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City	__/6

Normal ≥ 26 / 30 TOTAL __/30
Add 1 point if ≤ 12 yr edu

Appendix C: Case Report Form for Socio-Demographic and Clinical Characteristics

Office Use Only
ID Number: ________ **RAs Initials:** _________
Administration Date: _____________ **Data Entry Date:** ______________
MM/DD/YYYY **MM/DD/YYYY**

SOCIODEMOGRAPHIC CHARACTERISTICS			
1. Sex			
	Male		Female
2. Age in years: _______________			
3. Highest level of education			
	High school or equivalent		Post-secondary education (college diploma or university degree)
4. Independence			
	Independent (e.g., buying groceries, preparing meals, cleaning home, laundry, managing finances)		Requires family or caregiver assistance for instrumental activities of daily living
5. Employment status			
	Employed		Unemployed or retired
6. First language learned			
	English		Non-English

CLINICAL CHARACTERISTICS			
7. Procedure history			
	CABG (with or without previous PCI)		PCI (without previous CABG)
8. Left ventricular ejection fraction (%): __________________			
9. Lifetime smoking history in years: _____________________			
10. History of hypertension			
	Yes		No
11. Diabetes mellitus			
	Yes		No

12. Congestive heart failure			
	Yes		No
13. Obesity (Body mass index > 30)			
	Yes		No
14. Dyslipidemia			
	Yes		No
15. History of acute myocardial infarction			
	Yes		No
16. Peripheral vascular disease			
	Yes		No
17. History of atrial fibrillation			
	Yes		No
18. Chronic obstructive pulmonary disease			
	Yes		No
19. Connective tissue disease (e.g., arthritis, lupus) – Specify: ________________________			
	Yes		No
20. Peptic ulcer disease			
	Yes		No
21. Liver disease (e.g., cirrhosis, hepatitis) – Specify: _______________________________			
	Yes		No
22. History of cancer – Specify: _______________________________			
	Yes		No
23. Other comorbid conditions			

24. Total number of comorbid conditions		
25. HADS Scoring		
HADS-A: ____________/21	HADS-D: ____________/21	HADS-Total: __________/42
26. MoCA Scoring		
VE: _______________/5	Naming: _______________/3	Delayed Recall: _________/5
Attention: ____________/6	Language: ____________/3	Abstraction: ____________/2
Orientation: ___________/6		

Appendix D: Hospital Anxiety and Depression Scale (HADS)

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) ___________ Anxiety (A) ______________
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Appendix E: Age-Adjusted Charlson Comorbidity Index (ACCI) Scoring

Condition	Variable Name	Points	Notes
Myocardial infarction	MI	1	
Congestive heart failure	CHF	1	
Peripheral vascular disease or bypass	PVD	1	
Cerebrovascular disease or transient ischemic disease	CVA	1	CVA only
Hemiplegia	PLEGIA	2	If hemiplegia, do not count CVA separately
Pulmonary disease/ asthma	COPD	1	
Diabetes	DM	1	DM only
Diabetes with end organ damage	DMENDORGAN	2	If end organ damage, do not count DM separately
Renal disease	RENAL	2	
Mild liver disease	MILDLIVER	2	
Severe liver disease	SEVERELIVER	3	
Gastric or peptic ulcer	ULCER	1	
Cancer (lymphoma, leukemia, solid tumor)	CANCER	2	Non-metastatic cancer only
Metastatic solid tumor	METASTASES	6	If Metastatic, do not count cancer separately
Dementia or Alzheimer’s	DEMENTIA	1	
Rheumatic or connective tissue disease	RHEUMATIC	1	
HIV or AIDS	HIV	6	
Hypertension	HBP	1	
Skin ulcers/ cellulitis	SKIN ULCER	2	
Depression	DEPRESSION	1	
Warfarin	WARFARIN	1	

Age is adjusted by calculating each decade after 40 years of age as one point. For example, 1 point is added for age 50-59, 2 points are added for age 60-69, 3 points are added for age 70-79, etc.

Appendix F: Letter of Information and Consent Form

LETTER OF INFORMATION / CONSENT

Cognitive Deficits in Cardiac Rehabilitation

Investigators:

Local Principal Investigator:
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What am I trying to discover?

You have been invited to take part in my Master's thesis study because you are attending the cardiac rehab program at the Hamilton General and have had either a bypass or stent procedure. In this study, I want to compare the cognitive function of people who have had bypass with people who have had a stent procedure. I am hoping to learn about the cognitive problems that people may have when starting cardiac rehab. For example, they may have memory problems or trouble concentrating. They may find it difficult to keep up with activities in cardiac rehab, such as making lifestyle changes, remembering appointments, and taking medications. We know that some people in cardiac rehab may have cognitive problems, but we do not know the extent of the cognitive problems. We also hope to find out if these problems in cognitive function are only in people after they have bypass surgery.

Before you make your decision, you should learn about your role as a participant. After reading this letter, you will have time to ask questions. If you choose to participate, you will be asked to sign this consent form.

What will happen during the study?

If you choose to join the study, you will be asked to complete a brief test of your cognitive function. This should take about 10 minutes. I will ask you for some general demographic information, like your age and education. I may also ask you short questions about your health. After you complete the cognitive test, I will collect some basic health information about you from your health records at the Hamilton General like your past medical history and previous procedures. The cognitive test and questions should take less than 30 minutes of your time. After completing the cognitive test and answering the questions, you don't need to do anything else for this study.

Are there any risks to doing this study?

The risks involved in participating in this study are minimal. You may feel upset, frustrated or anxious when you complete the cognitive test. You will be asked to answer the questions to the best of your ability. You do not need to answer questions that you do not want to answer or that make you feel uncomfortable. You may stop taking part in the study at any time. If some of your answers suggest that you may have severe cognitive problems, we will ask Dr. McKelvie or the clinical nurse specialist, Karen Boyajian, to talk to you about your answers.

Are there any benefits to doing this study?

The research will not benefit you directly. I hope to learn more about cognitive problems that people may experience after bypass surgery. I hope that what is learned as a result of this study will help us to improve cardiac rehab programs for people who have some cognitive problems.

Do I get paid to join this study?

As a participant, you will not receive any money. However, we will provide you with a parking voucher to cover your hospital parking.

Will my personal information stay private?

Every effort will be made to protect your confidentiality and privacy. No one but myself will know whether you participated unless you choose to tell them. Personal information, such as your name, will be removed from the data and replaced with a number so that your data remains confidential. The information you provide will be kept in a locked cabinet where only I will have access to it. Information kept on a computer will be password protected on a secure hard drive. Once the study has been finished, any personal information will be destroyed. An archive of the data without identifying information will be kept and destroyed in 3 years following the completion of the study.

What if I want to withdraw from the study?

Your participation in this study is voluntary. It is your choice to be part of the study or not. If you decide to be part of the study, you can decide to stop (withdraw) at any time, even after signing the consent form or midway through the study. If you decide to withdraw, there will be no consequences to you. Information provided up to the point where you withdraw will be kept unless you request that it be removed. If you do not want to answer some of the questions, you do not have to, but you can still be in the study. Your decision whether or not to be part of the study will not affect your continuing access to services at the Hamilton General Cardiac Health and Rehabilitation Centre.

What if I have questions about the study?

If you have questions or need more information about the study itself, please contact me at: buim5@mcmaster.ca

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HiREB). The HiREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair of the Hamilton Integrated Research Ethics Board at 905-521-2100 Ext 42013.

CONSENT

I have read the information presented in the information letter about a study being conducted by Matthew Bui of McMaster University. I have had the opportunity to ask questions about my involvement in this study and to receive additional details I requested. I understand that if I agree to participate in this study, I may withdraw from the study at any time. I have been given a signed copy of this form. I agree to participate in the study.

______________________	______________________	____________
Name of Participant (Printed)	Signature	Date

Consent form explained in person by:

______________________	______________________	____________
Name and Role (Printed)	Signature	Date