PREDICTORS OF FIRST AMBULATION DURING HOSPITALIZATION AMONG PATIENTS ADMITTED FOR ACUTE MYOCARDIAL INFARCTION

By

OLGA LUCIA CORTES FERREIRA, RN, MSc

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AUTHOR: Olga Lucía Cortés Ferreira, RN (Universidad Industrial de Santander, Colombia), MSc (McMaster University, Canada).

SUPERVISOR: Maureen Markle-Reid, RN, MScN, PhD

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Abstract

Purpose: To determine the timing of first ambulation during hospitalization among patients admitted for acute myocardial infarction (AMI) and to identify the predictors of first ambulation.

Methods: This retrospective cohort study included 500 AMI patients admitted during 2004 to one of three hospitals that form the Hamilton Health Sciences Corporation in Hamilton, Ontario, Canada. The patients were randomly selected from a total of 1,014 charts from the Hamilton Health Sciences Computerized Health Records (SOVERA). Using a chart abstraction tool, the following data were collected from each patient's chart: demographic information, past medical history, treatment, complications, and patterns of ambulation while in hospital. The primary outcome was first ambulation, defined as the first time patients walked during their hospital stay. Secondary outcomes included heart rate at discharge and mortality during hospitalization. The relationship between patient and care-related factors and the time of first ambulation after AMI was explored through a time to event analysis using Cox regression; the associations were expressed as hazard ratios. The fit for the proportional hazard model was assessed and a stratified proportional hazard model was performed for age.

Results: Of the 500 charts, 60 were excluded. Of the 440 patients who were included in the final analysis, 340 (77.3%) walked during hospitalization. One hundred fifteen (26.1%) walked during the first 48 hours (early walking), 98 (22.3%) walked between 49-96 hours (intermediate walking), and 127 (28.9%)

walked after 96 hours (late walking). A total of 100 patients (22.7%) were categorized as non-walkers. Factors that emerged in the survival analysis that were positively associated with early ambulation after AMI and that proved the proportionality on the assessment of the fit of the model were: having a family history of cardiovascular disease (HR 1.33; 95% CI 1.00, 1.44; p=0.05), receiving thrombolysis (HR 1.47; 95% CI 1.11, 1.49; p=0.007), receiving nitroglycerin (HR 1.51; 95% CI 1.19,1.93; p<0.001), and taking calcium channel blockers (HR 1.58; 95% CI 1.22, 2.05; p<0.001). Factors that were negatively associated with early ambulation after AMI were age >59 years (HR 0.98; 95% CI 0.97, 0.99; p<0.001), having an arrhythmia in-hospital (HR 0.48; 95% CI 0.22, 0.94; p=0.04), taking inotropic drugs (HR 0.72; 95% CI 0.53, 0.98; p<0.001), and undergoing coronary artery bypass surgery (HR 0.51; 95% CI 0.33, 0.78; p=0.002).

Conclusion: There is variability in the timing of first ambulation among patients hospitalized with an AMI. Furthermore, those who walked early were more likely to have a family history of cardiovascular disease, have received thrombolysis, and be taking nitroglycerin or calcium channel blockers. Those least likely to walk early were older (>59 years), were more likely to have had an arrhythmia in-hospital, to be taking inotropic drugs, and to have undergone coronary artery bypass surgery.

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List of Abbreviations

ACC/AHA:	American College of Cardiology/American Heart Association
AMI:	acute myocardial infarction
BPM:	beats per minute
BRS:	baroreflex sensitivity
CABG:	coronary artery bypass graft
CCU:	coronary care unit
CEC:	circulating endothelial cell
CHD:	coronary heart disease
CI:	confidence interval
CICU:	cardiovascular intensive care unit
CIU:	coronary intermediate unit
CRP:	cardiac rehabilitation program
CVD:	cardiovascular disease
DBP:	diastolic blood pressure
EA:	early ambulation
ECG:	electrocardiogram
EMR:	electronic medical record
HHSC:	Hamilton Health Sciences Corporation
HIU:	heart investigation unit
HR:	heart rate
HRV:	heart rate variability
K:	Kappa statistic

LOS:	length of stay
LV:	left ventricle
LVEDV:	left ventricle end-diastolic volume
LVEF:	left ventricular ejection function
MET:	metabolic unit of energy cost or expended energy
MI:	myocardial infarction
NSTEMI:	non-ST elevation MI
PCI:	percutaneous coronary intervention
PCWP:	pulmonary capillary wedge pressure
PUMP:	Progressive Upright Mobilization Program
SBP:	systolic blood pressure
SD:	standard deviation
SDNN:	heart rate variability: mean 24 RR hour standard deviation
STEMI:	ST elevation MI
SV:	stroke volume

CHAPTER ONE

INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death worldwide accounting for 34% of total deaths (Leal, Luengo-Fernandez, Gray, Petersen & Rayner, 2006). Nearly 3.8 million men and 3.4 million women worldwide die each year from CHD. It is the main cause of years of life lost from early death in Europe. Furthermore, the cost of CHD is estimated to be $260 billion annually in Canada, 62% of which is attributed to health care expenditures and 21% to productivity losses (Leal et al., 2006).

About 60,000 patients with acute myocardial infarction (AMI) are admitted to hospital each year in Canada, with this number projected to rise with the aging population (Statistics Canada, 2005). About 95% of patients have uncomplicated AMI (Killip I-II) while the remaining 5% develop complications such as pulmonary edema or cardiogenic shock, sometimes requiring interventions such as mechanical ventilation (Berger et al., 2008; DeGeare, Boura, Grines, O'Neill & Grines, 2001; Kaul et al., 2004; Khot et al., 2003). There is a trend toward discharging patients with uncomplicated AMI early, defined by Kaul et al. (2004) as within four days of admission. However, while approximately 80% of AMI patients are eligible for early discharge, Kaul et al. (2004) found, in an international comparison, that less than 40% of patients eligible for early discharge were actually discharged early. They estimated the number of

potentially unnecessary hospital days to range between 65 (in New Zealand) to 839 (in Germany) per 100 patients admitted. Laarman and Dirksen (2009) reviewed trials evaluating early discharge after percutaneous coronary intervention (PCI) for AMI patients and suggested that in low-risk patients, discharge within 48 hours might be feasible and safe. The disadvantage of early discharge is the lack of opportunity to provide extended cardiac monitoring, early ambulation training, and to initiate cardiac rehabilitation (Kaul et al., 2004).

Since 1995, participation in a cardiac rehabilitation program (CRP) has been recommended in clinical practice guidelines from the U.S. Department of Health and Human Services, Agency for Health Care Policy and Research (AHCPR) and the National Heart, Lung, and Blood Institute. This has been characterized as an important component of the care of patients with cardiovascular disease to reduce mortality (Wenger et al., 1995). A CRP is a comprehensive program involving a medical evaluation, prescriptive exercise, cardiac risk modification, education counseling and behavioural interventions. Such programs were designed to initiate secondary prevention while AMI patients were still in hospital (phase I rehabilitation) (Thomas et al., 2007). Secondary prevention activities focus on early identification and prompt treatment of risk factors before they lead to another cardiovascular or cerebrovascular event. Hence, the goals of a CRP focus on limiting the adverse physiological and psychological effects of cardiac illness, reducing the risk of sudden death or re-infarction, controlling cardiac symptoms, stabilizing or reversing progression of

the atherosclerotic process, and enhancing the patient's psychological and vocational status (Thomas et al., 2007; Wenger, 2008).

Early and progressive ambulation during hospitalization is a major component of phase I of a CRP that is provided during the critical period after an AMI (Wenger, 1996; Wenger et al., 1995; Wenger, 2008). The ambulation program involves low intensity activities in the range of 1 to 2 METs (metabolic unit for energy cost, 1 MET = 3.5 ml O_2 consumed/kg body wt/min) in the coronary care unit (CCU) and 2 to 4 METs on the hospital ward (similar to the daily activities patients will resume early after discharge). A mobilization program usually begins with self-care activities such as bed-bathing, use of the bedside commode, sitting, and beginning walking steps (Wenger, 2008). This intervention is supervised by the unit nursing staff but sometimes involves a specialized rehabilitation team. The goal is to condition the patient for the exertional demands required after discharge and to link phase I activities and outcomes with the other rehabilitation phases (Cardiac Care Network of Ontario, 1999).

Although ambulation is a component of a phase I CRP, there are no specific guidelines about the optimal timing or intensity of in-hospital ambulation after an AMI. Although general guidelines for the care of patients with ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI) briefly mention the length of bed rest, these recommendations are not evidence-based (Anderson et al., 2007; Antman et al., 2008). While bed rest continues to be prescribed for some patients, nurses are often expected to implement a Phase I CRP that comprises

education, counseling, progressive mobilization and ambulation aimed at physically and mentally preparing patients to resume activities of daily living (Cardiac Care Network of Ontario, 1999; Carlsson, Lindberg, Westin & Israelsson,1997; Dusseldorp, van Elderen, Maes, Meulman & Kraaij, 1999; Johnston, Foulkes, Johnston, Pollard & Gudmundsdottir,1999; Scully, Vimr, Jutte & Thompson, 2000).

Progressive mobilization toward ambulation and the beginning of physical activity help to avoid physical disability by re-training the patient to orthostatic changes and exercising the skeletal muscle system. Physical activity may also be of benefit by promoting well being, preventing de-conditioning and preparing for return to normal life (Ades & Coello, 2000; Braun & Holm, 1989).

An added barrier to implementing a Phase I CRP is the reduced length of hospital stay for patients with AMI (Kaul et al., 2004). Although length of stay (LOS) in hospital for these patients varies worldwide from 4 to 21 days, practice guidelines for the management of patients with uncomplicated AMI patients recommend a LOS of 4 to 6 days (Anderson et al., 2007; Antman et al., 2008). Consequently, early ambulation (EA) is very important.

This thesis focuses on mobilization of the patient hospitalized with an AMI and will examine timing of first ambulation, predictors of ambulation, and the association between the initiation of ambulation and heart rate at discharge as well as in-hospital mortality. To date, there is limited information in this area.

Study Objectives

a) To describe the timing of first ambulation among patients admitted for AMI.

b) To identify patient and care-related factors that determines initiation of ambulation among patients with AMI.

c) To determine the association between initiation of ambulation and heart rate at discharge in patients with AMI.

d) To determine the association between initiation of ambulation and in-hospital mortality in patients with AMI.

Relevance of Study Objectives

The findings of this study will be important for health providers to predict functional recovery during the critical phase after an AMI, particularly from the point of view of optimizing specific interventions and available resources. Determining the time of first ambulation after an AMI makes it possible to calculate the time elapsed between time of admission with an AMI and the beginning of the first phase of rehabilitation.

The identification of predictors of first ambulation helps health care providers predict which patients are more likely to ambulate earlier or later after an AMI. This information will also assist in the identification of patients who might benefit from EA programs, considering their health status and preferences. This study will also identify the characteristics of those patients who do not ambulate early and could benefit most from targeted interventions to encourage EA. The exploration of associations between initiation of ambulation, heart rate at

discharge and in-hospital mortality will provide information regarding the safety of ambulation after an AMI.

By understanding which patients are likely to ambulate earlier and the influence of EA on heart rate and mortality, nurses and other members of the health care team will be in a better position to identify those patients most suited for early discharge, those who may need more time to initiate ambulation, those who may need assistance with ambulation during hospitalization and at home post-discharge, and those who may require prevention strategies for complications related to immobility.

Comprehensive CRPs have become a standard of care in the secondary prevention of AMI (Cardiac Care Network of Ontario, 1999). The Cardiac Care Network of Ontario, an evidence-based consensus panel on cardiac rehabilitation, identifies three types of settings for rehabilitation services: inpatient settings (formerly phase I); outpatient settings (hospital or community-based providers; known formerly as phases II and III with programs lasting for 3 to 6 months); and maintenance settings (offering long-term outpatient services, known as phase IV) (Cardiac Care Network of Ontario, 1999). Systematic reviews of randomized controlled trials show that comprehensive outpatient CRPs can reduce mortality of post AMI patients by up to 20% (Jolliffe et al., 2001; O'Connor et al., 1989; Oldridge, Guyatt, Fischer & Rimm, 1988).

The first phase of cardiac rehabilitation occurs during hospitalization through a comprehensive approach that includes education, counseling,

progressive ambulation toward physical training and orthostatic adaptation before hospital discharge and referral to an outpatient CRP (Antman et al., 2005; Cardiac Care Network of Ontario, 1999). However, little attention has been paid to the timing of initiation of ambulation during hospitalization and its impact on patient outcomes (Mark & Newby, 2003).

The specific aim of the first phase of rehabilitation is to condition the patient for the exertional demands that will be required for gradually increasing the level of activity after discharge. Although patient activities of daily living (ADL) that will be assumed in the home environment can be up to 7 METs, those activities that are carried out in the hospital environment are currently below the 3 to 4 MET level (Lakusic, Mahovic, Cerovec, Baborski & Majsec, 2005). These in-hospital activities of daily living include: dressing (2 METs), eating (1-2 METs), sitting (1-2 METs), showering (3-4 METs), lying awake (1-2 METs), hygiene (sitting) that includes shaving and brushing teeth (1-2 METs), and hygiene (standing) (2-3 METs). Following discharge from hospital, patients should be prepared for activities such as sexual intercourse (3-5 METs), walking 1 mile per hour (mph) (1-2 METs), walking more than 2 mph (2-4 METs), and climbing stairs (4-7 METs) (Lakusic et al., 2005).

Phase I rehabilitation begins in the CCU with activities that require fewer than 2 METS such as bed-bathing, sitting in a chair, and passive and active range of motion. These activities, as well as walking, are supervised by nurses or rehabilitation staff. Progressive ambulation, beginning with EA, is a decision

nurses are required to make in collaboration with the primary physician, based on the progress and assessment of the patient during the critical phase of their care (Smith, 2002; Stone et al., 2001; Swabey, Suskin, Arthur & Ross, 2004). However, there is no evidence about who (i.e., complicated or uncomplicated patient), when (before 12 or after 24 hours) and how (short walk, long walk) to best ambulate patients after their AMI.

The EA patterns of in-hospital patients with AMI are unknown and given the recent emphasis on early hospital discharge, may not even occur until the patient is at home or during phase II rehabilitation. Early discharge does not ensure a patient's physical training for tolerance of an orthostatic position, training ambulation to allow independence in activities of daily living, or training for more prolonged physical activity (Mark & Newby, 2003). The challenge for health care providers is to determine how to best prepare patients before discharge for an outpatient CRP, an intervention that improves patient outcomes and quality of life after hospital discharge (Gordon et al., 2004).

Content of Thesis

This thesis describes a retrospective cohort study designed to address the objectives listed above. Data were extracted from medical records of all patients with an AMI admitted to a CCU (or general intensive care unit) between January 1st and December 31st, 2004 in three hospitals in Hamilton, Ontario, Canada.

This thesis will include a summary of the current state of knowledge related to mobilization of the patient hospitalized with an AMI (Chapter 2), an outline of the methods used to conduct this study (Chapter 3), a description of the study findings (Chapter 4), and finally, a discussion chapter in which the study findings are interpreted, the strengths and limitations of the study are described, and the implications of the study findings for nursing practice are outlined (Chapter 5).

CHAPTER TWO

REVIEW OF THE LITERATURE

The literature related to in-hospital ambulation of patients who have had an AMI will be summarized under the following headings: (a) the physical and psychological effects of bed rest and restricted physical activity, (b) EA of hospitalized patients, (c) EA of hospitalized AMI patients, (d) timing of ambulation for hospitalized AMI patients, (e) factors associated with EA of hospitalized AMI patients, and (f) outcomes associated with EA of hospitalized AMI patients.

To identify relevant literature, I conducted searches of electronic bibliographic databases including CINAHL, Medline, and EMBASE back to 1966 and regularly updated the search throughout the conduct of this research project. I looked for narrative and systematic reviews, meta-analyses, and single studies that addressed the topics identified above (restricted to experimental and observational studies where appropriate). Keywords focused on the definition and description of EA; EA and bed rest as interventions for hospitalized patients and specifically those with AMI; AMI and in-hospital care and nursing care or caring; bed rest complications; risk classification after AMI; EA as a nursing intervention; cardiac rehabilitation in hospital, phase I CRPs, and outcomes related to CRPs; patterns of EA including types of activities, timing frequency and intensity; and factors determining EA.

Furthermore, I searched for studies in which the experimental intervention was EA, defined as programmed changes in position from bed to chair, bed to standing, or bed to walking added to conventional care while in hospital. The outcomes including risks and benefits of EA were explored including impact on heart rate and mortality. Eligible studies had to compare EA with prescribed bed rest or conventional care alone. I included experimental studies reported in the English language, allocating (at random or not) participants to EA or a control intervention. I also searched for systematic reviews reporting evidence about the effects of mobilization programs on cardiac patients or patients with other conditions.

Studies on the effectiveness of EA were identified by searching Medline (1966-2009), CINAHL Online (1966-2009), HealthStar (1975-2009), EMBASE (1966-2009), and the Cochrane Library Central Register of Controlled Trials (1980-2009). The search terms were myocardial infarction, ischaemic/ischemic heart disease, coronary disease, and medical procedures combined with ambulation, early ambulation, rehabilitation and bed rest in the title or abstract. The outcome was any beneficial or harmful event related to EA and to bed rest including mortality during hospitalization or after hospital discharge.

I also reviewed all existing clinical practice guidelines focused on the care of AMI patients, exploring terms such as bed rest, EA, progressive mobilization, or phase I CRP during hospitalization. When provided, the guidelines were carefully scrutinized for the quality of the evidence substantiating the

recommendations related to ambulation or bed rest after AMI or phase 1 CRPs. Fletcher & Fletcher (2005a) defined good, fair and poor quality evidence for studies evaluating the impact of an intervention or a risk on a given outcome. Good quality evidence is based on well designed, well conducted studies that yield consistent results in representative populations that directly assess effects on health outcomes. Fair quality evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect effect on health outcomes. Poor quality evidence is insufficient to assess the effects on health outcomes because of the limited number or power of studies, important flaws in their designs, gaps in the chain of evidence, or lack of information on important health outcomes (Fletcher & Fletcher, 2005a).

Physical and Psychological Effects of Bed Rest and Restricted Physical Activity

Information about the deleterious effects of prolonged bed rest changed practice in the 1930s and patients were no longer immobilized for up to several months (Mallory, White & Salcedo-Salgar, 1939). This knowledge stimulated research to compare the consequences of bed rest versus EA on the physiology of healthy people (Brieger, 1983). Most of these advances in knowledge related to bed rest complications were supported by research conducted by the National

Aeronautics and Space Administration (NASA) on astronauts in space. This research was designed to identify the cardiovascular changes in spaceflight and the way to modulate them. (Greenleaf, Brock, Sciaraffa, Polese & Elizondo, 1985; Greenleaf et al., 1988; Pavy-Le, Heer, Narici, Rittweger & Vernikos, 2007). Spaceflight was considered similar to bed rest or head-down bed rest in that the human body has to work without gravitational forces implicating physiological changes and adaptations of the cardiovascular system (Levine, Zuckerman & Pawelczyk, 1997).

Physiological implications of prolonged bed rest and the hemodynamic effects of postural changes in patients after prolonged bed rest may play a role in increasing secondary complications affecting the prompt recovery of patients (Saltin, Blomqvist, Mitchell, Johnson, Wildenthal & Chapman,1968). Complications of prolonged bed rest include cardiovascular atrophy and alteration of body fluid regulation leading to complications such as disrupted pulmonary regulation and endothelial dysfunction of the microcirculatory system. Prolonged bed rest can also lead to anemia and other metabolic disorders (Pavy-Le, Heer, Narici, Rittweger & Vernikos, 2007). The following section focuses on the physical and psychological effects of bed rest including its effects on body fluid regulation and cardiovascular changes, endothelial function, pulmonary function, anemia, metabolism, and psychological function. Some of the physiological processes described below occur fairly soon after the initiation of bed rest and some occur only with prolonged bed rest. Most AMI patients are not

on prolonged bed rest and therefore are not likely to develop all the complications described below; however, the following description provides general background for readers to understand the complexity of the associated physical and psychological mechanisms.

Body Fluid Regulation and Cardiovascular Changes

Distribution of pressure and volume in the cardiovascular system depends on gravitational and hydrostatic gradients which determine the body distribution of pressure and volume. Changes occur when these gradients are altered (removed or minimized) during bed rest (Levine, Zuckerman & Pawelczyk, 1997; Pavy-Le et al., 2007). Reductions in plasma volume may be related to changes in cardiovascular remodeling or changes in cardiac baroreflex after bed rest (Pavy-Le et al., 2007).

Cardiac atrophy

Levine et al. (1997) note that cardiovascular adaptation to bed rest leads to orthostatic intolerance characterized by an excessive fall in stroke volume (SV) in the upright position. They explain that with bed rest, a condition similar to spaceflight (except for weightlessness), a central fluid shift occurs leading to a neurohumorally mediated reduction in blood and plasma volume (observed during the first 24 to 48 hours of exposure). When an individual who has been on bed rest for 48 hours assumes a standing position, the gravitational forces from head-to-foot may lead to orthostatic intolerance (Levine, Zuckerman &

Pawelczyk, 1997). As a consequence, the upright SV is reduced, heart rate is increased, but with a variable ability to increase vascular resistance. Furthermore Levine et al. (1997) hypothesized that bed rest leads to a reduction in left ventricle (LV) volume and therefore a shift on the LV pressure-volume relationship further reducing SV and cardiac output. The decreased maximal SV and cardiac output can have a negative impact on the maximum oxygen uptake (VO2) (Levine et al., 1997).

Levine and colleagues (1997) set out to explain the cardiac mechanisms that cause the excessive fall in SV and orthostatic intolerance associated with bed rest. They measured pulmonary capillary wedge pressure (PCWP), SV, left ventricular end-diastolic volume (LVEDV), and left ventricular mass before and after 2 weeks of complete bed rest in 11 healthy men and 1 healthy woman with a mean age of 24+/-5 years. Bed rest led to a reduction in the following outcomes ($p<0.05$): plasma volume (17%), baseline PCWP (18%), SV (12%), LVEDV (16%), orthostatic tolerance (24%) and to a non-significant reduction in cardiac mass (5%). They concluded that bed rest led to a smaller, less distensible LV and along with a reduction in cardiac size, led to a greater decrease in SV at any given level of orthostatic stress, leading to orthostatic intolerance (Levine, Zuckerman & Pawelczyk, 1997).

The theory of cardiac atrophy induced by bed rest was also explored by Dorfman et al. (2007) who randomly assigned 24 healthy young women (32.1 +/- 4 years in age) to sedentary bed rest, exercise training, or protein

supplementation for 60 days. Measurements performed before and after the interventions included LV and right ventricular (RV) mass and volumes. After sedentary bed rest without nutritional supplementation, there were significant reductions in LV volume (96±26 to 77±25ml; p=0.03), RV volume (104±33 to 86±25ml; p=0.02), LV mass (2.2±0.2 to 2.0±0.2 g/kg, p=0.003), and RV mass (0.8±0.1 to 0.6±0.1 g/kg, p<0.001). The authors concluded that the rate of cardiac atrophy in women is similar to men following 60 days of bed rest. They also suggested that this myocardial atrophy likely contributes to the reduction in cardiac filling and the substantial drop in upright SV observed after bed rest. The drop in SV may also be explained by plasma reduction, a reduced central venous pressure, and higher venous compliance in the lower extremities (Levine et al., 1997).

Plasma volume

Levine and colleagues (1997) found a reduction in plasma from 3.16±0.45 L to 2.62± 0.43 L after bed rest. This is likely associated with reduced circulation and cardiovascular deconditioning with a reduction of extracellular volume (ECV) that could be observed after two days of bed rest (Fortney, Hyatt, Davis & Vogel, 1991; Greenleaf, Bernauer, Young, Morse, Stanley, et al., 1977; Hinghofer-Szalkay, Laszlo, Jezova, Rossler, Haditsch, et al., 2002). The mechanism of plasma reduction during bed rest may involve other changes such as an isocontent loss from the plasma of protein, albumin, globulin, urea, creatinine, sodium, chloride, osmolarity and glucose (Greenleaf, Bernauer, Young, Morse,

Stanley, et al., 1977). The body preserves extracellular volume at the expense of maintaining plasma volume (Greenleaf, et al., 1977). The unchanged total body fluid volume despite the reduction of ECV during bed rest may be explained by a fluid shift from extra- to intracellular compartments (Hinghofer-Szalkay, Laszlo, Jezova, Rossler, Haditsch, et al., 2002). This shift in volume occurs from the lower to the upper body, producing a compensatory redistribution of volume. The shift of intravascular fluid away from the extremities to the thoracic cavity is caused by the removal of gravitational stress (Hinghofer-Szalkay, Laszlo, Jezova, Rossler, Haditsch, et al., 2002).

Another mechanism that can explain the reduction of plasma volume is stimulation of diuresis and natriuresis (Pavy-Le et al., 2007). The effects of volume reduction derived from increased diuresis and natriuresis have repercussions such as orthostatic intolerance, reduced exercise capacity, and a decrease in body weight of 2% secondary to a loss of fluid derived from the extravascular and intravascular space (Pavy-Le et al., 2007). Furthermore, the volume shift is regulated by hormones. One of the regulations is mediated by the atrial natriuretic peptide (ANP) and plasma renin activity (PRA). After 24 hours, in response to the decrease in plasma volume, the PRA increases and remains high stimulating angiotensin without changes in aldosterone secretion (Pavy-Le et al., 2007). Additionally, at the beginning of this adaptation there is an increase in sodium (Na) excretion and return to baseline after 2-3 days (Pavy-Le et al., 2007).

Cardiovascular deconditioning

Cardiovascular deconditioning may be explained by an autonomic dysfunction with prolonged bed rest (Convertino et al., 1981; Convertino, 2003; Hung, Goldwater, Convertino, McKillop, Goris & DeBusk, 1983). The baroreflex system involves baroreceptors, the autonomic nervous system, heart rate and vessels. Baroreflex normally refers to the changes in R-R interval triggered by changes in systolic blood pressure that stimulate mechanoreceptors in the vessels (e.g., tachycardia after an acute drop in systolic blood pressure via increased sympathetic activity) (Convertino, 2003). After bed rest there is an attenuation of the carotid baroreflex during orthostasis (Convertino, 2003). The dysfunction can be measured through baroreflex sensitivity (the change in R-R interval in milliseconds for each mm of Hg in systolic blood pressure). In their study of 12 young, healthy subjects exposed to 2 weeks of bed rest, Levine et al. (1997) found no significant change in HR (74±13 to 75±7 bpm) or MAP (from 86±6 to 90±7 mmHg) after an orthostatic challenge. This finding is in contrast with a significant reduction in plasma volume, SV and total peripheral resistance ($p<0.05$ in all cases).

Although autonomic dysfunction is evident during the upright position with a low response baroreflex and greater orthostatic hypotension, this mechanism has been more controversial. Some mechanisms have been hypothesized as the cause for this autonomic dysfunction. The imbalance between the sympathetic and parasympathetic system may be explained by a decrease of the vagal

control of the heart or may be caused by hypovolemia (Iwasaki, Zhang, Perhonen, Zuckerman, Levine, 2004; Pavy-Le et al., 2007). In a study of six healthy patients, Iwasaki and colleagues (2004) measured heart rate by ECG, blood pressure, and plasma volume before and after two weeks of bed rest intervention. After bed rest, their plasma volume was restored with an infusion of dextran 40 (288± 31 ml). There was a significant normalization of the reduction of the transfer function gain (BP to R-R interval) used as an index of arterial-cardiac baroreflex sensitivity of 12.2± 3.6 ms/mmHg after volume restoration. The authors concluded that plasma volume reductions, rather than autonomic nervous system adaptation to bed rest, are responsible for the changes in arterial and cardiac baroreflex function after bed rest (Iwasaki, Zhang, Perhonen, Zuckerman, Levine, 2004).

Endothelial Function

Prolonged physical inactivity induced by bed rest causes endothelial dysfunction at the microcirculatory level (Demiot et al., 2007). This dysfunction is characterized by an increase of circulating endothelial cells (CECs), which is considered to be one index of endothelial damage (Demiot et al., 2007). Based on a study by Demiot et al. (2007), the alteration of endothelium is dependent on vasodilation of the microcirculation after two months of bed rest. This study also demonstrated a correlation between intima media thickness at the carotid level and physical activity. They investigated endothelial properties before and after 56

days of bed rest in eight healthy women who performed no exercise compared with eight subjects who performed treadmill exercise in a lower body negative pressure chamber and resistance exercise. The results showed a reduction in endothelium-dependent vasodilation in patients on bed rest (35.4% ± 4.8% vs 24.1% ± 3.8%, $p<0.05$) compared to those exposed to exercise. They also demonstrated a significant increase in the number of CECs (3.6 ± 1.4 vs 10.6 ± 2.7 ml^{-1}, $p<0.05$). Demiot et al. (2007) concluded that prolonged bed rest causes impairment of endothelium-dependent function at the microcirculatory level as well as an increase in circulating endothelial cells.

Pulmonary Function

Alteration in pulmonary function and of aerobic capacity is another complication secondary to bed rest. When moving to a supine position after bed rest, individuals experience decreased lung volume and increased airway resistance resulting from increases in intra-thoracic and pulmonary blood volumes and direct compression of airways by blood volume (Pavy-Le et al., 2007). Positive effects include decreased physiological dead space, improved ventilation-perfusion matching and lung diffusion capacity (Pavy-Le et al., 2007). After seven days of bed rest, changes in cardiopulmonary circulation include increased pulmonary arterial pressure, increased preload of left and right heart and increased right myocardial contractility. Congestion of the lungs occurs after

24 hours, after which right myocardial contractility decreases (Pavy-Le et al., 2007).

Beckett et al. (1986) conducted three studies, each with 6 healthy subjects, and assessed pulmonary function (forced vital capacity and total lung capacity measured by helium dilution) before, during and after 11-12 days of bed rest. They found a small significant increase in forced vital capacity and in total lung capacity while residual volume and functional residual capacity of the respiratory system did not change.

Anemia

Anemia secondary to immobilization is a complication that has been less explored. However, in some populations who are immobilized, such as patients with spinal cord injury, older adults, or patients with immobility secondary to obesity or prolonged bed rest (Ferretti et al., 1997; Penninx et al., 2004; Uebelhart, Miaux-Domenech, Roth & Chantraine, 1995), there is an association between disability, low physical performance and poor muscle strength with anemia. In those who are immobilized, an accumulation of fat in the bone marrow has been found (Payne, Uhthoff & Trudel, 2007). The adipocyte accumulation in the bone marrow both passively and actively impairs erythropoiesis leading to anemia secondary to immobility. Immobility induces adipocyte accumulation and in this way interferes with hematopoiesis by reducing the hematopoietic volume (Payne, Uhthoff & Trudel, 2007). Another explanation is that osteoblasts and

associated cytokines support hematopoietic stem cell proliferation and regulate hematopoiesis in vitro. Conversely, adipocytes in the bone marrow microenvironment inhibit hematopoiesis through adipokines by leptin and tumor necrosis factor-alpha and possibly inflammatory cytokines (Payne, Uhthoff & Trudel, 2007).

In their review of bed rest studies, Pavy-Le et al. (2007) reported an increase in abnormal erythrocytes, blood viscosity, hematocrit, fibrinogen, and red blood cell aggregation index. After nine days of bed rest, reduced cell deformation, reduced plasma viscosity and enhanced red cell aggregation were reported. After two weeks of bed rest, there was a transient decrease in erythrocyte metabolic activity. After 120 days of bed rest, there were reported shifts in the metabolic and structural parameters of erythrocytes leading to degradation of the functional state of erythrocytes such as changes in deformability and echinocytosis (Pavy-Le et al., 2007). Hemoglobin can drop by 9% after 42 days of bed rest in healthy people (Ferretti et al., 1997).

Metabolism

During bed rest, immobilization causes changes in energy requirements, protein metabolism, insulin resistance, calcium metabolism, metabolism of vitamins and minerals, and changes in the humoral regulating mechanisms (Pavy-Le et al., 2007). Energy requirement are reduced. Although metabolic alterations have been less explored, there is some evidence that these changes

during bed rest may begin after 3 to 7 days (Ferrando, Paddon-Jones & Wolfe, 2006). Alterations are more evident in long term in-hospital patients such as those who are critically ill in the intensive care unit (ICU) requiring mechanical ventilation (Ferrando, Stuart, Sheffield-Moore & Wolfe, 1999). Under special conditions in which there is a combination of bed rest (inactivity) and stress (critical illness), hypercortisolemia promotes muscle catabolism resulting in atrophy and impaired muscle protein synthesis (Paddon-Jones, Wolfe & Ferrando, 2005).

Over time, reduced physical activity leads to a loss of muscle mass and strength. Fatigue of the muscles and abnormal reflex patterns described by Pavy-Le et al. (2007) are attributed to significant atrophy observed in the early weeks of bed rest. Skeletal muscles during bed rest suffer alterations such as decreased maximal torque for ankle extensor (9%), decreased knee extensor (16%), and muscular atrophy (10%) (Ferrando et al., 1995).

The loss of muscle tissue generates a negative protein balance that can be measured by negative nitrogen balance and loss of fluid electrolytes. The loss of muscle mass with bed rest occurs during the first 7-14 days and is explained by a reduction in protein synthesis rather than an increase in protein breakdown (Biolo et al., 2004; Paddon-Jones, Wolfe & Ferrando, 2005; Stuart, Shangraw, Peters & Wolfe, 1990). For this reason, dietary recommendations include supplementing essential amino acids (Biolo et al., 2004). Patients who are restricted to bed rest require a proper diet in order to prevent loss of protein and

ultimately, loss of muscle strength and to avoid muscular deconditioning (Biolo et al., 2004).

Another metabolic alteration relates to insulin metabolism. Insulin's principal function is the regulation of energy storage and release. This hormone promotes energy for many metabolic processes through stimulation of glycogen synthesis, aerobic glycolysis, and protein and fatty acid synthesis in the liver (Pavy-Le et al., 2007). Further, insulin inhibits catabolic processes including glycogenolytic, gluconeogenic, proteolytic and lipolytic processes. Prolonged bed rest creates insulin resistance and low capacity of tissues to use insulin and produce energy as evidenced by increases in blood glucose level after the third day on bed rest (Pavy-Le et al., 2007). With bed rest, there is an increase in the level of C-peptide that is interpreted as a sign of insulin resistance resulting from low muscle activity (Mikines, Dela, Tronier & Galbo, 1989). Given that insulin also regulates protein metabolism, bed rest also affects this process. Insulin resistance produces low muscle protein synthesis during immobilization (Mikines, Dela, Tronier & Galbo, 1989).

Finally, other complications that may determine muscle atrophy and that have not been studied fully are related to calcium metabolism and pro-inflammatory cytokine secretion. Muscle fatigue and abnormal reflex patterns are attributed to significant muscle atrophy and deconditioning observed in the early weeks of bed rest (Dennis et al., 2004). Citokynes may stimulate or suppress inflammation. Pro-inflammatory cytokines like interleukin-1 (IL-1), interleukin-6

(IL-6) and tumor necrosis factor-x trigger the inflammatory mediators and may produce endothelium damage. The suppressor interleukins (IL-4, IL-10, IL-13) slow the cascade or suppress the inflammatory process.

Changes in the metabolism of vitamins and minerals due to bed rest have not been studied in detail. With prolonged bed rest, reductions in 25-hydroxy vitamin (25-OH D-) and 1,25-OH Dihydroxy-vitamin D (1,25-OH D) levels have been identified (Pavy-Le et al., 2007). This reduction is being evidenced by a bone reduction during bed rest that cannot be prevented by calcium dietary supplementation (Dennis et al., 2004; Pavy-Le et al., 2007).

Psychological Function

Research conducted by NASA suggests that bed rest is a form of sensory deprivation (Ishizaki et al., 1997). However, limited research has examined the psychological effects of prolonged bed rest. Ishizaki et al. (2002) evaluated the effect of bed rest on mood status and depressive and neurotic levels in nine young male subjects after 20 days on bed rest. Based on self-report psychometric inventories, depression, neurotic levels and confusion were increased during bed rest ($p<0.001$).

Early Ambulation of Hospitalized Patients

EA is considered a common practice in the care of hospitalized patients, and a practice that includes mobilization activities such as moving in bed, sitting

beside the bed, standing, ambulating on the spot, hallway ambulation and low intensive exercise (Browning, Denehy & Scholes, 2007). Its importance was demonstrated in the 1940s when upright mobilization was shown to reduce pulmonary complications in post-surgical patients (Browning et al., 2007). Furthermore, studies conducted on astronauts by NASA in the 1960s that identified the complications of bed rest and the benefits of EA and exercise made a major contribution to health care delivery (Pavy-Le et al., 2007).

Although existing studies have demonstrated benefits of EA, bed rest continues to be prescribed for medical conditions (Allen, Glasziou & Del Mar, 1999; Butson, 2000). A systematic review by Allen et al. (1999) compared bed rest to EA following medical procedures and for medical conditions. The study included 39 randomized controlled trials comparing ambulation with bed rest. Twenty-four trials were identified in which bed rest was ordered to prevent complications after a medical procedure and 15 trials were identified in which bed rest was part of the treatment regimen. In both groups of trials, outcomes for patients on bed rest were worse than those for patients who had EA. In the 24 trials of prophylactic EA compared with bed rest after a medical procedure, patients on bed rest were more likely to experience problems such as the following: nausea after a lumbar puncture (1 study; OR 0.51, 95%CI 0.28, 0.93), severe headache after spinal anaesthesia (2 studies; one for a urological procedure (OR 0.10, 95%CI 0.01, 0.82) and the second for an obstetric procedure (OR 0.19, 95%CI 0.065, 0.58)), dizziness after radiculography (1

study; OR 0.37, 95%CI 0.15, 0.94), haematoma (1 study; OR 0.33, 95%CI 0.11, 0.96) and back pain after cardiac catheterization (2 studies; OR 0.22, 95%CI 0.12, 0.40 and OR 0.002, 95%CI 0.002, 0.79).

In the 15 trials that evaluated the effectiveness of bed rest compared to EA as a treatment for medical conditions, patients on bed rest were more likely to experience problems such as the following: more disability on day 1 in patients treated for acute low back pain (percentage of difference in disability index 22%, 95%CI 1.5, 43, $p<0.05$), and prolonged recovery time in patients with acute infectious hepatitis (percentage of difference 10%, 95%CI 0.1, 19, $p<0.05$) (Allen et al., 1999).

Women on bed rest during the first stage of labour were more likely to have a longer first stage (6.7 vs 4.1 h, $p<0.001$), more frequent and weaker contractions ($p<0.01$), increased need for analgesia during labour ($p<0.001$), increased likelihood of assisted delivery ($p<0.01$), more fetal heart rate decelerations with contractions ($p<0.005$) and lower Apgar scores at 1 minute and at 5 minutes (7.5 vs 8.8, $p<0.001$; 9.4 vs 9.9, $p<0.05$) respectively (Allen et al., 1999; Flynn, Kelly, Hollins & Lynch, 1978). Overall, patients on bed rest for a prolonged time were more likely to have complications than patients who ambulated early, indicating little efficacy for bed rest as a therapy (Allen et al., 1999).

The benefits of EA when compared with prolonged bed rest have been shown in patients who had spinal anaesthesia. Six trials of spinal anaesthesia

identified between 1988 and 2005 showed a higher incidence of headaches in patients exposed to prolonged bed rest than in patients who were ambulated early (Cook, Davies & Beavis, 1989; Cramer et al., 2005; Fassoulaki, Sarantopoulos & Andreopoulou, 1991; Lindh, Andersson & Westman, 2001; Silvanto, Tarkkila, Makela & Rosenberg, 2004; Thornberry & Thomas, 1988). Patients who had hip replacement surgery who were ambulated early were compared to those who were ambulated later. Those who ambulated early had more favourable outcomes such as reduced length of stay from 8 to 5 days, ability to walk a longer distance, and less assistance required to progress to the next step in rehabilitation (Larsen, Sorensen, Hansen, Thomsen & Soballe, 2008; Oldmeadow et al., 2006).

Patients diagnosed with community acquired pneumonia who ambulated early (20 minutes in the first 24 hours of hospitalization) had shorter lengths of hospital stay than those who walked later (Mundy, Leet, Darst, Schnitzler & Dunagan, 2003). Furthermore, older patients with an acute exacerbation of chronic obstructive pulmonary disease showed a reduction in physical disability when ambulated early using walking aids compared to those ambulated later (Yohannes & Connolly, 2003).

The research studies described above demonstrate the benefits of EA as part of the treatment plan during hospitalization in order to prevent complications and rehospitalization among a general population of hospitalized patients.

Early Ambulation of Hospitalized AMI Patients

Functional decline is commonly observed after AMI. This is defined as a reduction in one's ability to care for oneself after a critical event and can occur during hospitalization. Functional decline after AMI may worsen with a prolonged hospital stay and bed rest that does not include a formal plan for ambulation.

With a focus on shorter hospital stays, there is a risk that some patients with AMI are discharged before they are mobilized and as a result, they do not receive Phase 1 of a CRP (early and progressive in-hospital mobilization). Other patients may have longer hospital stays but may not be mobilized (ambulated) according to the recommendations outlined in the American Heart Association Guidelines (Antman et al., 2008). Perhaps associated with the lack of emphasis on patient ambulation is the low referral rate to Phase II cardiac rehabilitation programs which can contribute to poor health outcomes (Cortés & Arthur, 2006).

In this section, autonomic changes after an AMI will be described followed by a summary of studies evaluating EA of AMI patients.

Autonomic Changes after AMI

After AMI, patients often experience functional decline that is due to alterations in the autonomic nervous system. The understanding of autonomic changes after AMI and autonomic alterations secondary to bed rest should help to inform decision-making regarding when to begin mobilization and what factors may be modified to facilitate this process.

Autonomic function is affected after AMI and is characterized by sympathetic hyperactivity and parasympathetic hypoactivity during the acute and recovery phases. The study of autonomic reflexes might contribute to the identification of high risk subgroups in the post AMI phase.

Autonomic dysfunction is associated with an increased risk of cardiac mortality and cardiac vulnerability that may lead to life-threatening arrhythmias (Kleiger, Miller, Bigger & Moss, 1987; La Rovere, Bigger, Marcus, Mortara & Schwartz, 1998). However, the pathophysiological implications of this dysfunction are still unclear. Studies have also demonstrated a decrease in baroreceptor sensitivity after AMI both in animals and humans. In the first hours after AMI in animal models, there is an attenuation or an activation of neural reflexes that may be explained by a denervation at the zone of infarction (Detollenaere, Duprez, De Buyzere, Vandekerckhove, De Backer & Clement, 1993a; Detollenaere, Duprez, De Buyzere, Vandekerckhove, De Backer & Clement, 1993b). In studies of the autonomic nervous system, the evaluation of heart rate variability (HRV) and baroreflex sensitivity (BRS) as parameters of parasympathetic cardiac control have been used as predictors of mortality after AMI.

Schwartz et al. (1988) showed that infarcted dogs with the lowest BRS were most likely to develop ventricular fibrillation spontaneously. These findings were compatible with multiple experimental studies showing that increased vagal stimulation post-infarction protected animals from ventricular fibrillation (Kleiger et al., 1992; Schwartz & La Rovere, 1998).

Parasympathetic hypoactivity after AMI leads to a relative increase in sympathetic nervous system activity resulting in ventricular vulnerability (La Rovere et al., 1998). Reduced parasympathetic responses are present in about 15% of AMI patients and contribute to arrhythmic death after AMI (La Rovere et al., 1992; La Rovere et al., 1998).

In a cohort study by Kleiger et al. (1987), 808 AMI patients who were less than 70 years of age and had survived the CCU phase were followed up for one year. Measurements of HRV (as a parameter of parasympathetic cardiac control) were made before discharge and at 11 days, 6 months, and 1 year (using a Holter monitor). Of patients with HRV less than 50 milliseconds, 34.4% (43/125) had died by the one-year follow-up (OR=5.3). Of those with HRV 50-100 milliseconds, 13.8% died (OR=1.6), and in those with HRV >100 milliseconds, 9.0% died (OR=1.0). No differences were found between patients receiving and not receiving beta-blockers (Kleiger et al., 1987).

La Rovere et al. (1998) later conducted an international multicentre prospective cohort study to evaluate autonomic response in 1,284 patients with a recent AMI (less than 28 days). HRV and BRS were evaluated during the 16 days after AMI. HRV was evaluated by determining the mean R-R interval 24 hour standard deviation (SDNN). During follow-up of about 21 months, there were 44 cardiac deaths and 5 non-fatal cardiac arrests. The risk of mortality in patients with low HRV (<70ms) was 3.2 (95%CI 1.42 to 7.36) and 2.8 (95%CI 1.24 to 7.36) in patients with low BRS (23 ms/mmHg). In patients with low SDNN or BRS

combined with a left ventricular ejection fraction (LVEF) <35%, the relative risk of mortality was RR 6.7 (95%CI 3.2 to 14.6) compared with patients with LVEF >35% (La Rovere et al., 1998; Maestri, Pinna, Mortara, La Rovere & Tavazzi, 1998).

Some beneficial effects of physical training have been reported to improve autonomic balance. Heart rate recovery after exercise (fall in heart rate during the first minute after exercise), particularly in the earliest stages after AMI, can serve as a simple indicator of parasympathetic activity. After the fourth week of training post AMI, patients recovered HRV (La Rovere et al., 1992; Sandercock et al., 2005). Another measure shown to be indicative of parasympathetic function recovery after exercise is increased BRS (La Rovere et al., 2002). Exercise training after AMI increases survival by modifying the autonomic balance and increasing vagal activity (La Rovere et al., 2002). Additionally, early rehabilitation in post PCI patients after first anterior AMI has resulted in positive clinical effects of reperfusion of the ischemic area (Malfatto, Facchini, Sala, Branzi, Bragato & Leonetti, 2000; Malfatto, Branzi, Bizzi, Valli & Facchini, 2005).

EA of AMI Patients

Overall, evidence supporting EA in the care of patients after AMI is considered weak (fair to poor grade for the overall quality of evidence) (New Zealand Guidelines Group, 2005; Scottish Intercollegiate Guidelines Network, 2002). The first study that specifically focused on EA after AMI was conducted by

Groden, Allison & Shaw (1967). This study failed to demonstrate the benefit of EA when compared with late ambulation. During the 1970s and 1980s, a series of randomized and non-randomized studies suggested that EA reduced the occurrence of death after AMI (Abraham, Sever, Weinstein, Dollberg & Menczel, 1975; Bloch, Maeder, Haissly, Felix & Blackburn, 1974; Ghose, Modak, Ganguli & Bagchi, 1980; Harpur, Conner, Hamilton, Kellett, Galbraith et al.,1971; Hayes, Morris & Hampton, 1974; Hutter, Sidel, Shine & DeSanctis, 1973; Lamers et al., 1973; Messin & Demaret, 1982; Pfisterer, Schweizer & Burkart, 1977; Sivarajan et al., 1981; West & Henderson, 1979). The goal of these studies was to assess the impact of EA on reduction of mortality and re-infarction in uncomplicated AMI. These studies were conducted in CCUs or on hospital medical wards. The mobilization protocols included activities described as any movement out of bed (Hayes et al., 1974), progressive activity (Pfisterer et al., 1977), and sitting in bed or a chair, walking (Abraham et al., 1975; Bloch et al., 1974; Ghose et al., 1980; Harpur et al., 1971; Hutter et al., 1973; Lamers et al., 1973; Sivarajan et al., 1981; West & Henderson, 1979) and climbing stairs (Harpur et al., 1971). Control group activity was defined as being on bed rest or receiving the current intervention (defined as late mobilization).

The effects of EA varied across the studies, most of which had small sample sizes. Timing of initiation of EA varied across studies with some initiating progressive mobilization as early as 0 hours (at admission) (Miller, 1976) and others at 24-48 hours (Bloch et al., 1974) or after 48 hours (Abraham et al., 1975;

Ahlmark, Ahlberg, Saetre, Haglund & Korsgren, 1979; Beckwith, Kernodle, Lehew & Wood, 1954; Harpur et al., 1971; Hutter et al., 1973; Messin & Demaret, 1982; West & Henderson, 1979). In some studies, exercise therapy was initiated while the patient was still in bed and these included arm and leg exercises (Bloch et al., 1974). In other studies, the patient moved from a lying to a sitting position while in bed or moved from the bed to a bedside chair before walking up to half an hour once a day (Harpur et al., 1971) or 1-2 hours twice a day (Abraham et al.,1975; Beckwith et al., 1954; Harpur et al., 1971).

In some studies, the patients walked to the toilet (Harpur et al., 1971), around the bed or ward (Hutter et al., 1973; West & Henderson, 1979; Messin & Demaret, 1982), or walked around freely (Abraham et al., 1975) including stair climbing (Rowe et al., 1989). Walking up one to three flights of stairs twice a day was part of the final training (Rowe et al., 1989) with a duration of 10 to 15 minutes per day. The initiation of discharge planning varied across studies with some beginning as soon as the patient was able to complete the walking activities (Harpur et al., 1971), some on the second to third day after hospitalization (Bloch et al., 1974; Ghose et al., 1980; Hayes et al., 1974; Pfisterer et al., 1977), some on the fourth to seventh day after hospitalization (Abraham et al., 1975; Harpur et al., 1971), and one on the ninth day (Hutter et al., 1973). In the control group, mobilization occurred 12 to 21 days after their AMI.

Although the studies did not find significant differences between the EA and control groups, there was a trend toward decreased mortality with EA. However, some of these studies are no longer relevant to care as it is currently delivered. There have been no recent studies comparing early versus late ambulation during the acute phase after an AMI. Yet, during this time, factors that could influence EA have evolved including early hospital discharge, the emphasis on cardiac rehabilitation, and the introduction of new treatments including thrombolysis, PCI and CABG surgery. This lack of recent evidence may explain the inconsistent behaviours of physicians and nurses regarding the EA of patients hospitalized with AMI.

Timing of Ambulation for Hospitalized AMI Patients

Existing guidelines state that physical activity for people with AMI should begin at low intensity and gradually increase over several weeks (grade C or low quality cohort or case control studies). There are statements that low to moderate intensity exercise training can be undertaken safely and effectively in the hospital setting for low and moderate risk patients (C or low quality; D recommendations based on expert opinion) (Scottish Intercollegiate Guidelines Network, 2002; New Zealand Guidelines Group, 2005; Fletcher & Fletcher, 2005a). Another guideline, based on grade C evidence, states that patients with S-T segment elevation with instability or continued ischemia should be mobilized to a bedside commode 12 to 24 hours after the AMI. Furthermore, it states that patients with AMI who are

free of recurrent ischemic discomfort, symptoms of heart failure, or serious arrhythmia should not be on bed rest for more than 12 to 24 hours. Patients with a low risk of complications may be candidates for early discharge (grade C recommendation) (Antman et al., 2008). For patients with non STEMI, bed rest is recommended when ischemia or arrhythmias are present or when patients have ongoing chest pain (Anderson et al., 2007; Antman et al., 2005). Overall, these guidelines suggest that stable patients with AMI can be mobilized and patients with complications should not be mobilized (Anderson et al., 2007; Antman et al., 2005).

Factors Associated with Early Ambulation of Hospitalized AMI Patients

Little is known about factors associated with early in-hospital ambulation of patients who have had an AMI. Given that in-hospital mobilization protocols are not evidence-based (Ehsani, 1984), nurses likely make decisions about patient ambulation on the basis of patients' personal factors (i.e., age, sex, health assessment), complications during hospitalization (i.e., arrhythmias, new ischemic event), and system-related factors (i.e., physicians´ orders regarding ambulation, early discharge policy). Also, nurses base the decision to ambulate a patient on their own clinical experience (Kneafsey, 2007; Lau-Walker, 2004).

Given that there have been no studies conducted to examine the predictors of EA in hospitalized AMI patients, I describe factors known to influence physical activity in hospitalized medical and critically ill patients and in

AMI patients attending outpatient CRPs. These include factors such as socio-demographic and health-related issues and health care provider recommendations.

Socio-Demographic Factors

Socio-demographic factors such as age and sex have been known to influence physical activity after AMI among patients attending outpatient CRPs. Those who do not attend CRPs are more likely to be older. Sex differences have been observed with females being less active than males (Marchionni, Fattirolli, Fumagalli, Oldridge, Del Lungo, Bonechi et al., 2000). Some studies have identified that less active women are older (> 85 years) and have higher post-AMI depressive mood scores (Jarrell, Hains, Kisilevsky & Brown, 2005; Norrman, Stegmayr, Eriksson, Hedback, Burell & Brulin, 2004). Although 40% of the coronary events occur in women, only 20% of them enter CRPs.

Patients living on their own were less likely to believe that exercise was important for their cardiac recovery and exhibited less confidence in their ability to manage exercise (Lau-Walker, 2004). Although less explored, marital and social support have been identified as important factors for recovery in cardiac illness (Akhtar, Malik & Ahmed, 2004; Rankin, Butzlaff, Carroll & Reedy, 2005).Being married has been shown to increase compliance of men with CRP attendance more than that of women (Akhtar, Malik & Ahmed, 2004; Rankin, Butzlaff, Carroll & Reedy, 2005). Patients with lower income tend to have lower levels of social

support, which has been identified as being negatively associated with involvement in a CRP (Shanks, Moore & Zeller, 2007). Patients who are employed have a more positive outlook and are better able to cope with the exercise regimen as part of their cardiac recovery (Cooper, Lloyd, Weinman & Jackson, 1999; Lau-Walker, 2004; Petrie, Weinman, Sharpe & Buckley, 1996; Wenger, 1996).

Health-Related Factors

Health-related factors are also important for determining initiation of physical activity. Disability one year before experiencing an AMI was associated with lower levels of physical activity, especially in older adults (Mendes de Leon, Bang, Bienias, Glass, Vaccarino & Kasl, 2005). Orthostatic hypotension among hypertensive patients may also influence decision-making about ambulation (Ades et al., 1999; James & Potter, 1999; Matsunaga et al., 2004). Furthermore, the presence of heart-related symptoms such as dyspnea or angina before and after AMI influence exercise activities and ambulation (Maeland & Havik, 1988).

A similar picture occurs with chronic heart failure where dyspnea and fatigue are associated with lower physical activity in cardiac rehabilitation (Clark et al., 1996). Former smokers and sedentary AMI patients are less likely to engage in physical activity (Goble & Worcester, 1992). Depression is present in 10% to 30% of patients after AMI and has been shown to negatively influence exercise and physical activity (Ades et al., 1999). Other health-related barriers to

physical activity among AMI patients are co-existing stroke and silent cardiac ischemia (Gordon et al., 2004). Factors such as postoperative atrial fibrillation and prolonged ventilator support are associated with increased stay in the ICU which could negatively impact EA of cardiac surgery patients (Nickerson et al., 1999). An individual's subjective perception of the severity of their illness is an indirect factor that can also determine when and how frequently they access a CRP (Cooper, Lloyd, Weinman & Jackson, 1999).

Other factors associated with the recovery of ambulatory ability prior to discharge in a general population of hospitalized patients ($\geq$ 55 years) included having normal mental status, not having a urinary catheter, not in restraints, mobilization in bed on admission, and higher physician-rated life expectancy (Brown, Roth, Peel & Allman, 2006).

Referral to CRP by Health Care Providers

Physician referral to a CRP is a very important factor influencing participation. Although 85% of physicians recommend exercise after uncomplicated AMI, only 7% of eligible cardiac patients are actually referred to a CRP. Furthermore, women are referred less often than men despite similarities in clinical condition and improvement in functional capacity (Daly, Sindone, Thompson, Hancock, Chang & Davison, 2002). A higher physician-rated life expectancy for the patient is a positive predictor for exercise prescription (Brown, Roth, Peel & Allman, 2006).

All the factors described above, while not examined in hospitalized AMI patients, may also influence EA of AMI patients during hospitalization. Based on the literature summarized above, factors that may influence EA are age, sex, severity of complications, depression, health care provider recommendations, level of self efficacy and motivation, and an individual's subjective perception of their illness.

Outcomes Associated with Early Ambulation of Hospitalized AMI Patients

Two systematic reviews and meta analyses of studies designed to evaluate the effects of EA have been completed to date and have been published in three papers (Herkner, Thoennissen, Nikfardjam, Koreny, Laggner & Mullner, 2003; Herkner, Arrich, Havel & Müllner, 2007; Cortés, Villar, Devereaux & DiCenso, 2009). Herkner et al. (2003) (2007) in a review of 15 studies from 1960 to 1980, evaluated the effect of short-term versus prolonged bed rest in patients with uncomplicated AMI. There were 120 (9.7%) deaths and 100 (8.5%) re-infarctions among 1233 and 1173 AMI patients on short–term bed rest respectively, compared with 133 (10.5%) deaths and 94 (7.8%) re-infarctions among 1261 and 1199 AMI patients on long-term bed rest respectively (risk ratio for death=0.94, 95%CI 0.75, 1.17 and risk ratio for re-infarction=1.14, 95%CI 0.87, 1.48). In addition, there were 24 (5.9%) episodes of venous thrombosis in 407 AMI patients exposed to short-term bed rest and 28 (8.0%) among 348 AMI patients exposed to long-term bed rest (risk ratio=0.76, 95%CI 0.44, 1.30). The

conclusion of this review was that bed rest ranging from 2 to 12 days was as safe as longer periods of bed rest. However, the studies, including the observational studies, were of low quality; the data extraction was inaccurate; and, the analysis did not adhere to the intention-to-treat principle.

We conducted a systematic review and meta-analysis that included 14 randomized controlled trials to compare AMI patients allocated to any in-hospital EA program (treatment group) with those patients allocated to a control group (bed rest or the current care in each institution) (Cortés et al., 2009) (Appendix A). The studies included in this review adhered to the intention-to-treat principle as did the data extraction for the review, with the number of participants initially randomized serving as the denominator for the event rates. Fourteen studies met the eligibility criteria, 13 of which were published before 1982. In total, there were 149 deaths (9.3%) and 82 non-fatal re-infarctions (5.1%) among 1,607 AMI patients receiving EA compared with 179 (11.6%) deaths and 80 non-fatal re-infarctions (5.2%) among 1,541 individuals allocated to the control group (RR for death=0.85, 95%CI 0.68, 1.05 and RR for non-fatal re-infarction=1.02, 95%CI 0.75, 1.39) after a year. This meta-analysis demonstrated a trend towards decreased mortality with EA after AMI.

Our study (Cortes et al., 2009) differs both conceptually and technically from the Herkner study (2003). Technically, we focused only on randomized controlled trials and followed the intention-to-treat principle for data extraction. Herkner et al. (2003) included observational studies and extracted outcome data

only for participants who were available for follow-up, which has been criticized (West, 2004). Moreover, we focused on the more reliably measured outcomes such as total mortality and non-fatal re-infarction. Results are based on small trials that were conducted more than two decades ago before thrombolysis and PCI were available (Aversano et al., 2002; Fernandez-Aviles et al., 2004).

Both systematic reviews (Herkner et al., 2003; Cortés et al., 2009) suggest that there is no conclusive evidence about the effectiveness or safety of EA within the context of modern cardiac care; however, this work does suggest that there is a trend towards decreased mortality with EA. This is consistent with the systematic review conducted by Allen et al. (1999) described earlier and four single studies (Cook, Davies & Beavis, 1989; Cramer et al., 2005; Fassoulaki, Sarantopoulos & Andreopoulou, 1991; Lindh, Andersson & Westman, 2001; Silvanto, Tarkkila, Makela & Rosenberg, 2004; Thornberry & Thomas,1988) in general medical patients which showed more complications with bed rest compared with EA.

Methodological problems identified in the individual studies included in the reviews by Cortés et al. (2009), Herkner et al. (2003) and Allen et al. (1999) need to be overcome in future studies. These problems may increase the noise and alter the signal of the results. Overall, these problems are related to small sample sizes of individual studies resulting in large confidence intervals around the estimates of effect. Potential bias and inconsistency in the ascertainment of outcomes were observed in some of the individual studies as outcome assessors

were not always blinded to patient outcome. Furthermore, the reviews by Herkner et al. (2003) and Cortés et al. (2009) restricted patient eligibility to relatively uncomplicated AMI patients with an average "baseline" risk of outcome events resulting in lower event rates among those receiving EA, late ambulation or bed rest. This methodological problem is a reflection of the fact that during the period of time that these studies were conducted, complicated AMI patients were not exposed to exercise in order to avoid complications (i.e., cardiac rupture, arrhythmia, death).

Uncertainty continues to exist about the effect of EA during the hospital stay of AMI patients. Furthermore, we do not know the effect of EA for complicated AMI patients or the best time to initiate EA to avoid complications. Lastly, we do not know the effects of early discharge on the pattern of bed rest or ambulation during hospitalization.

In a first attempt to understand the patterns of mobilization of post AMI patients while in hospital, I conducted the Progressive Upright Mobilization Program (PUMP) pilot study in 2002 (Cortés, 2002). This study involved patients from the CCUs in three hospitals in Hamilton, Ontario. The overall aim of this study was to identify patterns of mobilization during the first three days in the CCU (staying in bed, moving to a chair, and sitting/walking) in terms of time of day, frequency and duration. I also explored the association between mobilization and patient health factors such as age, sex, and physiological measures including heart rate (HR) and heart rate variation (HRV) on the third day in CCU. I

observed the patterns of daily mobilization of 31 patients for three consecutive days (a total of 2,232 patient-hours of observation). The mean age of participants was 67 years, 54% of whom were males and 71% with a Killip I (low risk rating). The pattern most frequently observed was bed rest (52%) and semi-fowler position (17.5%) for uncomplicated patients. Data were missing for 37% of the mobilization periods. Heart rate dropped significantly on the third day of hospitalization, while HRV, a measure of parasympathetic output, progressively increased. Preliminary associations that motivate continuation of this study were that: a) mobilization was negatively associated with male sex and Killip classes I and II, and b) HR was lowest among patients who were mobilized to a chair (70 bpm versus 73 bpm).

This pilot study suggested that additional research was needed to determine factors influencing the initiation of ambulation in hospital, to estimate their relative impact with better precision and to determine their association with overall patient outcomes during hospitalization.

Summary

There is increasing clinical evidence substantiated by pathophysiological rationale that bed rest is associated with more complications than EA. Current guidelines related to the timing of in-hospital ambulation of AMI patients are based on weak evidence. Furthermore, little is known about patterns of EA and factors that influence the initiation of in-hospital ambulation in patients after AMI.

The existing meta-analyses of randomized controlled trials comparing EA against bed rest showed a trend towards decreased mortality with EA. However, because trials included in the meta-analyses were small and conducted more than two decades ago, they do not reflect contemporary practice in cardiology and therefore their findings may not be applicable to the current AMI population. There is a need for a large randomized controlled trial to compare early and late ambulation in the current context of cardiology practice.

Given the paucity of evidence, this study uses existing data to learn more about the timing of first ambulation, patient and care-related factors that predict the initiation of ambulation, and the association between initiation of ambulation and heart rate at discharge and in-hospital mortality.

CHAPTER THREE

METHODS

Study Design

A retrospective cohort study design was chosen to address the study objectives. A cohort study is one of the strongest observational designs to determine relationships between exposure (i.e., demographic and health-related factors) and outcomes (i.e., initiation of ambulation) (Kelsey, Evans & Thompson, 1996). A prospective cohort study is a stronger design than a retrospective cohort study for addressing questions of prognosis because the exposure precedes the outcome (Fletcher & Fletcher, 2005b). However, for reasons described below, a retrospective cohort study design, involving the abstraction of data from the medical records of discharged AMI patients, was chosen to address the study objectives.

Ideally, this study would have been designed as a cohort study and all data related to timing and nature of mobilization would have been collected prospectively. However, short of having a research assistant observing every AMI patient 24 hours a day seven days a week in each of the possible units (i.e., CCU, step-down), these data would need to be provided by the nursing staff. When I used this data collection strategy in a pilot study (Progressive Upright Mobilization Program) (PUMP) that I completed in 2002, it became clear that these data were very difficult to collect accurately and comprehensively given the

many nurses involved in caring for the patient in the CCU and step-down units through to discharge who would have to complete the data collection forms. Therefore, I decided to use the electronic medical record (EMR) rather than a study specific instrument in order to reduce the possibility of missing data. In addition, by using the EMR, data could be extracted for the patient's entire hospital stay from the time of admission through to stays on the various units until discharge increasing the number of patient-days of observation. Experience with the pilot study indicated that first ambulation, as opposed to small changes of position (i.e., transfer to bedside chair), is consistently recorded in the EMR. This record includes activity sheets (same in all study hospitals) on which ambulation is recorded and these sheets are completed until the point of patient discharge from hospital. Finally, a retrospective review of chart data prevented biases arising from patients' and nurses' awareness of a mobilization study being underway, potentially modifying the mobilization patterns.

Experience with the PUMP pilot study led to the decision to select a retrospective cohort design to address the limitations in the quantity, precision and validity of the data (Cortés, 2002). This PUMP pilot survey aimed to identify the patterns of mobilization of AMI patients and their relationship with patient factors and outcomes. This study was a prospective observational study that included 31 patients diagnosed with AMI admitted to three CCUs in the Hamilton (Ontario) area. It described the mobilization patterns (including bed rest, semi-fowler position, transfer from bed to a chair, and standing/walking) documented

by CCU nurses for 72 consecutive hours after the patient's admission to the CCU. This pilot also explored relationships between mobilization patterns and heart rate as well as other factors. However, this study included a very small sample size (n=31). Furthermore, there was selection bias by the nursing staff due to the fact that they were recruiting patients for the study and caring for them. The follow-up period of 72 hours of hospitalization involved more than one nurse recording their observations about the patients' mobilization patterns. This led to incomplete forms and the possibility of recall bias because nurses often completed the forms much later than the actual mobilization activity.

A retrospective cohort study based on review of patient records was considered an option by which we could increase sample size, avoid recall bias, and improve precision about mobilization time because the first time the patient is ambulated is recorded. This time of ambulation is recorded more consistently and completely than other mobilization activities during hospitalization because it is one of the considerations for early discharge decisions.

Study Setting

Medical records were abstracted for patients admitted with AMI to one of three acute care hospitals that are part of the Hamilton Health Sciences Corporation (HHSC): Hamilton General Hospital (HGH), McMaster University Medical Centre (MUMC), and Henderson Hospital (HH).

The Cardiac and Vascular Program oversees cardiovascular care in all of these hospitals. HHSC is a tertiary care university-affiliated hospital that operates more than 1000 beds and is comprised of five unique hospitals and a cancer centre. It is situated in Hamilton, Ontario, Canada which has a population of about 500,000 people and serves approximately 2.2 million people living in Hamilton, central south and central west Ontario. Altogether, 700 nurses staff specialized units for patients with cardiovascular diseases at these three hospitals. These units include the coronary intermediate unit (CIU), the coronary care unit (CCU), the cardiovascular intensive care unit (CICU), the cardiorespiratory care unit, and the heart investigation unit (HIU). Nursing personnel include specialized critical care nurses and acute care nurse practitioners (ACNPs). The nurse-to-patient ratio varies according to the type of care and the characteristics of the unit of care. For example, ICUs located in each centre have a nurse-to-patient ratio of 1:1 whereas other units caring for AMI patients have a nurse-to-patient ratio of 1:3 or 1:4.

These specialized units are designed, equipped and staffed to provide care to patients with AMI, congestive heart failure, unstable angina, high risk arrhythmias, cardiomyopathies or valvular disease. Critically ill patients with multiple organ involvement post cardiac arrest, complications post angiogram, PCI, hemodynamic instability requiring monitoring, telemetry and mechanical ventilation are also admitted to these units.

Study Population

The study population included patients with a primary diagnosis of AMI on admission to a specialized care unit at any of the three Hamilton hospitals between January 1st and December 31st, 2004.

Inclusion Criteria

1. Diagnosis of AMI as the primary reason for admission. At least two of the following diagnostic criteria for AMI were recorded in the medical record (by a physician on first assessment within 12 hours of admission):

    a) clinical presentation suggestive of AMI (i.e., typical ischemic chest pain at presentation).

    b) acute elevation of the ST segment in at least two contiguous leads, newly appeared left bundle branch blockade, new Q waves or other persistent ECG changes, or acute and persistent changes in the T wave diagnostic of a non-Q wave MI.

    c) elevation of levels of cardiac enzymes (i.e., creatine kinase (CK) or diagnostic CK-MB fraction or Troponin I or T).

2. Admission to any of the aforementioned specialized units (CCU, ICU, HIU, CRCU) in one of the three acute care hospitals that are part of HHSC.

3. Availability of an EMR in the HHSC computerized system for patient information.

Data Collection Procedures

Ethics approval for the study was obtained from the McMaster University Research Ethics Board (CR Letter No 83/2005) (Appendix B). EMRs for eligible patients admitted with AMI between January 1st and December 31st, 2004 were requested from the health records office of each hospital and permission (Appendix C) to access these medical records using Sovera was obtained.

Eligible medical records were consecutive patients with a diagnosis of AMI on admission. For patients with more than one admission to the hospital for an AMI during the study period, only the data for the last hospitalization were used. Records were identified through a computerized search of the HHSC Information and Communication Technologies Department database by using the International Classification of Diseases Codes for AMI diagnosis (ICD-9-CM Diagnosis 410.0 to 410.9) (World Health Organization (WHO), 2007) (Appendix D). Records were accessed via the Meditech and Sovera systems. Meditech Health Care Information System is the clinical operations system for all the hospitals in the HHSC, and is a system implemented for record management problems. Sovera is an electronic health records management system that provides consolidated medical records and a simple consistent set of patient record indexing for the online storage and retrieval of patient health records across all HHSC facilities. In Sovera, all new health records are scanned and stored as electronic documents that can be accessed online anywhere and at anytime by authorized staff. The record information maintained by Sovera

complements the patient information already stored in the Meditech database (CGI G Group Inc, 2008).

Data Collection

A medical record abstraction form was developed by the investigator. The form consisted of five sections that included factors known to influence activity of hospitalized patients and AMI patients attending outpatient CRPs (Ades, Maloney, Savage & Carhart, 1999; Jolliffe, Rees, Taylor, Thompson, Oldridge & Ebrahim, 2001) (Table 1) (Appendix E). The record abstraction form also included factors related to first ambulation that were identified in the PUMP pilot study (Cortés, 2002). The first section included data regarding admission date and demographic variables such as age, gender, marital status, occupation, working status and ethnic background (i.e., language spoken at home) (Akhtar, Malik & Ahmed, 2004; Lau-Walker, 2004; Mendes de Leon, Bang, Bienias, Glass, Vaccarino & Kasl, 2005; Rankin, Butzlaff, Carroll & Reedy, 2005). This section also included both admission and discharge health status, location of the AMI, troponin, creatine kinase (CK) and CK-MB isoenzyme values, potential complications, as well as heart rate and blood pressure on admission. Finally, this section documented information related to the reported time of pain onset, time of arrival at the emergency department, and health status at discharge (i.e., alive or death).

Table 1. Factors associated with first ambulation

Aspect	Collected variables	Type of variable/units
Demography	Age Gender Marital status Language Work status	Continuous Categorical Categorical Categorical Categorical
Past Medical History	Previous disease Associated risk factors and treatment/procedures	Categorical Categorical Categorical
Physical Findings on Admission to Hospital	Time of onset (or event) Time of arrival to hospital. Heart rate from ECG at admission Systolic blood pressure at admission Elevated cardiac enzymes ST segment depression Type of MI	Continuous Continuous(hour) Continuous Continuous Categorical Categorical Categorical
In-Hospital Medical Therapy and Procedures	Bed rest prescription Re-perfusion therapy (thrombolysis) Catheterization Cardiac surgery Medication Heart rate from ECG at discharge	Categorical Categorical Categorical Categorical Categorical Continuous
In-Hospital Complications	Morbidity Mortality Use of devices	Categorical Categorical Categorical

The second section included past medical history (i.e., previous AMI, angina, cardiac surgery, diabetes, mental health problems) and risk factors (i.e., smoking) and cardiac or other procedure history (i.e., cardiac surgery) (Doering, Moser, Lemankiewicz, Luper & Khan, 2005; Blumenthal et al., 2004; Milani & Lavie, 2007). The third section included the interventions and procedures during hospitalization including medications, thrombolytics, and cardiac procedures such

as PCI. Other interventions included in this section were the recording of the bed rest prescription and activity as tolerated.

The fourth section included complications that occurred during hospitalization such as heart failure, pulmonary edema, arrhythmias, and stroke (Antman et al., 2005; Anderson et al., 2007). The final section included specific information on the date and time of the first ambulation and degree of assistance received during first ambulation. Information on the Killip class was collected from the physicians' records in each patient´s chart. The coding of Killip class included two categories: Killip III/IV (either pulmonary edema or cardiogenic shock post-AMI) or Killip I/II for patients without pulmonary edema or cardiogenic shock post AMI within the first 24 hours after admission. When information on the Killip class was not found in the chart, the record was reviewed for terms including "pulmonary edema", "shock", or prescription of intravenous diuretics or inotropic medications. Killip classification is a powerful independent predictor of all-cause mortality in patients with STEMI and NSTEMI (Khot et al., 2003; Killip and Kimball, 1967; DeGeare, Boura, Grines, O'Neill & Grines, 2001). A higher Killip class is independently associated with higher mortality in patients during hospitalization and at 6 months post AMI (2.4% and 4.0% Killip class I; 7% and 10% Killip class II, and 19% and 28% Killip class III/IV, respectively) (DeGeare et al., 2001; Khot et al., 2003).

Prior to commencing record abstraction, the terms in the form were defined and standardized. Variables included in the form were coded prior to

building the database (Appendix F). This data collection form was piloted on 40 randomly selected charts. The purpose of the pilot was to evaluate the completeness of data, the time required to complete the form, the ease of use of the data extraction form and the reliability of the outcome assessment. I abstracted these charts twice separated by a six month time interval. Intra-rater reliability was determined for this sample of charts using the kappa statistic for categorical data and intra-class correlation coefficient for continuous data (Streiner & Norman, 2001). I abstracted all medical records.

Sample Size

In 2004, there were 1014 charts of patients whose recorded diagnosis on admission was AMI at the three Hamilton hospitals. A sample of 382 charts would allow the identification of a positive association of 1.5 (hazard ratio) or larger (or a negative association of 0.67 or smaller) between explanatory (independent) variables (predictors) and initiation of ambulation present in at least 50% of the cohort, with at least 80% statistical power, at an alpha level of 5%. Allowing for the exclusion of a maximum of 15% of charts that failed to meet the inclusion criteria, the sample size increased to 450 charts (Hsieh & Lavori, 2000; Schoenfeld, 1983). We reviewed 500 charts for this study.

Outcomes

The primary outcome was first ambulation, defined as the first time AMI patients walked during their hospital stay. For wheelchair dependent patients, it was defined as the ability of the AMI patient to move from bed to chair, the current method for mobilization. An acceptable record of the first walk could come from the primary basic care nursing flow sheet or any record indicating a prescription for walking in any section of the EMR (i.e., interdisciplinary patient care notes, CRCU nursing kardex, doctors' orders, physicians' progress notes or cardiac care flowsheet) as noted by any health care provider. Patients were classified as not walking if there were no data in the chart indicating that they had walked during their hospitalization. Secondary outcomes included heart rate at discharge expressed as beats per minute (bpm) and mortality during hospitalization. Heart rate at discharge was collected from the electrocardiogram.

Plan for Statistical Analyses

Intra-rater Reliability

For the forty charts that were abstracted twice separated by a six month period of time, a kappa statistic was used to compare categorical data and intra-class correlation was used to compare continuous data. A kappa between 0.2 and 0.4 was considered fair; between 0.4 and 0.6 moderate; between 0.6 and 0.8 good; and higher than 0.8 excellent (Norman & Streiner, 2000).

Description of the Sample

Counts/percentages for categorical measures and means for continuous measures were used to describe baseline demographic, social, and clinical characteristics of the sample at hospital admission; AMI characteristics such as time of onset of the symptoms and activity recorded as the trigger for the event; and finally, treatment, procedures and complications during hospitalization.

Analysis of First Ambulation

Description of first ambulation included the distribution of the event by hour of occurrence, the number of hours before first ambulation occurred, the proportion ambulated on a weekday versus weekend and the proportion who ambulated independently versus with assistance.

Relationship Between Patient and Care-Related Factors and First Ambulation

Identification of these relationships comprised a number of steps with the final goal of establishing a model that best predicted the outcome of interest. For the first part of the analysis, independent t-tests (for continuous variables) and chi-square analysis (for proportions) were used to compare "walkers" and "non-walkers" with respect to the independent variables. Variables that showed significant differences (with an alpha level of 5% as the threshold for statistical significance) were included in the survival analysis.

The second part of the analysis tested the null hypothesis of no differences in independent variables among categories of time of ambulation (early, intermediate, late walkers and non-walkers). The categories defined according to data distribution were: 1) early walking time (within 48.99 hours of admission); 2) intermediate walking time (≥ 49 to 96.99 hours after admission); 3) late walking time (≥ 97 hours after admission); and, 4) no walking. Hypothesis testing used ANOVA (for continuous variables) and chi-square analysis (for proportions) with an alpha level set at 5% as the threshold for statistical significance.

Trend and Subgroup Analysis

In order to examine the trend among categories of walking (early, intermediate, late and non-walkers) and to take into account the analysis of ordinal or ranked categories, a chi-square test (Kendall's tau-b test), a correlation coefficient of independence was applied. It measures the degree of correspondence between two rankings or the strength of association of the cross tabulations when both variables are measured at the ordinal level. This analysis measured the degree of linear trend, or the correlation that fell between -1 and +1, for the variables that were significant in the bivariate analysis. Increasing values imply increasing agreement between the rankings. If the rankings are completely independent, the coefficient has a value of 0 on average. Furthermore, if the agreement between the two rankings is perfect, the coefficient

has a value of -1 or +1. The larger the correlation, the less independent are the variables in this linear dimension (i.e., a p-value of 0.01 suggests strong evidence of a non-zero correlation of about 2.5) (Norman & Streiner, 2000). Additionally, to examine the trend for continuous variables, a regression analysis was conducted for variables that were significant in the bivariate analysis. Variables that were included in the survival analysis model had a significance level of ≤ 0.05 and showed a significant (positive or negative) gradient through the time categories.

A post-hoc subgroup analysis was performed in order to better understand the differences between early, intermediate and late walkers and the related factors observed in the bivariate analysis. Post-hoc analysis was performed to determine which specific groups differed from one another when the difference was statistically significant. A Tukey test was performed to determine the difference between the three groups of walkers for the continuous variables. A pair-wise analysis (chi-square test) was performed to determine the difference between the three groups for the categorical variables (Norman & Streiner, 2000).

Time to Event Analysis (Survival Analysis)

The third part of the analysis included a survival analysis with pre-selected variables. The strength of this analysis is that it not only tests for the association between time of first ambulation and potential predictive factors, but it also tests for the time pattern of the occurrence of outcomes or endpoints (Hosmer &

Lemeshow, 1999). For consistency across participants, the time to first ambulation was set as the time difference (in hours) between the time of hospital admission and the occurrence of first ambulation in hospital. The time for patients who never walked was defined for purposes of the survival analysis as the length of their hospital stay.

In order to identify factors associated with time to first ambulation, a Cox regression proportional analysis was conducted. Cox proportional hazard model is a type of multivariable technique used for the analysis of factors acting together. This model is very useful for multivariable adjustment analysis when the outcome is time to an event (Fletcher & Fletcher, 2005b; Fletcher & Fletcher, 2005c). This is analogous to a multiple regression model and enables the difference between survival times of particular groups of patients to be tested while controlling for other factors. In this model, the result is presented as the "hazard ratio (HR)". In this study, the hazard at each time is the risk of walking given that the patient has not walked before that point.

We computed hazard ratios and their 95% confidence intervals (CIs) for each independent variable. Among entry factors into the models predicting EA, we included only variables shown in the previous analysis to be significantly associated (at a significance level $p \leq 0.05$).

The assessment of the proportional hazard model was performed to assure the correct hazard estimation for each predictor related to the first walk. This assessment of the fit of the proportional model included three phases. The

first was an evaluation of the proportional hazards assumption for the covariates, including a global test (Hosmer & Lemeshow, 1999). This numerical method used scaled schoenfeld residuals. To perform this analysis in Stata, global test (stphtest) and the schoenfeld (sch*) options had to be specified. Schoenfeld residuals are based on the individual contributions to the derivative of the log-partial likelihood (Hosmer & Lemeshow, 1999). The second was the assessment of the proportionality of the hazards by the graphical method using the scaled Schoenfeld residual plots for each covariate. Finally, the stratified analysis for proportional hazard model was planned in case some variables were identified as violating (affecting the outcome) the proportionality of the model (Hosmer & Lemeshow, 1999).

Analysis of Secondary Outcomes

Two secondary analyses were conducted to explore: (a) the relationship between first ambulation and heart rate at discharge; and, (b) the relationship between first ambulation and vital status (living, dead) at discharge. For these analyses, first ambulation is the exposure or independent variable and heart rate and death are the dependent variables.

The first of these analyses involved a bivariate comparison of heart rate at discharge between those who walked and those who did not walk. This analysis expanded to heart rate by categories of ambulation (i.e., early, intermediate and late walkers). A further step was to conduct a multivariate analysis using an

analysis of covariance (ANCOVA). Heart rate means (bpm) along with 95%CIs were computed, both unadjusted and adjusted by the factors influencing the time of first ambulation.

The relationship between ambulation and vital status (living, dead) at discharge involved a chi-square analysis by categories of ambulation, first as a dichotomous variable (walkers versus non-walkers) and then as time categories of ambulation (early, intermediate and late walkers). The influence of other variables was addressed through stratified analysis (i.e., mortality among walkers versus non-walkers within strata of Killip classes).

CHAPTER FOUR

RESULTS

This chapter begins with a summary of the intra-rater reliability testing of the data extraction process, followed by a description of the study sample. The findings related to each study question will then be summarized:

a) What is the timing of first ambulation among patients admitted for AMI?

b) Which patient and care-related factors determine initiation of ambulation among hospitalized patients with AMI?

c) What is the association between initiation of ambulation and heart rate at discharge in patients with AMI?

d) What is the association between initiation of ambulation and in-hospital mortality in patients with AMI?

Intra-rater Reliability Assessment

Overall agreement for categorical variables for 40 charts that were abstracted twice by the same chart abstractor separated by a six month period of time was excellent (Kappa statistic 0.80; 95%CI 0.76, 0.84). The kappa statistic varied between 0.24 and 0.89 for the individual variables that were selected. Two variables (past medical history of PCI; in-hospital PCI) showed moderate to fair agreement (K=0.44 and K=0.24, respectively). This finding is surprising given that this information is usually well documented. However, this may be related to the fact that it was difficult to find this information in the patient's chart. Given the

lower kappas for these variables and awareness of this problem, the 40 charts were reviewed a third time 6 months later and kappa statistics were calculated for these two variables again. For past medical history of PCI, the kappa statistic was 0.66 and for in-hospital PCI, the kappa statistic was 0.89.

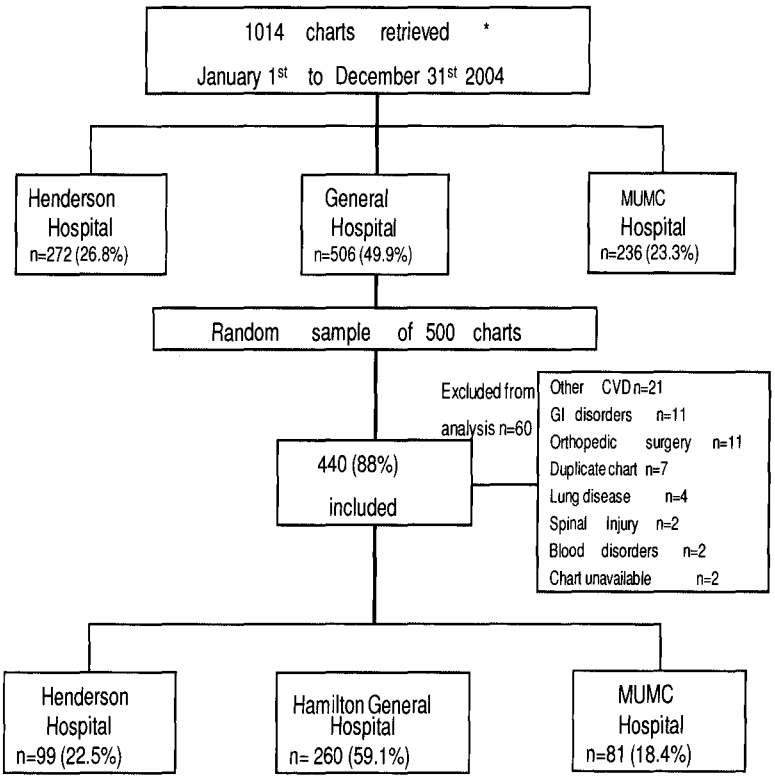
Overall agreement for continuous variables was also very good (intraclass correlation coefficient (ICC) = 0.96, 95%CI 0.92, 0.99). The ICC varied between 0.34 and 1.0 for the selected variables. The ICCs for two variables demonstrated fair to low reliability: the cardiac enzyme, creatinine kinase MB, and diastolic blood pressure at discharge, with ICCs of 0.42 and 0.34 respectively. Given the lower ICC for these variables, the 40 charts were reviewed a third time and ICC was calculated for these two variables again. For creatinine kinase MB, the ICC was 0.55 and for diastolic blood pressure at discharge, it was 0.70. This may be related to the fact that multiple laboratory values were reported in the charts for the same tests performed more than once as well as multiple recordings of vital signs increasing the chances of selecting different values each time the chart was abstracted. ICCs for the remaining variables ranged from 0.58 to 1.0.

Description of Study Sample

Five hundred medical records were identified from a total of 1,014 charts of patients with a diagnosis of AMI between January 1st and December 31st, 2004 at the three study sites (Figure 1). Fifty percent of patients with a diagnosis of AMI attended the Hamilton General Hospital (HGH); this is consistent with the fact

that it is the referral centre for patients from southern Ontario. Of these 500 charts, 88% (n=440) met the inclusion criteria. The reasons for exclusion of the remaining 60 (12%) charts are listed in Figure 1. The main reason for exclusion was the presence of other cardiovascular diseases that were initially miscoded as an AMI (n=21) (i.e., aortic dissection).

Figure 1. Flow Chart of the Sampling Process



* From the Hamilton Heatlh Sciences Computerized Health records (SOVERA)

Baseline Characteristics of the Sample

Table 2 summarizes baseline demographic characteristics of the 440 patients included in the study. Their median age was 68.0 years. Approximately two-thirds (66.1%) were males. The majority of the sample was married (67.9%), while 12.4% were single, 11.7% were widowed, and 6.7% divorced. Just over a third of the sample (38%) was employed. The data about employment status were missing in 35.4% of patients (n=156). Most patients reported English as their first language (95.9%). Other languages spoken at home included Italian (2.5%), Spanish (2.5%), Polish (2.0%), Russian (1.0%) and Portuguese (1.0%). Language information was not reported in 53 charts. The median length of stay was 6 days (1st and 3rd quartile between 3 and 11 days).

Table 3 summarizes the characteristics of the study participants at hospital admission. Over half (58%) came directly from home, 33.5% were referred from other hospitals, and 8.6% were referred from other places or by people (i.e., workplaces, bystanders on the street). Patients were more likely to arrive at the hospital on weekdays (75%). The most frequent mode of transportation to the hospital was by ambulance (72.7%), followed by car (18.2%), and walking (9.1%). Patients were admitted via the emergency department (58.1%), surgical unit (21.2%), CCU/CRCU (16.8%), ICU (1.8%) and a medical ward (2.1%). Patients were first admitted to the CCU or CRCU (70.2%), surgical unit (10.6%), medical wards (10.6%), or the ICU (7.8%).

Table 2. Demographic characteristics of the study participants recorded on admission

Characteristic	n (%) *
Age median (Q1-Q3)	68.0 (55-76)
Male, No (%)	291 (66.1)
Marital status n= 420[a]	
Married	285 (67.9)
Single	52 (12.4)
Widowed	49 (11.7)
Divorced	28 (6.7)
Common-law	6 (1.3)
Employed[b] n=284	
Yes	108 (38.0)
No	176 (62.0)
Reported English as their first language[c] n=387	371 (95.9)
LOS, median days (Q1-Q3)	6.0 (3-11)

Q1 and Q3: 1st and 3rd quartile, respectively. *Percentages are based on available data for each category. Numbers do not add to 440 as result of missing data on Marital status[a](n=20), Employed[b] (n=156); Reported English as their first language[c] (n=53).

Table 4 summarizes the past medical history of the participants at hospital admission. Conventional risk factors for CHD were, in order of frequency, hypertension (54.3%), hyperlipidemia (43.6%), diabetes (29.1%), former smoker (25.2%), current smoker (24.1%) and family history of CVD (21.1%). Just under a quarter of the study sample (23.2%) reported a previous AMI. Other prior CVDs included angina (8.9%), arrhythmia (6.6%), heart failure (5.2%), and stroke (4.3%). Forty patients (9.1%) had undergone CABG surgery and 36 (8.2%) had PCI.

Table 3. Characteristics of study participants on hospital admission

Characteristic	n (%)
Site of transference to the hospital[a] n=427	
Home	247 (58.0)
Other hospital	143 (33.5)
Other	37 (8.6)
Day of the week on arrival[b] n=437	
Weekday	328 (75.0)
Weekend	109 (25.0)
Way of arrival[c] n=385	
By ambulance	280 (72.7)
By car	70 (18.2)
By walking	35 (9.1)
Clinical service of admission[d] n=434	
Emergency department (ED)	252 (58.1)
Surgical unit	92 (21.2)
CCU/CRCU	73 (16.8)
ICU	8 (1.8)
Medical ward	9 (2.1)
First setting of hospitalization[e] n=396	
CCU/CRCU	278 (70.2)
Surgical unit	42 (10.6)
Medical ward	42 (10.6)
ICU	31 (7.8)
Emergency department	3 (0.8)

CCU: Coronary care unit; CRCU: Cardiac respiratory care unit;
ICU: Intensive Care Unit. Numbers do not add to 440 as result of missing data on Site of transference to the hospital [a](n=13);Day of the week on arrival[b] (n=3); Way of arrival[c] (n=55); Clinical service of admission[d](n=6); First setting of hospitalization[e] (n=44).

Table 4. Past medical history of study participants on admission to hospital

Antecedents (n=440)	n (%)
Conventional CVD risk factors	
Hypertension	239 (54.3)
Hyperlipidemia	192 (43.6)
Diabetes	128 (29.1)
Former smoker	111 (25.2)
Current smoker	106 (24.1)
Previous MI	102 (23.2)
CHD-family history	93 (21.1)
Previous CVD or procedures	
Angina	39 (8.9)
Arrhythmia	29 (6.6)
Heart failure	23 (5.2)
CABG	40 (9.1)
PCI	36 (8.2)
Stroke	19 (4.3)
Other medical conditions	
Mental disease	18 (4.1)
Alzheimer	9 (2.0)
Cancer	40 (9.1)
Pulmonary disease	33 (7.5)

The sum of percentages exceeds 100% because of the overlapping of some conditions in the same person.
CVD: Coronary vascular disease; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft

The mean time of symptom onset was at 11:30 hours (SD 6.3), median was 11:30 hours and the mode was 8:00 (Table 5). The largest proportion of AMIs occurred during the morning hours (7:01-13:00) (Figure 2). Mean heart rate on arrival was 82.6 bpm (SD 23.1); mean systolic blood pressure was 135.8 (SD 29.6) mmHg; mean diastolic blood pressure was 78.9 mmHg (SD 18.9). On admission, the mean peak cardiac enzyme levels were 74.1 ng/ml (SD 146.8) for troponin and 901.1 ng/ml (SD 1555.7) for creatine kinase (MB). The mean

ejection fraction was 43.8 (SD 12.8). On presentation to hospital, most patients arrived oriented (92.2%) and most patients (60.7%) were diagnosed with a STEMI. Patients were more likely to show inferior AMI (42.8%) than anterior and lateral side AMI (37.6% and 19.6%, respectively). Three hundred and forty-two (77.7%) of the patients were assessed as having a Killip I-II AMI and 98 (22.3%) had a Killip III-IV AMI (Table 5).

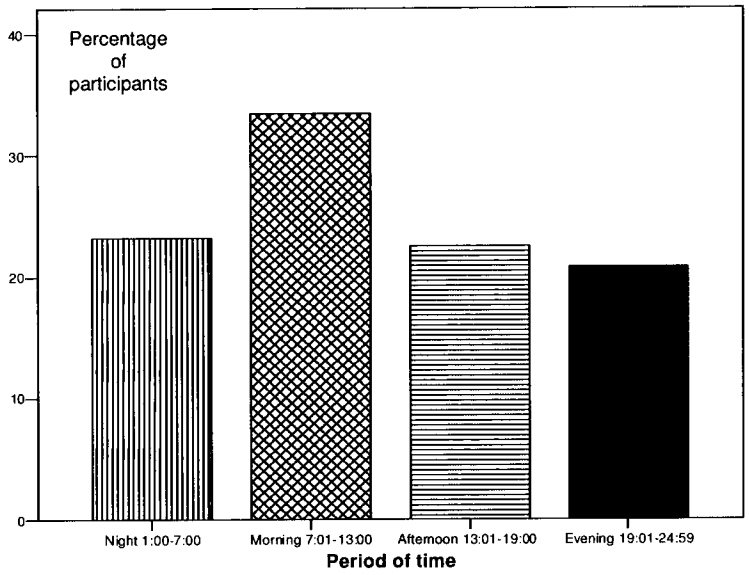
Symptoms most often described by patients upon arrival to ED included chest pain (75%). It was sometimes accompanied by other symptoms including shortness of breath (12.4%), nausea (4.3%), pain radiating to both arms (2.3%), pain radiating to the jaw (1.1%), and vomiting (2.5%) (data not shown). The activities reported as triggering the symptoms are shown in Figure 3. Most participants reported that their onset of pain occurred while sleeping (20.9%). This was followed by resting (18.4%), exercising (14.3%), working (6.4%), eating (2.5%), or experiencing strong emotional feelings (1.4%). Data regarding the types of activities triggering AMI were missing for 155 patients (35.2%).

Table 5. Characteristics of the study participants on admission to hospital

Characteristics	Mean (SD)
Mean time at onset of symptoms, hour (SD)	11:30 (6:38)
Mode	8:00
Vital signs on admission (n=440)	
HR mean (SD)	82.57 (23.1)
SBP mm Hg mean (SD)	135.82 (29.6)
DBP mm Hg mean (SD)	78.92 (18.9)
Cardiac specific enzymes on admission	
Peak Troponin, mean (SD) (n=426)[a]	74.10 (146.8)
Peak Creatine Kinase MB, mean (SD) (n=393)[b]	901.14 (1555.7)
Mean ejection fraction on admission (SD)	43.84 (12.82)
	n (%)
Level of consciousness on admission[c] n=387	
Oriented	357 (92.2)
Confused	21 (5.4)
Unconscious	9 (2.4)
Presence of ST Elevation[d] n=435	
STEMI/Q wave MI	267 (60.7)
Non STEMI/Non Q wave MI	173 (39.3)
Location of AMI[e] n=406	
Inferior	174 (42.8)
Anterior	153 (37.6)
Lateral	79 (19.6)
Killip class of AMI n=440	
Killip I-II	342 (77.7)
Killip III-IV	98 (22.3)

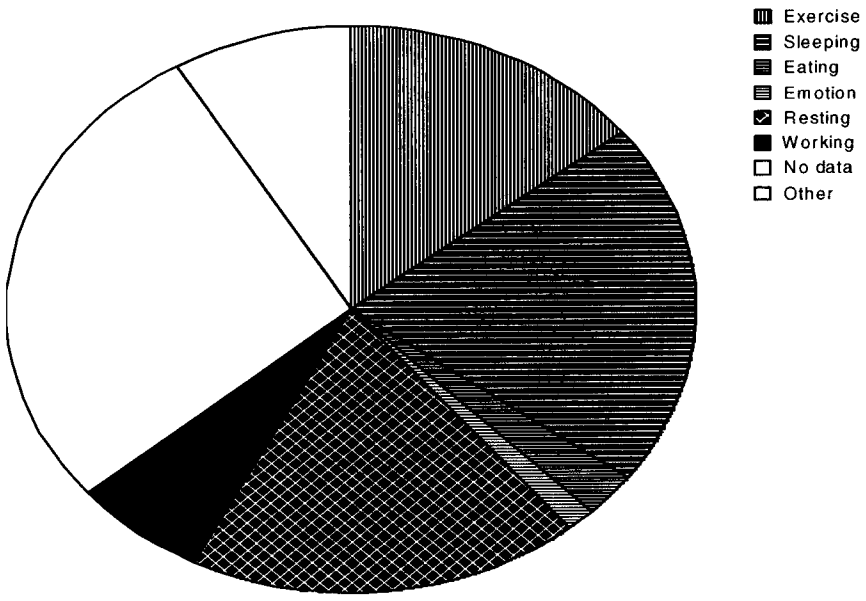
AMI: Acute myocardial infarction; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; QMI/STEMI, Acute myocardial infarction with Q wave or ST segment present on EKG, No QMI/Non STEMI, AMI without Q wave, without ST segment presentation.
Numbers do not add to 440 as a result of missing data in Peak Troponin[a] (n=13); Peak Creatinine Kinase[b] (n=47); Level of consciousness on admission[c] (n=53); Presence of ST elevation[d] (n=5); Location of AMI[e] (n=34)

Figure 2. Time of onset of AMI symptoms



Median time at onset 11:30 hrs; Q1-Q3 (7:00-18:00)

Figure 3. Activity reported as triggering the AMI



Most frequent trigger activities reported were sleeping (20.9%); resting (18.4%), and exercising (14.3%). Numbers do not add to 440 as a result of missing data (n=155)

In-Hospital Treatment

Table 6 shows that among the reperfusion strategies patients received during hospitalization, 210 (47.7%) had PCI; 103 (23.4%) had thrombolysis, and 32 (7.3%) had CABG. Almost three-quarters of the patients (n = 320; 72.7%) underwent coronary angiography. The most frequently prescribed medications during hospitalization were antiplatelets (96.4%), aspirin accounting for 88.9% of antiplatelets; beta blockers (77.3%); angiotensin converting enzyme (ACE) inhibitors (68%) and cholesterol lowering medications (59.3%). Other frequently prescribed medications were nitroglycerin (66.6%) and heparin (65.7%). Over two-thirds of patients (n=307; 69.8%) received calcium channel blockers.

Related to supportive treatment prescribed, 334 patients (75.9%) had analgesic agents, 210 (47.7%) had morphine, and 210 (47.7%) had sedatives. Furthermore 14% of patients (n=62) required mechanical ventilation, pacemaker 5.4% (n=24), or swan-ganz catheter 4.7% (n=21) as supportive treatment (not all in the table). Approximately one-half of patients (52.6%) were prescribed bed rest by a physician; 104 (23.6%) had a prescription of mobilization or activity as tolerated (AAT), and 105 (23.8%) did not have any prescription related to ambulation. In-hospital complications included kidney failure 2% (n=9), chest pain 6% (n=26), heart failure 12.9% (n=57), arrhythmias 12% (n=57), and death (n=32; 8%) (data not shown).

Table 6. In-hospital treatment prescribed for participants

Treatment n=440	n (%)
Reperfusion strategies	
PCI	210 (47.7)
Thrombolysis	103 (23.4)
CABG	32 (7.3)
Coronary angiography	320 (72.7)
Evidence-based interventions	
Anti-platelet agents	424 (96.4)
Aspirin	391 (88.9)
Beta-blocker	340 (77.3)
ACE inhibitor	299 (68.0)
Cholesterol-lowering agents	261 (59.3)
Other medical treatments	
Nitroglycerin	293 (66.6)
Heparin	289 (65.7)
Insulin	66 (15.0)
Inotropic agents	99 (22.5)
Antacid	68 (15.5)
Anti-arrhythmics	154 (35.0)
Calcium channel blockers	307 (69.8)
Supportive treatment	
Analgesic agents	334 (75.9)
Morphine	210 (47.7)
Lorazepan	170 (38.6)
Sedatives	210 (47.7)
Diuretics	125 (28.4)
Laxative	122 (27.7)
Mechanical ventilation	62 (14.0)
Prescription of bed rest	
Bed rest prescribed	231 (52.6)
Mobilization/AAT prescribed	104 (23.6)
None prescription for bed rest/AAT	105 (23.8)

PCI: Percutaneous coronary intervention;
CABG: Coronary artery bypass graft; AAT: Activity as tolerated.

Timing of First Ambulation During Hospitalization

A total of 340 patients (77.3%) walked during their hospitalization after their AMI. The mean hour of the day for the first walk was 1100 hrs (SD 5.4 hrs). The mean number of hours for all patients before the first walk following admission was 112.2 hours (SD 130.8 hrs), corresponding to 4.2 days; the median was 73.7 hrs (corresponding to 3.5 days). There were no differences in the mean number of hours to first walk between patients that had "bed rest" or "activity as tolerated" prescribed by a physician (110.2 hrs SD 134.9; 110 hrs SD 149.4 hrs) respectively (data not shown). The first walk was more likely to occur during the weekday (250 patients, 60%) than on weekends (90 patients, 40%).

In order to explore the associations of interest, the 24 hours of the day were divided into four categories of first walk time as follows: morning (07:00 to 11:59), afternoon (12:00 to 17:59), evening (18:00 to 23:59), and night (24:00 to 06:59). The first walk was taken during the morning by 50% of the patients (n=170), in the afternoon by 19.4% (n=66), in the evening by 27.6% (n=94), and during the night by 2.9% (n=10). The majority of patients who walked during their hospital stay (88.2%) mobilized for the first time in the ICU/CCU. Data regarding the circumstances surrounding first ambulation were missing for 106 (24.1%) patients. Approximately two-thirds of the patients mobilized independently (68%), 25.6% required assistance, and 6.4% required supervision.

Relationship Between Patient and Care-Related Factors and Initiation of Ambulation

Baseline Characteristics Stratified by Walkers and Non-walkers

There were no differences between those who walked ("walkers") and those who did not walk ("non-walkers") in terms of gender, marital status, and day of the week of admission (Table 7). However, there were significant differences in other demographic factors. Walkers were younger than non-walkers (difference 4.05 years; p=0.001). In addition, there was a higher proportion of employed individuals among the walkers compared with the non-walkers (41.3% vs. 25.4%; p=0.03) (Table 7).

A greater proportion of patients in the walker group were referred from home compared with the non-walkers (60.7% vs. 47.9%; p=0.001). Fewer walkers than non-walkers were referred from other hospitals (29.1% vs. 48.9%, p=0.001). Finally, a greater proportion of patients in the walker group were admitted from the emergency department compared with the non-walkers (62.4% vs. 42.6%; p=0.001) (Table 7).

Table 7. Comparison of patient characteristics between walkers and non-walkers on admission to hospital

	Walk while in hospital		p value
	Yes n=340 (77.3%)	No n=100 (22.7%)	
Demographic factors[a]			
Male, No (%). n=434	224 (66.9)	67 (67.0)	0.457
Age, mean (SD) n=431	64.85 (13.6)	68.9 (12.7)	0.001
Marital status[b] **(%) n=420**			0.972
Married	220 (67.9)	65 (67.7)	
Other (single, widow, divorced, common-law)	104 (32.1)	31 (32.3%)	
Employed[c] **n=284**			0.025
Yes	93 (41.3)	15 (25.4)	
No	132 (58.7)	44 (74.6)	
Day of the week of arrival[d] **n=437**			0.255
Monday-Friday	258 (76.3)	70 (70.7)	
Saturday-Sunday-Holidays	80 (23.7)	29 (29.3)	
Patient referred from[e] **n=427**			0.001
Home	202 (60.7)	45 (47.9)	
Other hospital	97 (29.1)	46 (48.9)	
Other	34 (10.2)	3 (3.2)	
Way of arrival[f] n=385			0.008
Ambulance	209 (69.7)	71 (83.5)	
Car	57 (19.0)	13 (15.3)	
Walking	34 (11.3)	1 (1.2)	
First setting at hospital entry[g] n=434			0.001
Emergency department	212 (62.4)	40 (42.6)	
Surgical unit	60 (17.6)	32 (34.0)	
Other : CCU, ICU, CRCU, med ward	68 (20.0)	22 (23.4)	
First setting for hospitalization[h] n=396			0.028
Emergency department	3 (0.9)	0	
Surgical unit	40 (12.5)	2 (2.6)	
CCU,ICU, CRCU, med ward	277 (86.6)	74 (97.4)	

CCU, Coronary care unit; ICU: Intensive care unit; CRCU: Cardiac respiratory care unit. Numbers do not add to 440 as a result of missing data in demographic factors[a] (n=7), marital status[b] (n=20), employed[c] (n=156), day of the week of arrival[d] (n=3), patient referral from[e] (n=13), way of arrival[f] (n=55), first setting of hospital entry[g] (n=6), first setting for hospitalization[h] (n=44).

With regard to the clinical presentation on admission to hospital (Table 8), there were some significant differences between walkers and non-walkers. Blood pressure levels were significantly higher among walkers compared with non-walkers (137 vs. 130, p=0.039 for SBP; 80 vs. 75, p=0.038 for DBP). Walkers had a higher, although not significantly different mean heart rate, compared with their counterparts. In general, patients arrived conscious to ED and no significant differences were observed between walkers and non-walkers (93.3% vs 88.5%). Although not statistically significant, more patients in the walker group fell in the Killip I-II classes (79.1% vs 73%, p=0.219). In support of this finding, the walker group had a higher ejection fraction than the non-walker group (mean 44.5%, SD 12.8% versus 41.8%, SD 12.7%, p=0.225). The mean total length of stay in days (LOS) was 9.6 (SD 9.1) in the walker group and 5.4 (SD 7.5) in the non-walker group ($p<0.001$) (Table 8). When those who died (n = 32) were excluded, the difference in mean total length of stay remained similar at 9.4 (SD 8.7) days in the walker group and 4.9 (SD 7.1) days in the non-walker group.

Table 9 shows the relationship between past medical history and walking events on admission to hospital. In general, there were no significant differences in the rates of conventional risk factors for CHD or in the history of having had reperfusion strategies. However, some clinically important differences are noteworthy. Fewer walkers had diabetes (27.4% vs. 35%), previous MI (21.2 % vs. 30%), arrhythmias (5.6% vs. 10%), mental disorder (3.5% vs. 6%) and cancer (7.6% vs. 14%), although these differences were not statistically significant. With

regard to reperfusion strategies, more walkers than non-walkers had a previous reperfusion strategy PCI (9.1% vs. 5%), although this difference was not statistically significant.

Table 8. Comparison of clinical characteristics between walkers and non-walkers on admission to hospital

	Walk while in hospital		p-value
	Yes n=340 (77.3%)	No n=100 (22.7%)	
Vital signs n=440			
HR, mean bpm (SD)	83.13 (23.6)	80.6 (21.1)	0.346
SBP, mean mmHg (SD)	137.39 (29.6)	130.3 (29.1)	0.039
DBP, mean mmHg (SD)	79.93 (18.9)	75.3 (18.7)	0.038
Level of consciousness[a] n=387			0.333
Oriented	280 (93.3)	77 (88.5)	
Confused	14 (4.7)	7 (8.0)	
Unconscious	6 (2.0)	3 (3.4)	
ST elevation n=440			0.641
STEMI	209 (61.5)	58 (58.0)	
Non STEMI	131 (38.5)	42 (42.0)	
Location of AMI			
Inferior	130 (38.3)	44 (44.0)	0.310
Anterior	119 (35.0)	34 (34.0)	0.839
Lateral	59 (17.4)	20 (20.0)	0.553
Killip Class n=440			0.219
Killip I-II	269 (79.1)	73 (73.0)	
Killip III-IV	71 (20.9)	27 (27.0)	
Cardiac specific enzymes			
Peak Troponin[b] (n=426), mean ng/ml (SD)	70.53 (140.5)	86.2 (166.9)	0.356
Creatine Kinase[c] (n=393), mean ng/ml (SD)	892.1 (1611.8)	930.7(1655)	0.835
Ejection fraction mean (SD)	44.5 (12.8)	41.8 (12.7)	0.225
Total LOS mean (SD)	9.6 (9.1)	5.4 (7.5)	<0.001

HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; STEMI/Non-STEMI: AMI with/without ST segment elevation on electrocardiogram; Killip: AMI prognostic classification based on clinical findings. Numbers do not add to 440 as a result of missing data in level of consciousness [a] (n=53); Peak Troponin[b] (n=13); Creatine Kinase[c] (n=47)

Table 9. Comparison of past medical history between walkers and non-walkers on admission to hospital

	Walk while in hospital		
	Yes n=340 (77.3%)	No n=100 (22.7%)	p-values
Risk factors for CVD			
Former smoker	87 (25.6)	24 (24.0)	0.748
Current smoker	89 (26.2)	17 (17.0)	0.059
Hypertension	187 (55.0)	52 (52.0)	0.597
Hyperlipidemia	149 (43.8)	43 (43.0)	0.884
Diabetes	93 (27.4)	35 (35.0)	0.168
CVD family history	76 (22.4)	17 (17.0)	0.249
Other CVD or medical conditions			
Previous MI	72 (21.2)	30 (30.0)	0.066
Heart failure	18 (5.3)	5 (5.0)	1.0
Arrhythmias	19 (5.6)	10 (10.0)	0.05
Stroke	15 (4.4)	4 (4.0)	0.559
Mental disorder	12 (3.5)	6 (6.0)	0.261
Cancer	26 (7.6)	14 (14.0)	0.073
Past reperfusion strategies			
CABG	31 (9.1)	9 (9.0)	0.576
PCI	31 (9.1)	5 (5.0)	0.218

CVD: Cardiovascular disease; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft

Table 10 describes the differences in the treatments and procedures received by the AMI patients during hospitalization by walking categories. The rates of use of beta-blockers (79.7% vs. 69%, p=0.03), ACE inhibitors (72.4% vs. 52.1%, p<0.001) and calcium channel blockers (74.1% vs. 55%, p<0.001) were significantly higher in the group of walkers than in the group of non-walkers.

With regard to supportive treatment (Table 10), more walkers received Ativan (41.2% vs. 30%, p=0.047). Walkers were less likely to have ventilatory support (11.8% vs. 22% p=0.014). The rates of tachy-arrhythmias (14% vs. 12.6%, p<0.001) and atrioventricular block (10.0% vs. 0.9%, p<0.001) were significantly higher in the group of non-walkers than in the group of walkers. Mortality rate was lower among the walkers compared with the non-walkers (2.1% vs. 25%, p<0.001) in-hospital. Bed rest prescription did not differ between the two groups while in hospital. However, the prescription of "activity as tolerated" (AAT) was more frequent among walkers than non-walkers (26.8% vs. 13%, p=0.005).

To better discriminate the time of first ambulation, four categories were created: 1) early walking time (within 48.99 hours of admission); 2) intermediate walking time (between 49 and 96.99 hours after admission); 3) late walking time (more than 97 hours after admission); and, 4) no walking. Of the 440 study patients, 115 (26.1%) walked during the first 48 hours (early walking); 98 (22.3%) walked between 49-96 hours (intermediate walking time); 127 (28.9%) walked after 96 hours (late walking); and 100 (22.7%) did not walk.

Table 10. Comparison of hospital treatment between walkers and non-walkers

	Walk while in hospital		
	Yes n=340 (77.3%)	No n=100 (22.7%)	p- values
Reperfusion strategies			
Thrombolysis n=103	75 (22.1)	28 (28.0)	0.228
PCI n=210	158 (46.5)	52 (52.0)	0.363
CABG n=32	30 (8.2)	2 (2.0)	0.191
Coronary angiography n=320	253 (74.4)	67 (67.0)	0.160
Evidence-based treatments			
Antiplatelet n=424	330 (97.1)	94 (94.6)	0.218
Aspirin n=391	304 (89.4)	87 (87.0)	0.475
Beta-blocker n=340	271 (79.7)	69 (69.0)	0.03
ACE inhibitor n=299	246 (72.4)	53 (52.1)	<0.001
Cholesterol lowering n=261	205 (60.3)	56 (56.0)	0.488
Other medical interventions			
Nitroglycerin n=293	233 (68.5)	60 (60.0)	0.118
Heparin n=289	228 (67.1)	61 (61.0)	0.282
Insulin n=66	52 (15)	15 (15.0)	1.0
Inotropic agents n=99	73 (21.5)	26 (26.0)	0.34
Antiarrhythmics n=154	117 (34.4)	37 (37.0)	0.635
Calcium channel blockers n=307	252 (74.1)	55 (55.0)	<0.001
Diuretic n=125	95 (27.9)	30 (30.0)	0.706
Supportive treatment			
Analgesic agents n=273	210 (61.8)	63 (63.0)	0.192
Morphine n=210	156 (45.9)	54 (54.0)	0.172
Ativan n=170	140 (41.2)	30 (30.0)	0.047
Sedative (Lorazepam) n=210	172 (49.7)	38 (40.4)	0.069
Mechanical ventilation n=62	40 (11.8)	22 (22.0)	0.014
Bed rest prescribed n=231	182 (53.5)	49 (49.0)	0.428
Mobilization (AAT) prescribed * n=104	91 (26.8)	13 (13.0)	0.005
Complications			
Mortality=32	7 (2.1)	25 (25.0)	<0.001
Arrhythmias n=57	43 (12.6)	14 (14.0)	<0.001
Atrioventricular block n=13	3 (0.9)	10 (10.0)	0.001
Kidney failure	6 (1.8)	3 (3.0)	0.425

Table 11 shows the differences among groups in demographic characteristics. Almost all demographic variables showed significant differences among the four categories including gender ($p<0.001$), age ($p<0.001$), marital status ($p=0.037$), employment ($p=0.001$), site from which patient was referred to hospital ($p=0.007$), hospital ($p=0.025$) and LOS ($p <0.001$). The table also shows significant trends for some covariates across the four categories of walkers (all p values were <0.001 and are not in the table). With respect to age, a trend was observed: as age increased so did the number of hours to ambulation ($F=22.9$, $p < 0.001$). The proportion of males who walked fell from 80.9% among early walkers to 72.3% among intermediate walkers to 49.6% among late walkers (trend $p<0.001$). The proportion of employed patients who walked also fell from 51.7% among early walkers to 29.2% among late walkers and the proportion of employed patients was lowest among non-walkers (25.4%) (p for the trend <0.001).

Table 11. Patterns of ambulation and characteristics of AMI patients on admission to hospital

	In-hospital walkers by time of first ambulation			Did not walk	p* values
	0-48.99 hours n=115 (26.1%)	49-96.99 hours n=98 (22.3%)	=97 hours n= 127 (28.9%)	n=100 (22.7%)	
Demographic factors					
Male, No (%) n=291	93 (80.9)¥	68 (72.3) ¥	63 (49.6) ¥	67 (67.0)	<0.001
Female, No (%) n=149	22 (19.1)	30 (30.6)	64 (50.4)	33 (33)	
Age, median/n (min-max)	59/111 (30-84)	65/95 (30-94)	70.5/126 (38-94)	70.5/99 (33-95)	<0.001
Marital status[b] (%) n=420					0.037
Married	82 (73.9)	69 (73.4)	69 (58.0)	65 (67.7)	
Other	29 (26.1	25 (26.6)	50 (42.0)	31 (32.3)	
Employed[b] n=284					
Yes	45 (51.7) ¥	27 (40.9) ¥	21 (29.2) ¥	15 (25.4)	0.001
No	42 (48.3)	39 (59.1)	51 (70.8)	44 (74.6)	
Arriving on weekdays n=328	90 (78.9)	74 (75.5)	94 (74.6)	70 (70.7)	0.584
Patient referred from[c] n=427					0.007
Home	66 (57.9)	65 (67.7)	71 (57.7)	45 (47.9)	
Other hospital	35 (30.7)	22 (22.9)	40 (32.9)	46 (48.9)	
Other	13 (11.4)	9 (9.4)	12 (9.8)	3 (3.2)	
Hospital					0.025
General	81 (70.4)	52 (53.1)	65 (51.2)	62 (62.0)	
McMaster	19 (16.5)	23 (23.5)	39 (30.7)	18 (18.0)	
Henderson	15 (13.0)	23 (23.5)	23 (18.1)	20 (20.0)	
Total	115	98	127	100	
LOS, mean (SD), n=433	6.35 (7.4)	8.53 (7.0)	13.4 (10.6)	5.4 (7.5)	<0.001

* p values for overall four group differences, shown if <0.05. ¥ Statistically significant <0.001 gradient trend only for Chi Square test (Kendall's tau-b test) and regression analysis between walkers group for categorical and continuous variables respectively. Numbers do not add to 440 as a result of missing data in marital status[b] (n=20); employed[b] (n=156); patients referred from[c] (n=13).

With regard to their clinical status on admission (Table 12), there were significant differences among the four categories in systolic blood pressure ($p=0.017$), diastolic blood pressure ($p<0.001$), and Killip functional class ($p<0.001$). This table also highlights the variables that showed significant trends along the four categories of walkers (all p values were<0.001 and are not in the table). In systolic ($F= 9.87$, $p<0.001$ for trend) and diastolic blood pressure ($F=19.9$, $p<0.01$ for trend) it was evident that as blood pressure measures went

down, patients were likely to take longer before beginning to walk. The proportion of patients with Killip I-II scores among those who walked early was highest (91.3%) and fell significantly to 66.9% among those who walked late (Chi Square test=4.34, p for a trend <0.001).

Table 12. Patterns of ambulation and characteristics on admission to hospital

	In-hospital walkers by time of first ambulation			Did not walk	
	0-48.99 hours n=115 (26.1%)	49-96.99 hours n=98 (22.3%)	=97 hours n= 127 (28.9%)	n=100 (22.7%)	p-value *
Level of consciousness n=387					0.373
Alert	99 (96.1)	74 (90.2)	107 (93.0)	77 (88.5)	
Other consciousness levels	4 (3.9)	8 (9.8)	8 (7.0)	10 (11.5)	
Type of MI n=440					0.409
STEMI	76 (66.1)	61 (62.2)	72 (56.7)	58 (58.0)	
Non-STEMI	39 (33.9)	37 (37.8)	55 (44.3)	42 (42.4)	
Cardiac specific enzymes					
Troponin, mean ng/ml (SD)/n	92 .3 (168.9)/111	71.57 (147.5)/93	50.4 (99.6)/125	86.2 (166.9)/97	0.130
Creatin Kinase MB,mean ng/ml (SD)/n	867.8 1049.2)/105	819.5 (1311.6)/89	976.3 2198.1)/107	939.7 (1364.05)/92	0.903
Vital signs on admission (n=440)					
Mean heart rate, bpm (SD)/n	82.09 (24.3)/112	81.2 (19.4)/98	85.5 (25.9)/ 127	80.6 (21.07)/98	0.372
Mean systolic blood pressure, mmHg, (SD)/n	141.4 (30.6)/114 ¥	139.1 (27.1)/97¥	132.4 (29.9)/127¥	130.3 (29.1)/96	0.017
Mean diastolic, blood pressure, mmHg, (SD)/n	84.5 (17.7)/114¥	81.8 (19.2) ¥	74.3 (18.4) ¥	75.3 (18.7)/96	<0.001
AMI Killip class (n=440)					
I-II	105 (91.3) ¥	79 (80.6) ¥	85 (66.9) ¥	73 (73.0)	<0.001
III-IV	10 (8.7)	19 (19.4)	42 (33.1)	27 (27.0)	

p-values for overall group differences, shown if <0.05.¥ Statistically significant <0.001 gradient trend only for Chi Square test (Kendall's tau-b test) and regression analysis between walkers group for categorical and continuous variables respectively .

Table 13 shows the relationship between past medical history and time of first ambulation. Significant differences (Chi square) in walking behaviour are observed for cardiovascular family history (p<0.001) and stroke (p=0.02). The table also highlights the variables that showed significant trends along the four categories of walkers (all p values were <0.001 and are not in the table). A

significant trend (decreasing direction from early walkers) was observed for two variables – family history of CVD and current smoker. The proportion of patients with a family history of CVD was higher among early walkers (31.3%), and decreased across the other categories of walkers showing a significant trend (Chi Square =3.45, p for a trend <0.001). Furthermore, a significant decreasing trend was observed for the group of current smokers. A larger proportion of current smokers were intermediate walkers (31.6%) compared with the other categories of walkers (Chi Square trend analysis=2.40, p= 0.016).

Table 13. Patterns of ambulation and past medical history

Factor	In-hospital walkers by time of first ambulation			Did not walk	p-value*
	0-48.99 hours n=115 (26.1%)	49-96.99 hours n=98 (22.3%)	≥97 hours n=127 (28.9%)	n=100 (22.7%)	
Conventional CVD risk factors					
Former smoker, n=111	30 (26.1)	24 (24.5)	33 (26)	24 (24.0)	0.979
Current smoker, n=106	32 (27.8) ¥	31 (31.6) ¥	26 (20.6) ¥.	17 (17.0)	0.055
Hypertension, n=239	57 (49.6)	64 (65.3)	66 (52)	52 (52.0)	0.097
Hyperlipidemia, n=192	54 (47.0)	50 (51)	45 (35.4)	43 (43.0)	0.103
Diabetes, n=128	28 (24.3)	27 (27.6)	38 (29.9)	35 (35.0)	0.376
CVD family history, n=93	36 (31.3) ¥	27 (27.6) ¥	13 (10.2) ¥	17 (17.0)	<0.001
Previous heart disease					
Previous MI, n=102	23 (20.0)	23 (23.5)	26 (20.5)	30 (30.0)	0.285
Angina, n=39	9 (7.8)	10 (10.2)	10 (7.9)	10 (10.0)	0.877
Heart failure, n=23	4 (3.5)	4 (4.1)	10 (7.9)	5 (5.0)	0.427
Arrhythmias, n=29	3 (2.6)	7 (7.1)	9 (7.1)	10 (10)	0.176
Other medical conditions					
Stroke, n=19	3 (2.6)	1 (1.0)	11 (8.7)	4 (4.0)	0.027
Mental disease, n=18	4 (3.5)	2 (2.0)	6 (4.7)	6 (6.0)	0.528
Cancer, n=40	10 (8.7)	5 (5.1)	11 (8.7)	14 (14.0)	0.183
Past reperfusion strategies					
CABG, n=40	10 (8.7)	11 (11.2)	10 (7.9)	9 (9.0)	0.852
PCI, n=36	11 (9.6)	13 (13.3)	7 (5.5)	5 (5.0)	0.102

* p-values for overall group differences, shown if <0.05. ¥ Statistically significant gradient <0.001 trend only for Chi Square test Kendall"s tau-b test) for categorical variables. CVD: Cardiovascular disease; PCI: percutaneous coronary intervention; CABG: Coronary artery bypass graft

Many in-hospital treatments were significantly related to the time of first ambulation (Table 14), but only some of the factors exhibited an increasing significant gradient from early walkers to non-walkers and others showed a decreasing significant gradient. The proportion of patients who underwent cardiac angiography fell from 83.5% in early walkers to 67% in late walkers (Chi Square test=3.11, p=0.015). More patients who walked early (before 49 hours) compared to those who walked later received reperfusion therapies such as thrombolysis (p=0.009) and PCI (p<0.001). However, the trend was only significant for PCI (Chi Square Test=1.92, p=0.05).

Table 14. Patterns of ambulation and hospital treatment (I)

Factor	In-hospital walkers by time of first ambulation			Did not walk	p-value*
	0-48.99 hours N=115 (26.1%)	49-96.99 hours N=98 (22.3%)	≥97 hours N= 127 (28.9%)	n=100 (22.7%)	
Reperfusion strategies					
Thrombolysis n=103	35 (30.4)	22 (23.5)	17 (13.4)	28 (28.0)	0.009
PCI n=210	71 (61.7) ¥	42 (42.9) ¥	45 (35.4) ¥	52 (52.0)	<0.001
CABG n=32	4 (3.5)	8 (8.2)	16 (12.6)	4 (4.0)	0.023
Cardiac angiography n=320	96 (83.5) ¥	72 (73.5) ¥	85 (66.9) ¥	67 (67.0)	0.015
Medical treatment					
Evidence-based interventions					
Antiplatelet n=424	112 (96.5)	95 (96.9)	124 (97.6)	94 (94.0)	0.516
Aspirin n=391	103 (89.6)	88 (89.8)	113 (89)	87 (87.0)	0.920
Heparin n=289	73 (63.5)	66 (67.3)	89 (70.1)	61 (61.0)	0.488
B-Blocker n=340	98 (85.2) ¥	79 (80.6) ¥	94 (74) ¥	69 (69.0)	0.024
ACE inhibitor n=299	89 (77.4)	66 (67.3)	91 (71.7)	53 (53.0)	0.001
Other interventions					
Nitroglycerin n=293	85 (73.9) ¥	73 (74.5) ¥	75 (59.1) ¥	60 (60.0)	0.013
Insulin n=66	10 (8.7) ¥	13 (13.3) ¥	28 (22) ¥	15 (15.0)	0.033
Inotropic agents n=99	17 (14.8) ¥	16 (16.3) ¥	40 (31.5) ¥	26 (26.0)	0.005
Antiarrhythmics n=154	42 (36.5)	28 (28.6)	47 (37)	37 (37.0)	0.513
Calcium channel blockers n=307	90 (78.3) ¥	69 (70.4) ¥	93 (73.2) ¥	55 (55.0)	0.002
Cholesterol lowering n=261	77 (67) ¥	64 (65.3) ¥	64 (50.4) ¥	56 (56.0)	0.031
Diuretic n=125	18 (15.7) ¥	31 (31.6) ¥	46 (36.2) ¥	30 (30.0)	0.003

* P values for overall group differences, shown if <0.05. ¥ Statistically significant <0.001 gradient trend only for Chi Square test (Kendall's tau-b test) and regression analysis between walkers group for categorical and continuous variables respectively.
PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft.

There was a downward trend from early walkers to non-walkers in the proportion of patients treated with nitroglycerin (73.9% to 60%, Chi Square test=2.89, p=0.004); calcium channel blockers (78.3% to 55%, Chi Square test=3.27, p<0.002); cholesterol lowering drugs (67% to 56%, Chi Square test = 2.37, p=0.018); and beta-blockers (85.2% to 69%, Chi Square test=3.11, p=0.02). There was an upward trend from early walkers to non-walkers in the proportion of patients treated with insulin (8.7% to 15%, Chi Square test=-2.08, p=0.03); inotropic agents (14.8% to 26%, Chi Square test = -2.91, p<0.001); and diuretics (15.7% to 30%, Chi Square test= -2.76, p=0.003) (Table 14).

Finally, related to supportive treatment (Table 15), two variables (mobilization/AAT, mechanical ventilation) differed significantly across walker categories (p= 0.025 and p<0.001 respectively) and showed significant trends. The proportion of patients having a prescription in their chart for mobilization or activity as tolerated showed a decreasing trend from 27.8% in early walkers to 23.6% in late walkers (Chi Square test=2.8, p=0.005) to 13% in non-walkers. Patients receiving mechanical ventilation showed a trend from 3.5% in early walkers to 22.8% in late walkers (Chi Square test=-5.2, p<0.001) to 22% in non-walkers (Table 15).

Tabla 15. Patterns of ambulation and hospital treatment (II)

Factor	In-hospital walkers by time of first ambulation			Did not walk	p-value *
	0-48.99 hours n=115 (26.1%)	49-96.99 hours n=98 (22.3%)	≥ 96 hours n= 127 (28.9%)	n=100 (22.7)	
Supportive treatment					
Analgesic agents n=332	92 (80)	78 (79.6)	89 (70.1)	73 (73.0)	0.213
Morphine n=210	53 (46.1)	50 (51)	53 (41.7)	54 (54.0)	0.266
Lorazepam n=170	50 (43.5)	38 (28.8)	52 (40.9)	30 (30.0)	0.206
Laxative n=122	27 (23.5)	36 (36.7)	31 (24.4)	28 (28.0)	0.127
Bed rest prescription n=231	64 (55.7)	54 (55.1)	64 (50.4)	49 (49.0)	0.696
Mobilization/AAT prescription n=104	32 (27.8) ¥	29 (29.6) ¥	30 (23.6) ¥	13 (13.0)	0.025
Complications					
Mechanical ventilation n=62	4 (3.5) ¥	7 (7.1) ¥	29 (22.8) ¥	22 (22)	<0.001
Pacemaker n=24	5 (4.3)	4 (4.1)	9 (7.1)	6 (6.0)	0.718

* p-values for overall group differences, shown if <0.05. ¥ Statistically significant <0.001 gradient trend only for Chi Square test (Kendall"s tau-b test) and regression analysis between walker groups for categorical and continuous variables respectively.

Post-hoc Analysis

A post-hoc subgroup analysis was performed in order to examine the differences between early, intermediate and late walkers in terms of patient and care-related factors observed in the bivariate analyses. Post-hoc analysis was performed to evaluate the differences observed between the walking categories and the related factors. Tukey-HSD test was performed to examine differences among the three groups of walkers with respect to the quantitative factors following ANOVA analysis. A pair-wise analysis was performed to determine the difference in categorical factors across the three categories of walking: early, intermediate, and late (Norman & Streiner, 2000).

Post-hoc analysis did not reveal significant differences between early and intermediate walkers or between intermediate and late walkers. With respect to early and late walkers, post-hoc analysis of continuous variables identified differences in age and diastolic blood pressure (Table 16). Early walkers were younger than late walkers (59.0, SD 12.6 vs. 70.5, SD 12 years; F=24.3, $p<0.001$). Early walkers had a higher diastolic blood pressure compared to late walkers (84.5 SD 2.3 vs 74.3 SD 2.6; F =26.2, $p<0.001$).

The pair-wise analysis for categorical variables was performed selecting the early walkers category as the reference group and comparing it first with intermediate and then with late walkers (Table 16). The aim of this analysis was to examine more closely the differences in the factors that were significant in the bivariate analysis. Significant differences were observed between early and late walkers for the following factors: more men walked earlier (80.9%) than later (49.6%) (Chi square 5.32, $p<0.001$). Killip class I-II (uncomplicated) patients walked earlier (91.3%) than later (66.9%) (Chi square 4.91, $p<0.001$). Patients with a family history of CVD walked earlier (31.3%) than later (10.2%) (Chi Square 4.11, $p<0.001$). Those who received thrombolysis walked earlier (30.5%) than later (13.4%) (Chi square 3.22, $p<0.001$) as did those who had a cardiac angiography (83.5% vs. 66.9%) (Chi square 3.08, $p < 0.002$). Patients who received PCI walked earlier (61.7%) than later (35.4%) (Chi square 4.1, $p<0.001$). In terms of medical treatment, patients who received nitroglycerin walked earlier

(73.9%) than later (59.1%) (Chi square 2.40, p<0.016) and patients taking beta-blockers walked earlier (85.2%) than later (74.0%) (Chi square 2.22, p= 0.02).

Table 16. Post- hoc analysis between early and late walkers

Factor	In-hospital walkers by time of first ambulation		p-value
	0-48.99 hours n=115 (26.1%)	**≥ 96 hours n= 127 (28.9%)**	
Demographic factors			
Age, mean (SD)	59 (12.6)	70.5 (12)	<0.001
Male, No (%)	93 (80.9)	62 (49.6)	<0.001
Vital signs			
Diastolic blood pressure, mean (SD)	84.5 (2.37)	74.3 (2.65)	<0.001
Killip I-II n (%)	105 (91.3)	84 (66.9)	<0.001
Conventional CVD factors, n (%)			
CVD family history	36 (31.3)	13 (10.2)	<0.001
Reperfusion strategies, n (%)			
Cardiac angiography	96 (83.5)	85 (66.9)	0.002
PCI	71 (61.7)	45 (35.4)	<0.001
Medical treatment, n (%)			
Thrombolysis	35 (30.5)	17 (13.4)	<0.001
B-Blockers	98 (85.2)	94 (74.0)	0.02
Nitroglycerin	85 (73.9)	75 (59.1)	0.016

Time to Event Analysis

The survival analysis comprises the analysis of accumulated data that takes into account the timing of events. The weighted relative risk over the entire study is presented as a hazard ratio (Guyatt & Rennie, 2002; Hosmer & Lemeshow, 1999). Survival analysis provides a method to compare the risk of an event in different groups, where the risk changes over time. The Cox regression analysis (for proportionality of hazards) used walking or not walking as the status variable and the difference in time between hospital admission and first walk as the time to event variable.

The primary goal of this analysis was to estimate the effect of study variables on first walk. Variables were selected for the multivariate time-to-event model analysis if they were significant in the bivariate analysis ($p \leq 0.05$) and in the post hoc analysis or if they were associated with an increasing or decreasing significant gradient. The selected variables included: gender, age, smoking status, referral source, employment status, marital status, systolic and diastolic blood pressure, length of hospital stay, Killip functional class, family history of cardiovascular disease, arrhythmia and stroke. The treatment and in-hospital procedure variables were thrombolysis, PCI and CABG. Treatment variables that were also included were cardiac angiography, beta-blockers, ACE inhibitors, nitroglycerin, calcium channel blockers, cholesterol lowering drugs, insulin, diuretic, inotropic drugs, mechanical ventilation, arrhythmias-in hospital and prescription of activity as tolerated.

A number of factors emerged in the survival analysis as positively associated with EA after AMI (Table 17). Males were 47% more likely to walk early than females (hazard ratio (HR) 1.47; 95%CI 1.15, 1.87, p=0.002). Patients with a family history of CVD were 33% more likely to walk early compared with patients who did not have this family history (HR 1.33; 95%CI 1.00, 1.44 p=0.05). Factors related to treatment during hospitalization show that patients having thrombolysis were 47% more likely to walk early compared with patients not receiving thrombolysis (HR 1.47; 95%CI 1.11, 1.49 p=0.007). Patients receiving nitroglycerin were 51% more likely than patients not receiving this treatment to walk early (HR 1.51; 95%CI 1.19, 1.93 p<0.001). Patients receiving calcium channel blockers were 58% more likely to walk early than patients not receiving calcium channel blockers (HR 1.58; 95%CI 1.22, 2.05 p < 0.001).

Factors were also negatively associated with EA (Table 17). Patients > 59 years of age were 2% less likely to walk early (HR= 0.98; 95%CI 0.97, 0.99 p<0.001); those having arrhythmia in hospital were 52% less likely to walk early (HR= 0.48; 95%CI 0.24, 0.94 p<0.041). Those receiving inotropic drugs were 28% less likely to walk early (HR= 0.72; 95%CI 0.53, 0.98, p<0.001). Finally, those who had CABG were 49% less likely to walk early (HR= 0.51; 95%CI 0.33, 0.78, p=0.002).

Table 17. Factors associated with early ambulation on multivariate survival analysis

Factors	Hazard Ratio	95% CI	p-value
Positively associated			
Male sex	1.47	1.15-1.87	0.002
CVD family history	1.33	1.00-1.44	0.050
Thrombolysis	1.47	1.11-1.49	0.007
Nitroglycerin	1.51	1.19-1.93	0.001
Calcium channel blockers	1.58	1.22-2.05	<0.001
Negatively associated			
Age > 59 years	0.98	0.97-0.99	<0.001
In-hospital arrhythmia	0.48	0.24-0.94	0.041
Inotropic drugs	0.72	0.53-0.98	<0.001
CABG	0.51	0.33-0.78	0.002

Proportional Hazard Assessment

The assessment of the fit of the proportional model included first an evaluation of the proportional hazards assumption for the covariates, including a global test. The overall test with nine degrees-of-freedom was not significant at p=0.15 which demonstrates the proportionality of the Cox regression model (Table 18). However, the individual tests demonstrated that the model was marginally non-proportional in gender with a significant p-value of 0.01 (Table 18). Based on the assumption that the model was not completely proportional in gender, I performed a stratified proportional hazard model to analyze the model without the gender variable (Table 19). From this analysis, I observed that the overall test with eight degrees-of-freedom was not significant at p=0.66. Thus, the overall and the individual tests for each covariate demonstrated that the model

was proportional. The general stratification on gender improved the adherence to the proportional hazard assumption to the point that we are comfortable making inferences on the remaining covariates (Hosmer & Lemeshow,1999). The plots of the scaled Schoenfeld residuals illustrated in Figure 4 additionally supported the assumption of proportional hazards for each of eight covariates. The graphs proved that all covariates have zero slopes. (Hosmer & Lemeshow, 1999, p. 213).

Overall, this analysis supports the survival analysis model, with the exception of the gender variable (Table 19). The final model includes factors that were found to be positively associated with EA including family history of cardiovascular disease and treatment factors such as thrombolysis, and taking calcium channel blockers or nitroglycerin. The model also supports factors that were negatively associated with EA including being over 59 years of age, having arrhythmias while in hospital, receiving inotropic drugs and having a CABG.

Table 18. Test of proportional hazards assumptions

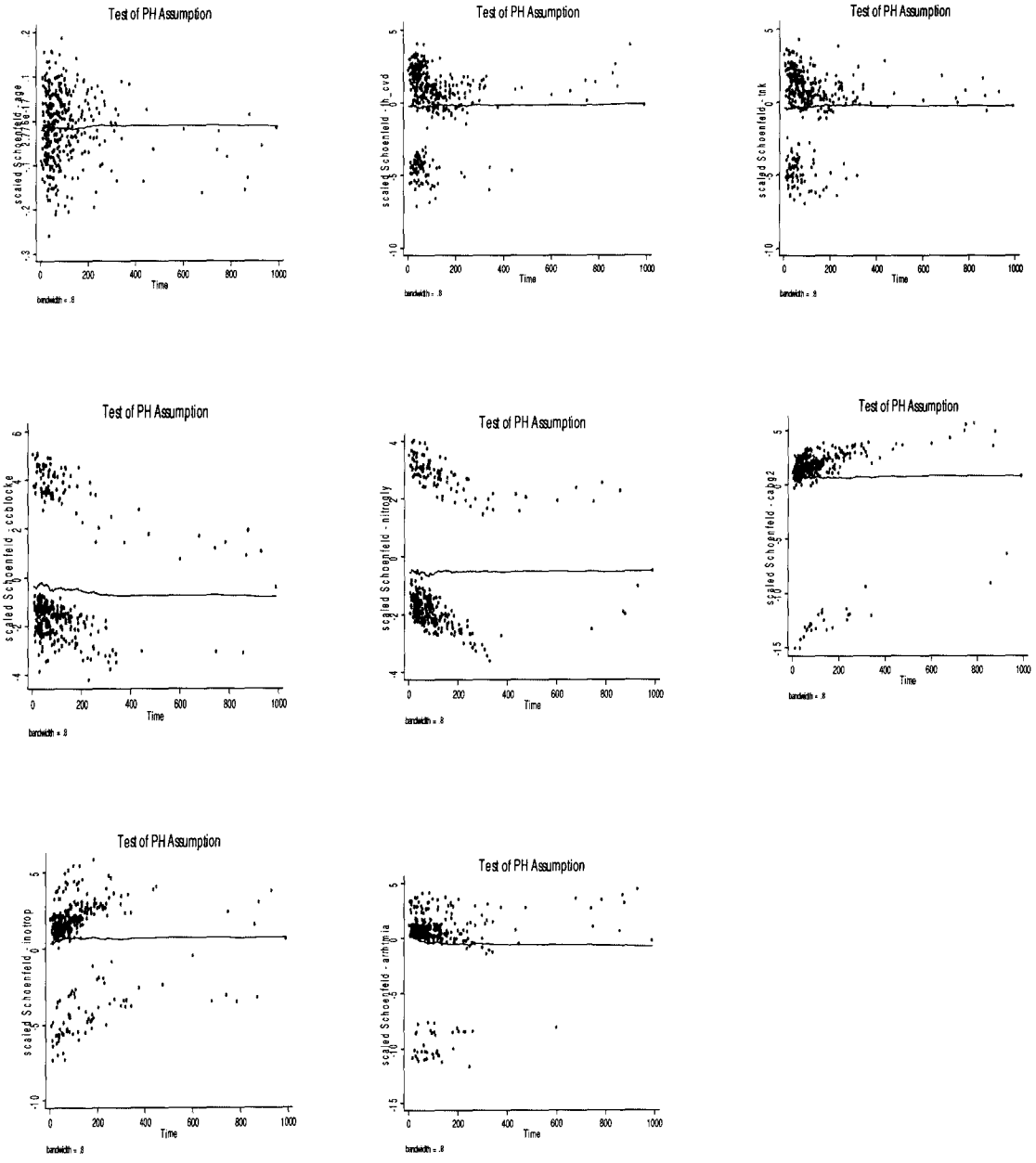
Covariates	rho	Chi2	dif	Prob> Chi2
Gender	-0.13263	5.79	1	0.0161*
Age	-0.01373	0.06	1	0.8052
Family history CVD*	0.05125	0.92	1	0.3377
Thrombolysis	0.02967	0.31	1	0.5797
Calcium channel blockers	-0.09080	3.02	1	0.0821
Nitroglycerin	-0.01027	0.03	1	0.8527
Inotropics	0.02668	0.26	1	0.6121
CABG*	0.01036	0.04	1	0.8459
In Hospital arrhythmias	-0.04696	0.79	1	0.3739
Global test		12.23	9	0.1527

*CVD: Cardiovascular disease; CABG: coronary bypass graft. Gender p value is significant and violates the Proportionality of the model

Table 19. Test of stratified proportional hazards. Final model

Variable	rho	Chi2	df	Prob>chi2
Age	-0.00638	0.01	1	0.9090
Family history CVD	0.05027	0.88	1	0.3470
Thrombolysis	0.03229	0.36	1	0.5472
Calcium Channel blockers	-0.09480	3.26	1	0.0709
Nitroglycerin	-0.00528	0.01	1	0.9244
Inotropics	0.02330	0.19	1	0.6589
CABG	0.00446	0.01	1	0.9341
In-hospital arrhythmia	-0.04411	0.70	1	0.4027
Global test		**5.83**	**8**	**0.6660**

Figure 4. Proportionality assessment of the model



Secondary Analysis

Association Between Initiation of Ambulation and Heart Rate at Discharge

There was no statistically significant difference in mean heart rate at discharge among groups (70.9 bpm for early walkers; 71.9 bpm for intermediate walkers, 73.6 bpm for late walkers, and 72.4 bpm for non-walkers p=0.503).

Association Between Initiation of Ambulation and In-Hospital Mortality

There were 32 in-hospital deaths (7.3%) among the study participants. The mortality rate was lower for those who walked (2.1%) compared with those who did not walk (25%) (RR 12.4, 95%CI 5.41-27.2; $p < 0.001$) (Figure 5). Mortality was more frequent during the first week (59.4%), followed by the second week (21.8%) and beyond the fourth week (12.5%) (Figure 6). For patients who walked and then died there were 2 deaths (28.5%) before 49 hours, 2 deaths (28.5%) between 49 and 96 hours, 3 deaths (43%) after 96 hours (data not shown). Of the 25 deaths among those patients who did not walk, 20 (80%) occurred during the first week after admission (Figure 7).

Figure 5. Relationship between mortality and walking status

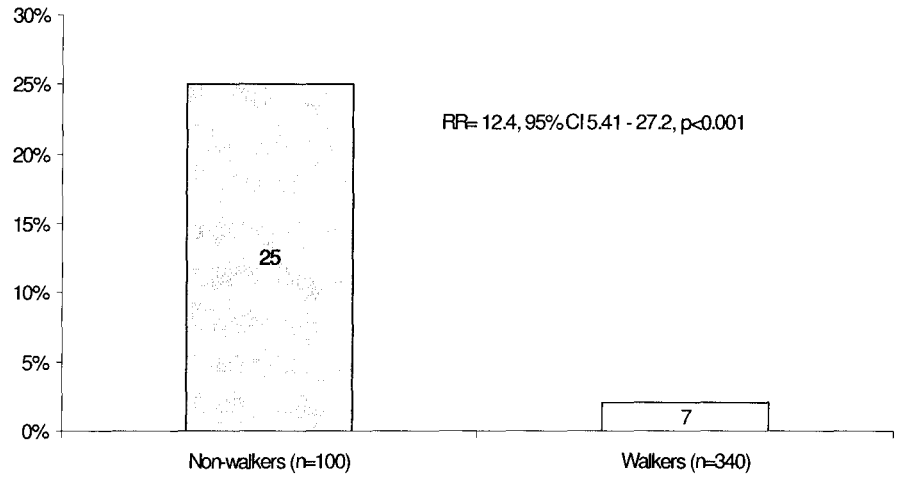


Figure 6. Time distribution of 32 fatal cases after admission

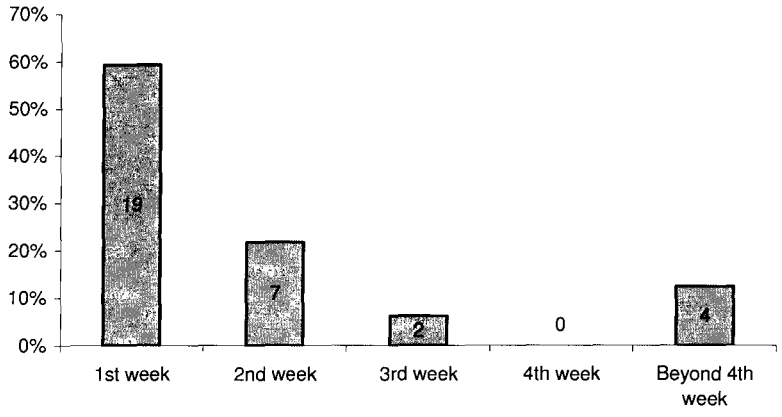
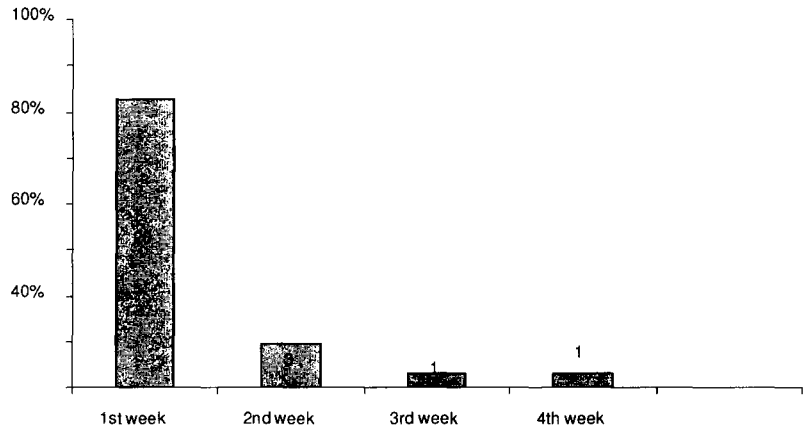


Figure 7. Time distribution of 25 fatal cases of non-walkers after hospital admission



Patients who died and those who survived were compared in terms of selected characteristics on admission, complications and in-hospital events (Tables 20 and 21). This exploration was done in order to identify possible reasons for death after an AMI that could have affected the probability of walking. Patients who died were more likely to arrive at the emergency department (ED) from home than those who did not die (63.3% vs 57.4%, p <0.022) and correspondingly, fewer of those who died were transferred from other hospitals compared with those who did not die (26.7% vs 34%). Furthermore, patients who died were more likely to be confused on arrival to the hospital compared with those who did not die (92.3% vs 71.3, p=0.005).

With respect to past medical history, patients who died were more likely to have had diabetes (50% vs 27.5, p=0.008) and a previous MI (37.5% vs 22.1%,

p=0.043). Although there were no significant differences, patients who died were more likely to have had previous PCI (12.5% vs 7.8%) and CABG (15.6% vs 8.6%) (Table 20).

Table 20. Comparison of admission factors between patients who did and did not die after AMI during hospitalization

Aspect	Factors	Dead	Alive	p-value
Transferred from other hospital, n(%)	Home Other Hospital	19 (63.3) 8 (26.7)	228 (57.4) 135 (34.0)	0.022*
Past medical history, n(%)	Hypertension Diabetes Previous MI Previous PCI Previous CABG	19(59.4) 16 (50.0) 12 (37.5) 4 (12.59 5 (15.69	220 (53.99 112 (27.59 90 (22.1) 32 (7.8) 35 (8.6)	0.58 0.008 0.043 0.260 0.153
Physical findings on admission to hospital, n(%)	Oriented Confused Unconscious	0 24 (92.3) 2 (7.7)	35 (9.7) 256 (71.3) 68 (18.9)	

MI: Myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft.

Those who died were more likely to have been assessed as Killip III-IV compared with those who did not die (75% vs 18.1%, p<0.001). Consistent with this, these patients had more complications during hospitalization than those who did not die such as cardiogenic shock (31.3% vs 6.6%, p<0.001), atrioventricular block (21.9 vs 1.5%, p<0.001), recurrent ischemia (6.3% vs 0.2%, p=0.015) and kidney failure (9.4% vs 1.5%, p=0.022). As a result, they were more confined by devices such as a pacemaker (12.5% vs 4.9%, p=0.087), mechanical ventilation (47% vs 11.5%, p<0.001), a central line (37.5% vs 16.7% p=0.006) and a swan ganz catheter (6.3% vs 4.7%, not significant) compared with those who did not die (Table 21).

Table 21. Comparison of complications and fatal events between patients who did and did not die after AMI during hospitalization

Complications and events	Dead n=32	Alive n=408	p-value
Killip n (%)			<0.001
I-II	8 (25.9)	334 (81.9)	
III-IV	24 (75.0)	74 (18.1)	
Devices and procedures, n (%)			
Pacemaker	4 (12.5)	20 (4.9)	0.087
Mechanical ventilation	15 (46.9)	47 (11.5)	<0.001
Complications n (%)			
Cardiogenic shock	10 (31.3)	27 (6.6)	<0.001
Atrioventricular block	7 (21.9)	6 (1.5)	<0.001
Recurrent ischemia	2 (6.3)	1 (0.2)	0.015
Kidney failure	3 (9.4)	6 (1.5)	0.022
Catheters, n (%)			
Central line	12 (37.5)	68 (16.7)	0.006
Swan ganz	2 (6.3)	19 (4.7)	0.462

Summary

Of the 440 patients who were included in the final analysis, 77.3% walked during hospitalization. One hundred fifteen (26.1%) walked during the first 48 hours (early walking), 98 (22.3%) walked between 49-96 hours (intermediate walking), and 127 (28.9%) walked after 96 hours (late walking). A total of 100 patients (22.7%) were categorized as non-walkers. There were 32 in-hospital deaths (7.3%) among the study participants. The mortality rate was lower for those who walked (2.1%) compared with those who did not walk (25%) (RR 12.4; 95%CI 5.41-27.2; $p < 0.001$). The majority of patients who died and had not walked died during the first week after admission (n= 80%). There was no statistically significant difference in mean heart rate at discharge between groups.

Factors that emerged in the survival analysis that were positively associated with EA after AMI were: having a family history of CVD, receiving thrombolysis, receiving nitroglycerin, and taking calcium channel blockers. Factors that were negatively associated with EA after AMI were age >59 years, having an arrhythmia during hospitalization, taking inotropic drugs, and undergoing coronary artery bypass surgery.

CHAPTER FIVE

DISCUSSION

Patterns of care in the treatment of AMI have evolved from promoting bed rest in the 1930s to promoting EA beginning in the 1970s (Wenger, 1996). Although over the years, EA has become a critical component of Phase I in-hospital CRPs (Wenger, 2008; Horton, 1999; Plowright, 2009), little is known about the patterns of in-hospital ambulation or the factors associated with ambulation of patients who have had an AMI. To the best of our knowledge, this is the first study that describes the timing of first ambulation during hospitalization among patients admitted for AMI, the predictors of first ambulation, and the association between initiation of ambulation and heart rate at discharge and between initiation of ambulation and in-hospital mortality.

Patient Characteristics

This retrospective cohort study involved the examination of the medical records of 440 patients who had been admitted with an AMI to one of three sites of a large tertiary hospital in Hamilton Canada during the year 2004. The study population is comparable to post-AMI patients described in the scientific literature as reflected by their median age (68 years old), the proportion of male patients (66.1%), and the prevalence of conventional risk factors (hypertension, smoking, dyslipidemia, diabetes) (Bramkamp, Radovanovic, Erne, Szuc, 2007; Meier et al., 2002). Patients with Killip class I-II AMIs (77.7%), indicating a lower risk of heart

failure, were slightly fewer than the proportion reported in the literature (80-90%) (Bramkamp, Radovanovic, Erne, Szucs, 2007; Meier et al., 2002). This may be because Hamilton Health Sciences is a tertiary referral hospital as opposed to a community hospital. The prevalence of STEMI (60.7%) was similar to that described in the literature (Bramkamp et al., 2007; Meier et al., 2002). Almost two-thirds were married (67.9%) and not employed (62%) and most were English-speaking (95.9%). About one-quarter had experienced a previous AMI (23.2%), about half had hypertension (54.3%) and hyperlipidemia (43.6%), and almost 10% (9.1%) had previously had CABG surgery or PCI (8.2%).

With respect to treatments for the current AMI, almost 50% had PCI (47.7%), about a quarter (23.4%) had thrombolysis, and 7.3% had a CABG. The current literature about discordance between treatment and level of risk of AMI patients showed that high risk patients receive treatment less frequently than those at low and moderate risk (Rogers, Canto, Lambrew, Tiefenbrunn, et al., 2000; Scott, Derhy, O'Kane, Lindsay, Atherton, Jones, 2007). Only one quarter of the charts (23.6%) included a prescription for ambulation or activity as tolerated.

The median length of hospital stay was 6 days, which is similar to the data presented by Tiemann (2008) for other countries such as England and France (6.0 days) and lower than Germany (6.9), Hungary (8.9), Italy (7.0), Poland (11.0), Spain (8.2) and Japan (11.0) (Tiemann, 2008). Laarman and Dirksen (2009) reported that in low-risk AMI patients, discharge within 48 hours of PCI might be feasible and safe. Out of interest, I examined LOS specifically for those

who had PCI (n=210) and found they had an average LOS of 5.9 days (SD 7.0 days) and for those who did not have PCI (n=229), the average LOS was 11.0 days (SD 9.9).

Patterns of Walking During Hospitalization

The first question this study sought to address was timing of first ambulation. About three-quarters (n=340; 77.3%) of 440 patients walked during their hospital stay. First ambulation tended to occur around 1100 hours (mean; SD 5.4 hours) about 3.5 days (median) into their hospital stay. About a quarter of the patients (26.1%) were "early walkers" walking within 49 hours of admission, another quarter (22.3%) were "intermediate walkers" walking within 97 hours of admission, another quarter (28.9%) were "late walkers" walking after 97 hours of hospital stay. The last quarter (22.7%) did not walk during their hospital stay.

There are at least three possible explanations for these differences in the timing of first ambulation. One might simply be that inadequate attention was paid by the health care providers to this aspect of care and orders for ambulation were not provided as early as they perhaps should have been or not provided at all and patients were ambulated in a happenstance manner. Noteworthy is that there were many inconsistencies between the physician orders related to bed rest and ambulation and the patients' actual mobilization pattern. About half the patients (n=231; 52.6%) were prescribed "bed rest"; 104 were prescribed "ambulation as tolerated (AAT); and 105 of the patients´ charts (23.8%) did not have any

prescription for ambulation. It is interesting to note that 78.8% of patients with a prescription for bed rest had walked and 87.5% of patients who had a prescription for ambulation/AAT had walked.

While there may have been verbal discussions related to mobilization, the order may not have been recorded in the medical chart. An argument against the happenstance approach to ambulation orders is the fact that "activity as tolerated" was ordered significantly more frequently for walkers (26.8%) than non-walkers (13%) indicating that there may have been clinical indications that prompted physicians to keep the non-walkers on bed rest. A future research study could use qualitative interviews of cardiologists to learn more about their prescribing habits related to ambulation and the criteria they consider when writing these orders.

Another explanation could be that some patients were discharged so early that they did not have time to ambulate. Interestingly, there was a statistically significant gradient in length of stay (LOS) with the non-walkers having the shortest mean LOS of 5.4 days while LOS for early walkers was 6.35 days, intermediate walkers 8.53 days and late walkers 13.4 days. This could imply that non-walkers were healthiest and therefore discharged early and that late walkers were least healthy requiring the longest LOS and time to ambulation. However, there were no statistically significant differences between walkers and non-walkers in clinical characteristics at baseline (i.e., vital signs, level of

consciousness, ST elevation, location of AMI, cardiac specific enzymes), Killip class, or receipt of reperfusion strategies.

A third explanation could be that non-walkers were the most severely ill with a large proportion dying before they could walk. Significantly more walkers came to hospital directly from home (60.7% for walkers vs. 47.9% for non-walkers) while more non-walkers were transferred from another hospital (48.9% for non-walkers vs. 29.1% for walkers) and significantly more non-walkers were first seen in a surgical unit (34% for non-walkers vs 17.6% for walkers) while walkers were first seen in an emergency department. Based on Killip class data, a larger proportion of non-walkers had a more severe AMI with 27% falling into the Killip III-IV class compared with 8.7% of early walkers and 19.4% of intermediate walkers. Consistent with this, 22% of non-walkers were put on mechanical ventilation compared with 3.5% of early walkers and 7.1% of intermediate walkers. However, the trend does not extend to the late walkers as more of them had a Killip class III-IV AMI (33.1%) than the non-walkers (27%) and a similar proportion were put on mechanical ventilation (22.8% for late walkers vs 22% for non-walkers). An analysis of patient data for non-walkers with a Killip III-IV classification indicated that about one quarter of them (27.6%) had important complications including mechanical ventilation (35.5%), pacemaker (25%), arrhythmias (76.9%), kidney failure (42.9%), heart failure (28.1%) and intra-aortic balloon pumping (29.4%) with a prolonged LOS of 12.45 days. These conditions are included in the definition of complicated AMI patients (Newby,

Califf, Guerci et al., 1996) and are consistent with the decision not to ambulate them early.

Another possible explanation why non-walkers had the shortest LOS may be that, given the patient's condition or the hospital's need for beds, s/he may have been transferred to their community hospital. Unfortunately, transfer data were not extracted from the charts.

One important difference is the mortality rate between the walkers (2.1%) and non-walkers (25%). However, when mean LOS was recalculated for non-walkers after excluding the patients who died, it did not change substantially (5.4 days for all non-walkers vs 4.9 days excluding those who died).

About 100 patients had no record of walking. There are a multitude of reasons for this. First, one quarter of these patients died (n=25). As mentioned above, some may have been transferred to their community hospital before walking. Although there were few statistically significant differences between those who walked and those who did not walk, those who did not walk tended to be sicker (e.g., cancer, on mechanical ventilation). Finally, there is the possibility that some of these patients did walk but it was not recorded on the medical record.

Predictors of First Ambulation

The second study question sought to identify the patient and care-related factors that determine initiation of ambulation. Those factors positively associated

with EA included the following: having a family history of CVD, received thrombolysis, and taking calcium channel blockers or nitroglycerin. Those factors negatively associated with EA were the following: being over the age of 59 years, experiencing an arrhythmia during their hospital stay, receiving inotropic drugs, and having CABG.

Patients with a family history of CVD were 33% more likely to walk early. This factor is a non-modifiable risk factor due to its genetic origin. While this has not been studied in previous research, a hypothesis is that patients who are aware of this family history may be more aware of the importance of exercise in cardiac rehabilitation after an AMI which may have prompted them to push for earlier ambulation (Hollman, Olsson, Ek, 2006).

Patients who had thrombolysis were 47% more likely to walk early than those who had not had this intervention. Pharmacological reperfusion using thrombolytic therapy within 12 hours of symptom onset decreases mortality rate in AMI patients. Studies have found that thrombolysis reduces the occurrence of arrhythmic events independent of left ventricular function (Fuster, 1993; Chesebro, Badimon, Ortiz, Meyer & Fuster, 1993). This effect may be the result of a favourable action on the cardiac sympathovagal balance (Pedretti, Colombo, Sarzi Braga & Carù, 1994). Although we did not record the time of thrombolysis administration in the emergency room, it is known that rapid initiation of thrombolysis at the earliest presentation increases activity status (Avorn, Knight, Ganz & Schneeweiss, 2004). Timely administration of this therapy decreases

myocardial infarct size and lessens the incidence of congestive heart failure thereby optimizing functional status (Avorn, Knight, Ganz & Schneeweiss, 2004). It would stand to reason that patients who have had thrombolysis might ambulate earlier given that its administration reduces or avoids many of the negative effects of an AMI that might complicate EA (i.e., infarct size, arrhythmias) and improves other effects (i.e., preservation of left ventricular function).

Those who received nitroglycerin were 51% more likely to walk early than those who did not receive it. Nitrates have been used to treat CAD for more than a century (Murrell, 1879). Nitroglycerin is indicated for patients with unstable angina and NSTEMI within the first 48 hours for treatment of persistent ischemia. Studies have shown how this intervention relieves ischemic discomfort, controls hypertension, improves pulmonary congestion, and also preserves the left ventricular function (Yusuf, Collins, MacMahon & Peto, 1988). This is likely because administration of nitroglycerin in the acute phase of AMI produces a rapid effect lowering the pulmonary artery wedge pressure concomitant with decreasing systemic blood pressure without affecting total peripheral vascular resistance, cardiac output and heart rate. Furthermore, the benefit of nitrates may be related to the concomitant use of aspirin, thrombolytics and beta-blockers (Morris, Zaman, Smyllie & Cowan, 1995). It may be that through reduction of ischemia and its associated discomfort and improvement in pulmonary congestion, AMI patients are better able to ambulate than those who did not receive nitroglycerin.

Patients who received calcium channel blockers were 58% more likely to walk early than those who did not receive them. The positive action of calcium channel blockers is more difficult to explain due to its associated treatment limitations. Calcium channel blockers do not reduce the risk of initial recurrent infarction or death when given routinely to patients with AMI or unstable angina. For example, verapamil and diltiazem, both calcium channel blockers given to patients in whom beta-blockers are ineffective or contraindicated, relieve ischemia and control the rapid ventricular response associated with atrial fibrillation (Mehta, Bossone & Eagle, 2000). Both, however, are contraindicated in patients with STEMI and associated systolic left ventricular dysfunction.
The positive effect on EA is explained by a study by Nolan et al. (2007). In their study, Nolan et al. (2007) assessed HRV in patients after an AMI. Approximately 15% of patients had a decreased HRV resulting from a withdrawal of vagal efferent activity and vagal antagonism secondary to sympathetic overactivity. They reported that HRV increases as a consequence of compound treatment (i.e., beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors) and exercise. It would support the reason why patients who have had calcium channel blockers, concomitant with beta-blockers, thrombolysis, and angiotensin converting enzyme might ambulate earlier given that its administration improves HRV allowing a proper response to exercise.

Patients over 59 years of age were 2% less likely to ambulate early (before 49 hours) than patients less than 59 years of age. This is consistent with other

studies in which older individuals have lost their ambulatory ability secondary to an acute condition (Brown et al., 2006). Comorbidities such as hypertension and diabetes in older adults slow orthostatic responses when standing after several days in bed (Ferrer-Hita, Domínguez-Rodríguez, García-González, Abreu-González, Samimi-Fard & Marrero-Rodríguez, 2008). Scott et al. (2007) identified increasing age as the most frequent and independent predictor of the omission of treatments such as fibrinolytic therapy, primary angioplasty and referral to cardiac rehabilitation after discharge. It is possible that the older patients could be perceived as having more health-compromising factors and could receive less attention related to mobilization, especially if the care provider perceives that it would require more time and more than one person to provide this care to these patients.

Patients who experienced an arrhythmia during hospitalization were 52% less likely to walk early after their AMI. Arrhythmia commonly presents after AMI. AMI patients who report sustained ventricular tachycardia, atrioventricular block, fibrillation, electromechanical dissociation, or asystole within the first four days after admission are considered complicated and not eligible for early discharge (Kaul et al., 2004). These complications can be precipitated by structured degeneration of the conduction system related with AMI. Given that some type of arrhythmias decrease cardiac output and tissue perfusion acutely and can lead to stroke and/or sudden death, it is likely that care providers would keep these

patients on bed rest and that they would not be ambulated early (Saczynski et al., 2009).

Patients who were prescribed inotropic drugs, used to treat patients with heart failure, were 28% less likely to walk early after their AMI. This treatment improves contractile function, cardiac output and left ventricular diastolic pressure (Chatterjee & De Marco, 2003). Exposure to inotropic drugs can lead to functional decline particularly among individuals with co-morbid health problems and systemic failure. Functional decline could hinder EA (Perme & Chandrashekar, 2009). In this study, patients taking inotropic drugs had a longer length of stay than those who did not receive this treatment (12.5 days SD 12.1 vs 7.48 days SD 7.5, $p < 0.001$).

Those who had CABG surgery were 49% less likely to walk early than late (12.5%) after their AMI. CABG surgery has been identified as a significant independent predictor of increased postoperative LOS (Nickerson, Murphy, Davila, Schechtman & Kouchoukos, 1999). The average length of hospital stay after CABG is seven days (Ovrum, Tangen, Schiøtt & Dragsund, 2000). These patients may need more time in bed given that some require mechanical ventilation and others have mediastinal drains and arterial lines. Although some literature states that these patients can be ambulated on the third day (Ovrum et al., 2000) in the current study, those who had CABG had a LOS of 14.9 days (SD 9.67), which is longer than those having PCI with a LOS of 6.0 days (SD 7.0) and longer than those having thrombolysis with a LOS of 5.6 days (SD 5.5). About a

third of patients who had CABG (37.5%) were classified as Killip III-IV. This procedure impedes EA (Morris, 2007) which likely explains the low hazard ratio of 0.51.

Through their awareness of the factors that predict EA of hospitalized AMI patients, clinicians can identify those patients who would benefit more from participating in the first phase of cardiac rehabilitation. Perhaps more importantly, knowing the factors that negatively influence walking may help clinicians to focus on the patients less likely to walk to provide the support and assistance they may require for clinically appropriate ambulation and rehabilitation. Given that this is one of the first studies to identify such predictors, these data may form the beginning of an algorithm for identifying patients who can be ambulated early. As more studies are completed with varied populations and other non-medical predictors that were not available in these medical records (i.e., depression, stress), the algorithm can be refined.

Association Between First Ambulation and Heart Rate at Discharge

The secondary analysis identified a non-statistically significant gradient in mean heart rate at discharge between groups of walkers (70.9 bpm for early walkers, 71.9 bpm for intermediate walkers, 73.6 bpm for late walkers, and 72.4 bpm for non-walkers p=0.503). The reduction of heart rate at discharge was expected in this study as a result of treatment (i.e., beta blockers). While there was no significant difference between groups of walkers, there was a significant

reduction in heart rate for the entire sample from the time of admission to discharge (mean difference -10.5, SD 25.1 (82.5 vs 72, p=0.009). The reduction in HR is a positive effect secondary to taking beta-blockers in all patients having AMI. Although some studies by La Rovere et al. (2002) have identified a relationship between exercise and heart rate and HRV, there are no studies indicating modifications in favour of HR reduction during phase I cardiac rehabilitation.

The management strategies for AMI are aimed toward establishing and maintaining reperfusion in the infarct-related artery. This also includes early prevention of arrhythmias, maintaining satisfactory balance between myocardial oxygen consumption and the recovery of the vagal tone after AMI. Exercise, in terms of walking early after AMI, would sustain the reason for beginning phase I rehabilitation in terms of improving parasympathetic responses (i.e., increasing vagal tone) which stimulates an increase in HRV. This would prepare the individuals for discharge and to assume daily activities by the time they are discharged home.

Association Between First Ambulation and In-Hospital Mortality

There were 32 in-hospital deaths among the study participants (7.3%), with a mortality rate of 2.1% in those who walked and 25% in those who did not walk (RR 12.4, 95%CI 5.41-27.2; $p < 0.001$). The in-hospital mortality rate (7.3%) was lower than the 9.7% in-hospital post-AMI death rate reported for Canada

during 2004 (Tu, Nardi, Fang, Liu, Khalid, Johansen, 2009). The majority of patients who died (25/32 = 78%) did not walk at any time during hospitalization and 59% (19/32) died during the first week after admission. This is consistent with our results that showed a shorter LOS for patients who died after AMI. For patients who walked and then died, there were 2 deaths (1.7%) before 49 hours, 1 death (1%) between 49 and 96 hours, and 3 deaths (3.2%) after 96 hours.

Furthermore, patients who died were classified as Killip III-IV indicating that they were at greater risk. They had more complications than the survivors (i.e., cardiogenic shock, atrioventricular block, recurrent ischemia and kidney failure) which is associated with a poor prognosis (Attaran et al., 2009). Patients who are this sick are not able to walk and health care providers are not likely to assume the risk of mobilizing them. Mortality is more frequent in this group given their complex health status.

Strengths and Limitations of the Study

The main strengths of this study were the retrospective cohort design, the high degree of intra-rater reliability in chart abstraction, and the planned survival analysis. Although generally perceived as a limitation, the retrospective data collection using charts added both efficiency and quality to this study for the following reasons: first, the chosen endpoint (first walk) was sufficiently important that nurses would record it. The first ambulation post-AMI is seen as an expression of achieving a level of physical well-being, confidence and recovery

that is likely to reflect important clinical changes. Therefore, using this event as the primary outcome enhanced internal validity and the chance to identify associated factors.

Second, the retrospective cohort study eliminated the chances of both recall and awareness bias from the nurses as the persons who had to provide ambulation as part of their practice. In other words, they did not have to recall when they first ambulated a patient (recall bias) and if they knew that this was the study's outcome of interest, it avoided their possibly ambulating patients earlier than they might ordinarily do (awareness bias).

Third, the use of medical records also offered the chance to observe a large number of patients increasing the power of the study to detect important factors. It is possible that ambulation may not have been recorded for all patients and that some of those labeled as non-walkers may have indeed walked and it may be possible that data regarding independent variables were also missing from the EMR. Although this may be a major threat to the study's validity, a chart review of patients observed to be walking on the wards showed that this event was generally recorded within about half an hour.

There was a lack of precision in the medical record about secondary aspects such as the distance walked or the assistance a patient received when ambulating. Therefore, a decision was made to not use these imprecise data. Survival analysis is intended to incorporate baseline risk differences. However, errors can occur in the measurement of time intervals for the occurrence of the

events. This potential source of imprecision was minimized by setting the time of "admission" to hospital as "zero time" for reference.

By study design, the relationship between ambulation and heart rate at discharge included more observations among patients with a better prognosis. The confounding effect of the time of recovery was treated by describing this relationship by strata of time (i.e., time in hospital and time of death for non-survivors). Data about important non-medical factors that could have influenced the timing of ambulation were not available due to incomplete recording of data by health providers, i.e., patient's language, religion, educational status, socio-economic status, and health-related factors such as depression and stress, or even having previously participated in a CRP. These data were not reported on admission making it impossible to explore their association with the first walk. Employment status was not recorded in sufficient detail to understand the nature of the patient's job. Other factors that were not recorded as well as they might have been were the timing of the beginning of symptoms. It is probable that patients had experienced pain 12 to 24 hours before arriving at the emergency department increasing the gap between cardiac ischemic and the beginning of the first phase of cardiac rehabilitation.

The validity of this study weighs heavily on the accuracy and consistency of the chart abstraction process. While many of the measures of intra-rater reliability indicated a high level of consistency in my abstraction of data twice from the same 40 charts, there were some kappas that indicated poor

consistency which led to re-abstraction of the 40 charts. It would have strengthened the study to have had a second individual abstract data from all the charts after we had both participated in a structured training program, assessed our inter-rater agreement initially and periodically throughout the abstraction process, and developed a process for dealing with discrepancies in our chart abstractions. Prior to beginning abstractions, we would also obtain a measure of the validity of our abstraction by asking a clinical expert to independently abstract a specified number of charts and then comparing our abstractions.

Implications of Study Findings for Practice

More than 30 years of research have shown the benefits of cardiac rehabilitation after AMI (Wenger, 2008). The National Institute for Health and Clinical Excellence (NICE, 2007) guideline for the management of secondary prevention following an AMI recommends that implementation of all phases of cardiac rehabilitation should be a key priority. This guideline highlights the importance of EA during phase I and II of cardiac rehabilitation in preparation for phases III and IV. In light of this recommendation, the findings of this study suggest there is work to be done to increase the number of patients ambulated sooner after their AMI.

Study findings confirmed that only a small proportion (26.1%) of uncomplicated patients walked within 48 hours of hospitalization. This is not consistent with the recommendations of the American Heart Association (AHA)

and the American College of Cardiology (ACC). Patients with uncomplicated STEMI, who are free of recurrent ischemic discomfort, symptoms of heart failure, or serious disturbances of heart rhythm should not be on bed rest for more than 12 to 24 hours (Level of evidence C) (Antman et al., 2008). Based on this recommendation, many of the intermediate and late walkers could have been ambulated earlier.

A significant challenge is the development, implementation and evaluation of an ambulation program for use in the intensive care unit (ICU) and on the wards. This includes the development of assessment tools and criteria for beginning and stopping mobilization of AMI patients. Educational programs are needed to teach all health care providers how to use the assessment tools, apply the criteria for initiating mobilization, overcome barriers to mobilization, and deal with particularly challenging situations such as multiplicity of vascular access, sedation, mechanical ventilation, obesity and time restraints (Morris, Zaman, Smyllie & Cowan, 1995).

There is recent emphasis on the involvement of an interprofessional team including physicians, nurses, physiotherapists, respiratory therapists, and nutritionists to organize an early mobility and walking program, based on an effective communication strategy among team members, the patient and his/her family. Perme & Chandrashekar (2009) describe an interprofessional rehabilitation program for intensive care patients including early mobility and walking. They propose a program that includes classifying patients based on

physical and hemodynamic assessments. They underline the importance of progressive mobility, individual functional capability (phases), and ambulation of patients according to specific criteria. Nurses assess the patients by reviewing their medical and surgical history, mental status, skin integrity, medications, and neurological status before initiating the program. The ambulation program can be modified for patients with special health issues (Perme & Chandrashekar, 2009).

Future Research

There is much research to be done in this area. While EA is supported by biological rationale and studies conducted in a general population of hospitalized medical patients (Allen et al., 1999), two systematic reviews (Herkner et al., 2003; Cortés et al., 2009) suggest that there is no conclusive evidence about the effectiveness of EA within the context of modern cardiac care. A well-designed trial is required.

This retrospective cohort study has begun to identify predictors of EA but more research is needed to examine other potential predictors that were not included in this study (i.e., depression, stress). As the predictors are identified, an algorithm could be created and tested to help clinicians identify which patients should be ambulated and the best time to initiate ambulation for patients with varying levels of AMI severity. Related to this is the need for further research to examine the relationship between patterns of EA and client outcomes such as health-related quality of life. Further research is also needed to determine the

quantity, duration and frequency of ambulation as well as strategies to facilitate progressive ambulation prior to discharge. Passive exercises may be warranted for those patients who cannot be ambulated earlier.

A qualitative study is needed to learn more about physician and nurse behaviours related to mobilization of AMI patients. For physicians, interviews might identify the criteria they consider when writing orders on the chart for bed rest or activity as tolerated and how consistently they update these orders. For both physicians and nurses, barriers and facilitators to mobilizing patients can be explored. More research is required to understand the patient, provider, and health system factors that explain why uncomplicated AMI patients are not ambulated.

Once an ambulation program is developed, its effectiveness in terms of patient/family (in-hospital and post-discharge health status, quality of life, and satisfaction), provider, and health system (e.g., LOS, rehospitalization, post-discharge resource utilization) outcomes should be evaluated using a randomized controlled trial. This program should focus not only on in-hospital care but also on the provision of family support and training for post-discharge care.

Although mobilization of AMI patients during hospitalization is an important step in initiating phase I of a cardiac rehabilitation program, not all patients are mobilized. This important aspect of recovery may become more challenging as hospitals continue to reduce the length of hospital stay for this population. This

study has provided data about the timing, predictors and outcomes associated with in-hospital ambulation and forms a foundation for future research in this area to evaluate the effectiveness of EA in the context of in-patient and out-patient cardiac rehabilitation programs.

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APPENDIX A

Early Mobilisation for Patients Following Acute Myocardial Infarction: A Systematic Review and Meta-analysis of Experimental Studies. ***International Journal of Nursing Studies, 2009.*** **Cortés, O.L., Villar, J.C., Devereaux, P.J., DiCenso, A.**

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Review

Early mobilisation for patients following acute myocardiac infarction: A systematic review and meta-analysis of experimental studies

Olga L. Cortes [a,b,*], Juan C. Villar [c], P.J. Devereaux [d], Alba DiCenso [e]

[a] School of Nursing, Universidad Industrial de Santander, Bucaramanga, Colombia
[b] School of Nursing, McMaster University, Hamilton, Ontario, Canada
[c] Grupo de Cardiologia Preventiva, Universidad Autónoma de Bucaramanga, Colombia
[d] Departments of Medicine and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada
[e] Nursing and Clinical Epidemiology & Biostatistics, McMaster University, Hamilton, Ontario, Canada

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ABSTRACT

Objective: To determine the impact of early mobilisation (EM) on total mortality and non-fatal re-infarction after acute myocardial infarction (AMI).
Design: Systematic review and meta-analysis.
Data sources: MEDLINE, CINAHL, HealthStar, EMBASE, the Cochrane Library Controlled Trials Registry and experts.
Methods: Target studies included published and unpublished experimental, controlled studies in any language comparing AMI patients allocated to any in-hospital early mobilisation or a control/standard treatment. Two reviewers independently assessed study eligibility and quality and performed data extraction. We calculated relative risks (RRs) and 95% confidence intervals (CIs) using the random-effects model.
Outcomes: All-cause mortality or re-infarction up to 1-year post-AMI.
Results: Out of 385 potentially relevant studies, 14 met our eligibility criteria (13 published before 1983). There were 149 deaths (9.3% of 1607) and 82 non-fatal re-infarctions (5.2% of 1580) among post-AMI patients receiving EM, compared with 179 deaths (11.6% of 1541) and 80 non-fatal re-infarctions (5.3% of 1518) among AMI patients receiving control treatment (RR = 0.85, 95% CI 0.68, 1.05 and RR = 1.02, 95% CI 0.75, 1.39 respectively).
Conclusion: Our meta-analysis demonstrated a trend towards decreased mortality with EM after AMI. However, there is uncertainty about early mobilisation and more research should be developed having into account all kind of differences among patients receiving treatment after AMI worldwide.

What is already known about the topic?

- Early ambulation is considered a common practice in the care of hospitalized patients having non-complicated acute myocardial infarction.
- During the hospital stay of the patient with acute myocardial infarction, there are no specific guidelines about bed rest or mobilisation.
- Some of the general guidelines for the care of patients with ST-MI or non-ST-MI briefly mention length of bed rest but the recommendation is not evidence-based.

What this paper adds

- The effect of early ambulation during the hospital stay of AMI patients remains uncertain, but it may be clinically important (15% reduction in total mortality).

* Corresponding author at: School of Nursing, Universidad Industrial de Santander, Faculty of Health Sciences, Carrera 32 # 29-31, Room 5 floor, Bucaramanga, Santander, Colombia. Tel.: +57 7 634 5745; fax: +57 7 634 5745.
E-mail address: cortesol@mcmaster.ca (O.L. Cortes).

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- Since early ambulation is an inexpensive and plausible intervention, this study should be seen as a call for new studies to rule out a potential benefit under the current standards of care.

1. Introduction

Major medical advances throughout the last 2 decades in the management of acute myocardial infarction (AMI) have resulted in a decrease in AMI mortality (Braunwald, 2002). In addition to reperfusion strategies (i.e. percutaneous transluminal coronary intervention [PTCI] or thrombolysis) and effective medications, other effective treatments include educational programs, targeted management of risk factors and the implementation of outpatient cardiac rehabilitation programs (Jollife et al., 2001; Oldridge et al., 1988; Taylor et al., 2004). In general, the earlier the initiation of these interventions after an AMI, the greater the benefit (Aversano et al., 2002; Fernandez-Aviles et al., 2004). Despite these significant advances, mortality after AMI remains substantial, and access to therapies is still limited. There is a need for further cost-effective interventions to ensure patients suffering an AMI survive.

Although bed rest has been less recommended as part of the in-hospital treatment to AMI patients, is still practiced and prescribed. Over the last decades there has been a trend to reduce the extent of the recommended bed rest, and the length of hospital stay for AMI patients towards the early discharge, not assuring with this the beginning of phase I rehabilitation at home. Mostly nurses have to make the decision of early ambulate these patients, but the guidelines to base this intervention even for complicated or uncomplicated AMI cases is very lack.

The American College of Cardiology/American Heart Association current guidelines for the care of patients after ST-segment elevation MI (STEMI) recommend bed rest for the first 12–24 h for uncomplicated patients and discourage mobilisation for complicated patients (level of evidence C) (Antman et al., 2005). The recommendation for patients with unstable angina and non-STEMI is bed rest with no specifics regarding timing or level of activity (level of evidence C) (ACC/AHA, 2002).

Although the introduction of reperfusion strategies has led to shorter hospital stays (thus reducing the bed rest) (Spencer et al., 2004), an average AMI patient in western countries stays, at the turn of this century, for about a week in hospital (Kauf et al., 2006), and even a month in Japan (Kinjo et al., 2004). Currently only half of AMI patients of developed countries (35% with STEMI and 60% with non-STEMI) undergo reperfusion strategies, which partially explains hospital stays longer than recommended (Kaul et al., 2004).

Prolonged bed rest, described as varying between 6 and 20 h, is associated with cardiac deconditioning (Chobanian et al., 1974; Saltin et al., 1968; Convertino et al., 1981; Allen et al., 1999; Miller et al., 1976). Studies have shown reduced stroke volumes (Chobanian et al., 1974) and oxygen peak uptake (VO_2) (Saltin et al., 1968) and increased heart rates among individuals exposed to prolonged bed rest (Convertino et al., 1981). A systematic review of 39 randomised controlled trials studying the effects of bed rest in a variety of clinical problems ($n = 5777$) showed a number of unfavourable results associated with bed rest (Allen et al., 1999). Prolonged bed rest has also been associated with increased risk of pulmonary embolism and cardiac arrhythmic death (Miller et al., 1976).

Despite the evolving patterns of care, a substantial group of AMI patients may still be exposed to prolonged bed rest. Since AMI patients are at higher risk of death during the first week after the event, determining the relative impact of mobilisation as part of their initial treatment remains important. We therefore undertook a systematic review and meta-analysis to address the following question: is there an impact on mortality and re-infarction rates among patients receiving early mobilisation after an AMI?

2. Methods

2.1. Eligibility criteria

We included studies of AMI inpatients receiving the conventional treatment at the time, in which the experimental intervention was early mobilisation (EM), defined as programmed changes of position from bed to chair, bed to standing, or bed to walking added to conventional care while in hospital. Eligible studies had to compare EM with prescribed bed rest or conventional care alone. We included experimental studies reported in any language, allocating (at random or not) participants to early mobilisation or a control intervention. Studies were eligible regardless of their language, time of publication, or publication status.

2.2. Study identification

We searched for eligible studies in MEDLINE (1966–2007), CINAHL (1966–1982), CINAHL online (1982–2008), HealthStar (1975–2008), EMBASE (1966–2008), and The Cochrane Library Controlled Trials Registry. The search terms were "myocardial infarction", "ischaemic/ischemic heart disease", "coronary disease", combined with "mobilisation/mobilization", "ambulation", "early ambulation", "rehabilitation" and "bed rest" in the title or abstract. We also searched manually for references in review articles, and asked experts for published or unpublished material with relevance for this review.

2.3. Study selection, quality assessment and data extraction

Our search strategy identified 385 unique citations. Two reviewers independently screened the titles and abstracts of each citation and identified all citations possibly containing studies of interest with any type of acute MI. All abstracts judged as potentially relevant for at least one reviewer were eligible for further appraisal using the full text version of the study. This screening process yielded 17 full text publications identified by one or both screeners for full review (Fig. 1). To determine eligibility, both reviewers independently evaluated these 17 full text

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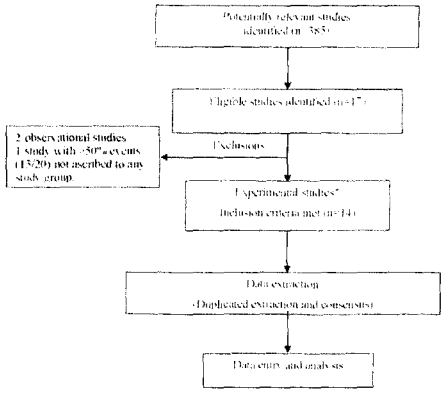

Fig. 1. Flowchart for selection of studies. Asterisk represents either randomised or pseudo-randomised

articles. Articles in languages different to English were screened and read by a collaborator. Discrepancies were discussed jointly until consensus was achieved.

Reviewers independently evaluated study quality by assessing whether patients were randomised to comparison groups, allocation was concealed, physicians were blinded to group allocation, and withdrawals and drop-outs were described (Jadad et al., 1996). We extracted data on the general characteristics of the studies, their population, intervention and outcomes. The outcomes of interest were all-cause mortality and non-fatal re-infarction during the first year after AMI. We followed the intention-to-treat principle, with the number of participants initially randomised serving as the denominator for the event rates. All disagreements were resolved using the consensus process described above. We computed Kappa agreement statistics for decisions on inclusion and quality appraisal.

2.4. Statistical analysis

Two pre-specified conditions determined the decision to pool individual study findings: (a) having more than 100 events overall and (b) finding symmetry in a funnel plot of the effects reported in the included studies (Oxman and Guyatt, 1992). Effect size estimates for the two outcomes of interest were computed for individual studies and the combined data. We computed relative risks (RRs) as summary measures of effect along with their 95% confidence intervals (95% CI) using the random-effects model. We pre-defined two subgroup analyses: (a) by categories of study quality: high, middle and low, and (b) by time when mobilisation was started (before versus after day 5 post-AMI). We also tested heterogeneity of the effect sizes computing Chi-square statistics. We entered data in duplicate and all calculations were done using Review Manager version 4.2 (The Cochrane Collaboration, Oxford, UK).

3. Results

3.1. Characteristics of the included studies

We identified 14 studies including 3148 patients that fulfilled our eligibility criteria (Fig. 1). The Kappa statistic for agreement on study eligibility was 0.77 (95% CI 0.26, 100). The reports of the included studies were published in English ($n = 12$) (19–30) and German ($n = 2$) (31–32). Ten of the studies were published before 1980 and only 1 after 1982. All studies enrolled patients defined as having uncomplicated AMI, except for Abraham et al. (1975), who enrolled patients with both complicated and uncomplicated AMI. Most studies included patients aged 55–65 years, with at least 70% male participants, except for one study that included only male participants (Messin and Demaret, 1982). The experimental intervention was similar across studies (stand up, move to chair, and walk) with the only difference being how many days post-AMI their EM intervention was initiated. The general characteristics of the included studies are shown in Table 1.

3.2. Quality assessment

Eleven of the experimental studies were reported as randomised, but only three reported blinding of outcome assessors. Of the 11 reported as randomised, the method of randomisation was described in 10, but 4 of these reports described a method that led to predictable treatment allocation (e.g. by arrival day/time or admission order). Participant losses were 5–20%, and no study described the characteristics of those lost to follow up. Overall, no study was scored as being of high quality; 7 studies were rated as intermediate in quality (at least 2 of the quality features met) and 7 were rated as low quality. Details of the quality assessment are summarised in Table 2.

3.3. Outcome data

All studies reported data on total mortality and non-fatal re-infarction, except for Rowe et al. (1989) (only mortality reported). A total of 328 deaths and 162 non-fatal re-infarctions were reported in the studies. The funnel plot of the effect sizes for individual studies was of acceptable symmetry for both study outcomes (Appendix A) and we therefore pooled data.

There were 149 deaths (9.3%) among 1607 AMI patients allocated to EM, compared with 179 deaths (11.6%) among 1541 individuals receiving control treatment (RR = 0.85, 95% CI 0.68, 1.05, X^2 for heterogeneity 13.31, df = 13, $p = 0.42$). For studies in which EM was started on day 5 or earlier, the effect size was 0.93 (95% CI 0.70, 1.25) and for those studies in which EM was started after day 5, the effect size was 0.75 (95% CI 0.50, 1.11), as shown in Fig. 2. When considering study quality, the RR for studies classified as intermediate in quality was 0.78 (95% CI 0.51, 1.19) compared with 0.85 (95% CI 0.61, 1.18) for studies classified as low in quality (Fig. 3).

There were 82 non-fatal re-infarctions (5.2%) among those receiving EM and 80 non-fatal re-infarctions (5.3%) among individuals allocated to the control intervention

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Table 1
Characteristics of included studies.

Reference, country	N (% males)	Setting[a] (mean age, years)	Mobilisation protocol	Day post-MI mobilisation started		Follow-up
				Active	Control	
Abraham et al. (1975), Israel	129 (73)	CCU (61.2)	Sitting on chair, walking	5	12	12 months
Bloch et al. (1974), Switzerland	158 (89)	CCU (57.7)	Moving legs, sitting on chair, Walking	2–3	12	11 months
Ghose et al. (1980), India	84 (92)	In-hospital (53.9)	Sitting on bed, Increasing walking	3	8	6 months
Glasgow (1973), England	538 (78)	CCU (53.6)	Leg movements, sitting on chair, walking	7	21	12 months
Harpur et al. (1971), England	262 (87)	CCU (65.5)	Sitting on chair, walking, Climbing stairs	8	21	4–6 months
Hayes et al. (1974), England	189 (85)	CCU (56.8)	Any movement out of bed	2	9	6 weeks
Hutter et al. (1973), USA	138 (75)	CCU (60[b])	Dangling, sitting on chair, walking	7–9	10–12	6 months
Lamers et al. (1973), Netherlands	203 (72)	In-hospital (62.1)	Dangling legs, sitting on chair, walking	10	20	19 months
Messin and Demaret (1982), Belgium	98 (100)	Hospital wards (57.5[b])	Early ambulation	5	8	12 months
Pfisterer et al. (1977), Switzerland	200 (78)	CCU, hospital wards (63.4)	Progressive activity	3	8	In-hospital
Rowe et al. (1989), England	48 (91)	CCU (56.6)	Any activity out of bed	4	8	3-6 months
Schaumann (1978), Germany	101 (NA)	Medical wards (NR)	Sitting on chair, Walking	7	21	In- hospital
Sivarajan et al. (1981), USA	258 (80)	Medical wards (56.2)	Exercise prescribed and supervised	Days 4–5	After day 5	12 months
West and Henderson (1979), England	742 (85)	Hospital wards (65.1)	Sitting on chair, Walking	5	10	12 months

NR, Not reported.
[a] All studies included uncomplicated AMI patients, except Abraham.
[b] Reported as categories originally (approximated median).

(RR = 1.02, 95% CI 0.75, 1.39, X^2 for heterogeneity 9.39, df = 12, $p = 0.67$). For studies in which EM was started on day 5 or earlier, the effect size was 0.96 (95% CI 0.57, 1.60) and for those studies in which EM was started after day 5, the effect size was 1.05 (95% CI 0.68, 1.63). When considering study quality, the RR for studies classified as intermediate in quality was 1.08 (95% CI 0.73, 1.59) compared with 0.95 (95% CI 0.40, 2.26) for studies classified as low in quality (Fig. 4).

4. Discussion

Our systematic review demonstrates a trend towards lower mortality in AMI patients receiving EM. If true, the 15% relative risk reduction could save thousands of lives annually. The biology of EM would suggest that AMI patients at different absolute risk levels receiving different background treatments may benefit from it. The data presented in this systematic review, from experimental

Table 2
Quality assessment[a] of included studies.

Reference	Randomisation		Blinding reported	Withdrawals/dropouts described?
	Reported?	Randomisation likely?		
Intermediate quality (2+ characteristics present)				
Ghose et al. (1980)	Yes	Yes	Yes	No
Hutter et al. (1973)	Yes	Yes	Yes	No
Sivarajan et al. (1981)	Yes	Yes	Yes	No
Bloch et al. (1974)	Yes	Yes	No	No
Glasgow (1973)	Yes	Yes	No	No
Schaumann (1978)	Yes	Yes	No	No
West and Henderson (1979)	Yes	Yes	No	No
Low quality (<2 characteristics present)				
Abraham et al. (1975)	Yes	No (pseudo")	No	No
Harpur et al. (1971)	No	No (pseudo")	No	No
Hayes et al. (1974)	Yes	No (pseudo")	No	No
Lamers et al. (1973)	No	No (pseudo")	No	No
Pfisterer et al. (1977)	Yes	No (pseudo")	No	No
Rowe et al. (1989)	Yes	No (pseudo")	No	No
Messin and Demaret (1982)	No	No (pseudo")	No	No

[a] Pseudo": pseudo-randomised allocation.

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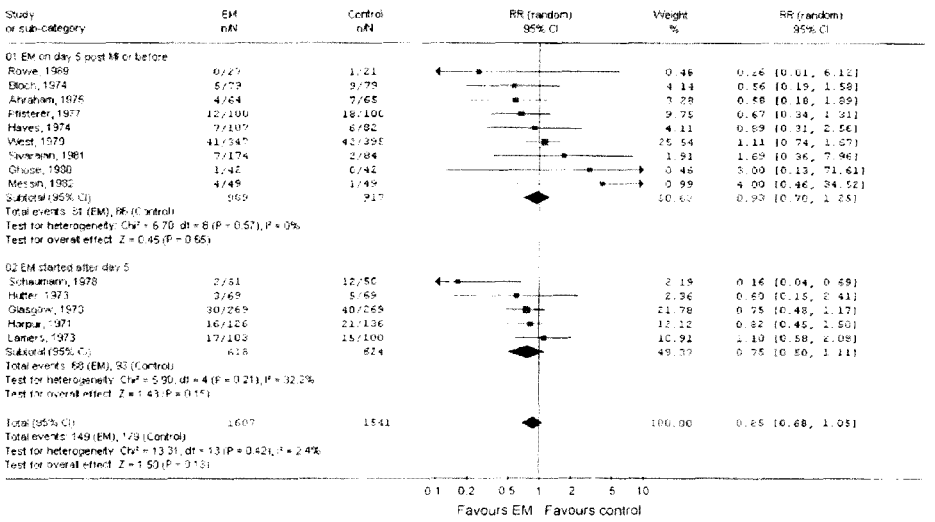

Fig. 2. Effect sizes of the included studies for mortality by time when early mobilisation (EM) initiated.

studies prior to the use of reperfusion strategies, emphasise the need for updated randomised controlled trials evaluating the effects of EM for AMI patients treated with the current standard of therapy.

This meta-analysis involving 328 deaths and 162 non-fatal re-infarctions in 3148 patients suggests that EM may reduce mortality, but not non-fatal re-infarction. Although studies did not report cardiac and non-cardiac deaths separately, the number of non-cardiac deaths in this population while in hospital is likely minimal. Despite the evolution in the care given to AMI patients in the recent decades, results for total mortality show no evidence of

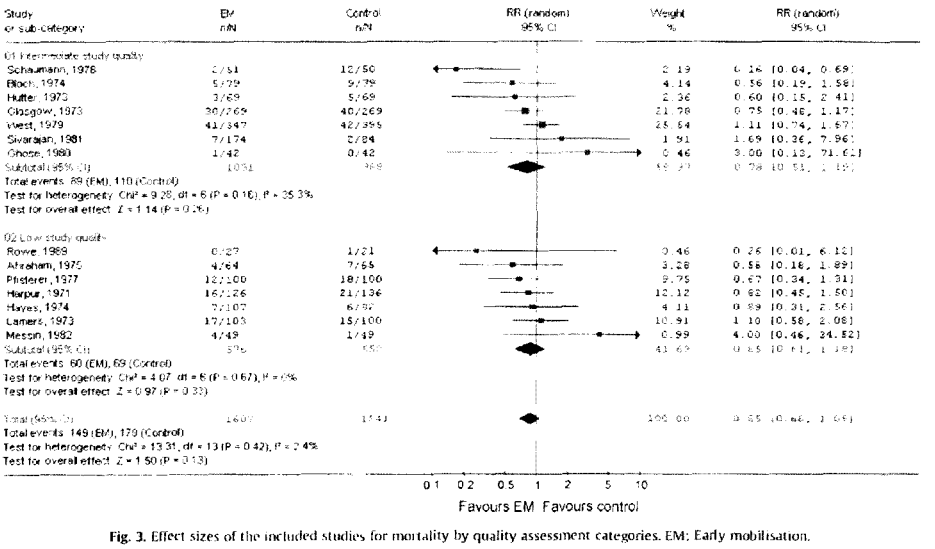

Fig. 3. Effect sizes of the included studies for mortality by quality assessment categories. EM: Early mobilisation.

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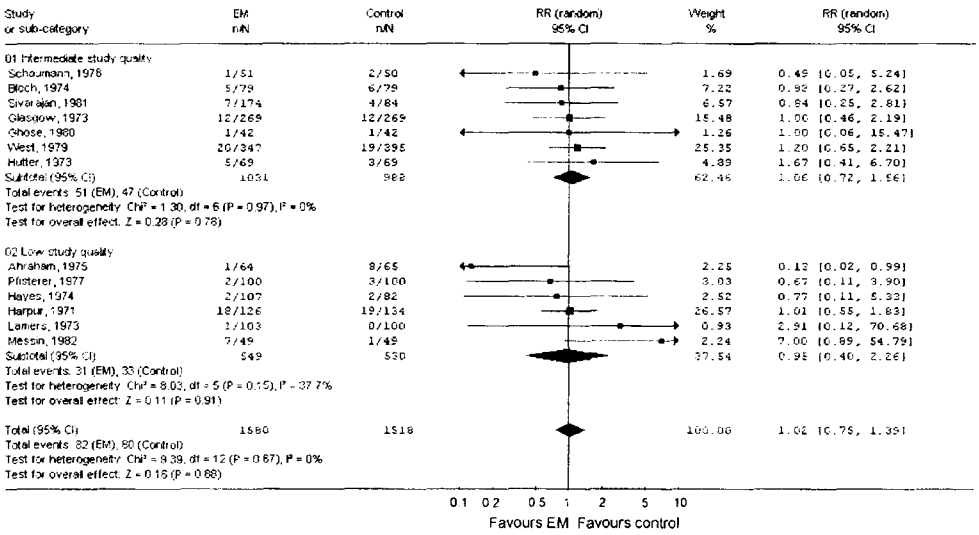

Fig. 4. Effect sizes of the included studies for non-fatal re-infarction by quality assessment categories. EM: Early mobilisation.

differences in the effect size across studies ($I^2 = 2.4\%$ for this outcome in all studies included), nor a trend in the baseline risk of participants over time. Therefore, if beneficial, the potential impact of EM is likely via reduction of cardiac deaths following AMI. Arrhythmic death after AMI is thought to occur via increased myocardial vulnerability triggered by acute ischemia (Schwartz et al., 1988; De Ferrari et al., 2007).

Since the included studies were conducted before the use of reperfusion strategies worldwide, it is unlikely that spontaneous re-perfusion had occurred before day 5 post-AMI. Acute occlusion of coronary arteries in dogs has been associated with an immediate fall in baroreflex sensitivity (BRS) and such a response discriminated dogs developing ventricular tachycardia from those who did not (Schwartz et al., 1984). Acute drops in BRS have also been documented in humans after acute coronary artery occlusion during angioplasty (Airaksinen et al., 1998). About 15% of post-AMI patients may exhibit impaired BRS (Rothschild et al., 1988), which is an independent predictor of mortality post-AMI (La Rovere et al., 2003). However, both physical training and re-perfusion improve BRS (La Rovere et al., 1992; Iellamo et al., 2000; Loimaala et al., 2003). These relationships support the hypothesis that EM might reduce arrhythmic deaths by improving BRS once re-perfusion has occurred. If that is the case, the benefit of EM might have great potential in the current thrombolytic/PTCI era, with more patients having an earlier reperfusion. EM, a simple and widely practicable intervention to AMI patients, may have an additive effect in mortality reduction to other life-saving interventions, such as PTCI that target other mechanisms. This further supports the need for contemporary studies testing the effect of EM on post-AMI patients.

4.1. Study limitations

Although our findings regarding mortality are encouraging, readers should view our results only as hypothesis-generating. Our systematic review is based on small rather than large trials that were conducted more than two decades ago. Although the funnel plot suggests a small chance of publication bias, important studies might still have been missed. Although the included studies had relatively high event rates, small studies are at greater risk of bias (as shown by our quality appraisal) and error (alpha or beta). This may be critical when the effect size reported is relatively modest, such as the 15% reduction in mortality in this systematic review. The comparability of the effect sizes by categories of study quality might indicate similar biases, whose effect would be comparable across studies, although difficult to weight. Finally, the date of the studies included in this review creates two major difficulties: lack of access to original data sets and difficulty interpreting the pooled effect sizes in light of modern AMI treatments.

The included studies do not reflect contemporary practice in cardiology. In particular, mortality rates are lower and hospital stays are shorter. Although these limitations might shift the effect size, changes in the direction of the effect are unlikely. Consequently, it is still justifiable to recommend that the uncertainty around EM be addressed in future research within the context of current practice.

4.2. Implications for research and practice

If found effective, establishing EM programs might benefit clinical practice in several ways. This intervention would help bridge the existing gap between hospital

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discharge, referral and enrolment in the so-called phase II of cardiac rehabilitation (Pearson, 2002). The in-hospital phase of cardiac rehabilitation is not yet a standardised practice based on high-quality evidence. Although hospital stays for AMI patients is actually shorter than in the 1970s or 1980s, wide variations in hospital stay across countries remain. Moreover, other factors affecting the cardiovascular care, such as inequities (e.g. sex or race) may affect hospital stays (Kaul et al., 2004). EM programs developed currently by nurses (as part of in-hospital components of cardiac rehabilitation), may improve not only physical and cardiac outcomes but also mental and psychological wellbeing before hospital discharge. This intervention may reduce the gap between hospital discharge and the beginning of cardiac rehabilitation phase II. The effect of EM for discharged patients that are not referred (or are unable to participate) in cardiac rehabilitation phase II programs remains uncertain. In the absence of evidence of harm and the potential benefits, nurses should provide and promote EM to AMI patients across their hospital stay.

Expansion of EM programs might lead to a more systematic and universal approach to cardiac rehabilitation as well as increasing the enrolment in these programs. While EM may have some contraindications (e.g. for patients with AMI Killip III and IV), it may also be synergistic with other BRS-enhancing interventions, such as beta-blockers (Malfatto et al., 1998) as well as other accepted treatments.

A large randomised controlled trial (RCT) is in order when uncertainty remains after several smaller studies (Yusuf et al., 1984). We believe this is the case for EM for patients after AMI, where we are unable to exclude a clinically important benefit (i.e. RR < 0.85). This is especially true when the existing data are potentially incomplete, biased and outdated with respect to current cardiology practice. The complexity of such a trial would require, however, a deeper understanding of the patterns and determinants of mobilisation of AMI patients in the thrombolytic/PCI era.

4.3. Conclusion

This systematic review of experimental data from studies conducted in the 1970s and 1980s showed a trend towards an increased survival of AMI patients receiving EM relative to those who do not. We believe these results may renew the interest of researchers, grant agencies and decision makers in understanding the access, patterns, determinants, and impact of EM, an inexpensive and widely applicable intervention in the current context of cardiology practice.

Conflict of interest

None declared.

Acknowledgements

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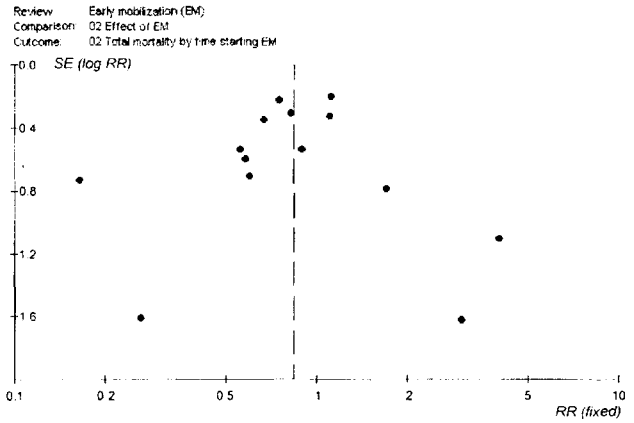
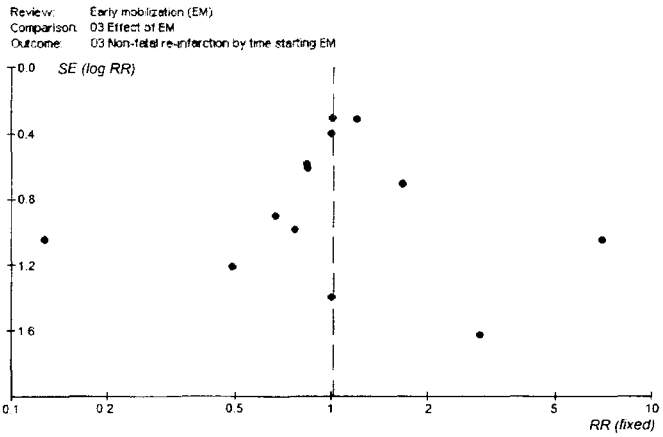
Appendix A

Funnel plots for the effect sizes of the included studies on mortality (top) and non-fatal re-infarction (bottom)





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APPENDIX B

Ethics Approval

Maureen Markle-Reid

From: 'O.L. Cortes" <cortesol@univmail.cis.mcmaster.ca>
To: <dicensoa@mcmaster.ca>; <mreid@mcmaster.ca>; <markerob@hhsc.ca>; <canesnn@mcmaster.ca>
Sent: Friday, September 02, 2005 8:48 AM
Subject: Re: REB Application

Good news: the project was accepted by the REB and at the same time I have received the password to enter to Health Records. Thanks for your help and contributions. Ready to go for the next steps.

Olga C.

On Thu, 1 Sep 2005 10:15:58 -0400
Mazzetti Deborah <mazzedeb@HHSC.CA> wrote:
> This will confirm receipt of your REB application for retrospective
> review
> of medical charts/health records for the study entitled "The
> PRogressive
> Upright Mobilization Program (PUMP Phase I)". This study has been
> reviewed
> and approved by the REB Executive. The project number is CR-83 and
> has been
> forwarded on to Health Records at MUMC. To followup please contact
> MUMC
> Health Records, Jane Yeomans at x75121 or yeomans@hhsc.ca
> <mailto:yeomans@hhsc.ca>. Please refer to the project number CR-83.
>
>
> Deborah Mazzetti
> Coordinator, Research Ethics Board
> Henderson Site, 90 Wing, Room 1
> 711 Concession Street
> Hamilton, Ontario
> L8V 1C3
> 905-527-4322 Ex. 42013
> Fax 905-574-5645
> mazzedeb@hhsc.ca
> http://www.fhs.mcmaster.ca/rsd/ethics/reb/
>
>
> The Cornerstone of Care Campaign for Hamilton Health Sciences needs
> your
> support. Please, visit hamiltonhsc.thsciences.ca today and help make
> something great even greater.
>
> This information is directed in confidence solely to the person named
> above
> and may not otherwise be distributed, copied or disclosed.

APPENDIX C

Permission Request to Access Medical Records Using SOVERA

Hamilton Health Sciences
Information & Communication Technologies Department
Computer Access Request Form

All fields are mandatory, if not fully completed by a Manager, Supervisor or Clinical Educator it will be returned and not processed.

First Name: Cortés **Last Name: Olga**

Employee I.D. Number: 026302 Phone Extension:

Job Title: Nurse student – Graduate Stud. **Discipline: School of Nursing**

Program or Department: Nursing RN **Site: McMaster**

Manager's Name: Dr. Robert McKelvie **Ext: 44583**

Please Check:

☐ **New Access** ☐ **Modify Existing Access - list username**

☐ **Email** ☐**NT Network Access only, not including Email.**

Meditech:
X Clinical ☐ **Stores Access** ☐ **Purchasing Access**

If you require Material Management - Stores and Purchasing Access, list cost center(s) If you are requesting purchasing access, please ensure you have updated the "Signing Authorization Form" with Finance. Access will not be granted if this has not been completed.

☐ **IWT Workload** include preferred ward. Ward

Peoplesoft:
☐ **H.R.** Time & Labour
Financials ☐General Ledger Query Reporting

Sovera for HIM Retrieval X No Print ☐ Retrieval Print ☐ Physicians – staff only
Other Health Records staff only – specify template

Other Applications – list here:

If you are not sure of Access required, list the name of an employee who currently has this application and access. If there is more than one application, list ALL of the applications required.

Application name: Olga Cortés

Employee name: Dr. Robert S. McKelvie

Non HHS Employees

If you are not an HHS employee, please list employer's name, address and phone number in space below. Authorization is required from a Manager, Supervisor or Clinical Educator.

Name:

Job Title:

Program or Department:

Phone Extension:
This form must be emailed by an authorized Requestor or authorized delegate to Password Admin on the Global Address List or Passadmin@hhsc.ca. If email is not available please call the ICT Helpdesk at Ext 43000. Please do not send this form in Interoffice Mail.

October 2004

APPENDIX D

Classification of Diseases: Codes for AMI Diagnosis

ICD-9-CM International Classification of Diseases

(390-459) Diseases of the Circulatory System

410 Acute myocardial infarction

- 410.0 Acute myocardial infarction of anterolateral wall
- 410.1 Acute myocardial infarction of other anterior wall
- 410.2 Acute myocardial infarction of inferolateral wall
- 410.3 Acute myocardial infarction of inferoposterior wall
- 410.4 Acute myocardial infarction of other inferior wall
- 410.5 Acute myocardial infarction of other lateral wall
- 410.6 True posterior wall infarction
- 410.7 Subendocardial infarction
- 410.8 Acute myocardial infarction of other specified sites
- 410.9 Acute myocardial infarction of unspecified site

411 Other acute & subacute forms of ischemic heart disease

- 411.0 Postmyocardial infarction syndrome
- 411.1 Intermediate coronary syndrome
- 411.8 Other acute & subacute forms of ischemic heart disease

412 Old myocardial infarction

413 Angina pectoris

- 413.0 Angina decubitus
- 413.1 Prinzmetal angina
- 413.9 Other & unspecified angina pectoris

414 Other forms of chronic ischemic heart disease

- 414.0 Coronary atherosclerosis
- 414.1 Aneurysm of heart
- 414.8 Other specified forms of chronic ischemic heart disease
- 414.9 Chronic ischemic heart disease, unspecified

http://www.biblioteca.anm.edu.ar/frames/circul.htm

APPENDIX E

Data Collection Form

Mobilization of Patients After an AMI

Time abstraction began_____ Time abstraction ended _____

I. Hospital Admission and Demographics

Hospital (√ check one)			Henderson			McMaster				General			
Patient initials			Patient ID										
Date of Hospitalization for AMI	Day/_____ Month/_____ Year/_____												
Reviewers initials													
Date of data collection	Day/_____ Month/_____ Year/_____												

Gender (√)	Male		Female		**Age**				
Marital status	Single		Widowed		Married		Divorced		
Occupation	Employed?	Yes		No		ND			

Occupation	Work part time		Retired		Work full time		On disability		ND	

English Language	Yes			No			Language spoken in Home			
Patient Came to Hospital From	Home		Other Hospital		Dr. Office		Workplace		Other:	
Patient arrived at this hospital by	Walking		By ambulance		By car		Air ambulance			

Patient arrived	Oriented or alert (answer questions on own behalf)		Confused		Unconscious	

Patient was admitted to this service	**Number of times (√)**	**Date (day/month/year)**	**Hour (in 24 hours)**	**Length of Stay (LOS)**	**Reason for Hospitalization in Each Setting (if apply)**
Emergency (ER)	First_____ Second_____	Day/____ Month/_____Year/_____ Day/ ____Month/_____Year/_____	_____ _____	_____ _____	Dx:_____ Dx:_____
Surgical	First_____ Second_____	Day/____Month/_____ Year/_____ Day/____ Month/_____ Year/____	_____ _____	_____ _____	Dx:_____ Dx:_____
Intensive care unit					

ICU	First_____ Second_____	Day/____Month/____Year/____ Day/____Month/____Y ear/____	_____ _____	_____ _____	Dx:_____ Dx:_____
Coronary care unit (CCU or CRCU)	First_____ Second_____	Day/____Month/_____Year/____ Day/____Month/_____Year/____	_____ _____	_____ _____	Dx:_____ Dx_____
Medical ward	First_____ Second_____	Day/____ Month/_____ Year/____ Day/____Month/_____Year/____	_____ _____	_____ _____	Dx_____ Dx_____
Total LOS	→				

Discharge from hospital	**Alive**		**Dead**		**Date**	Day/____Month/_____Year/_____	

Emergency Room reason for admission	Q MI		Non Q MI		Unstable Angina	
AMI localization	Anterior		Lateral		Inferior	
AMI confirmation	Troponin (value)		Creatin Kinase (value)			
Vital signs	Heart rate		Blood pressure			

Time of the beginning of heart pain	Day/_____ Month/_____ Year/_____						**Hour of trigger of pain**					
Activity that the patient was doing when the pain started (select only one)	Exercise		Sleeping		Having sex		Eating		Other:			
	Emotion		Daytime nap		Resting		Working		ND			

II. Past Medical History. Please check as many as applicable. (√)

Risk Factors		**Diagnosed**		**Cardiac or Other Procedures**	
1. Former smoker		1. Myocardial Infarction		1.Coronary artery bypass graft (CABG)	
2. Current Smoker		2. Diabetes		2. PCI or Coronary Angioplasty	
3. Hypertension		3. Heart Failure (HF)		3. Abdominal surgery:	
4. Hyperlipidemia		4. Arrhythmia (TIA/CVA)		4. Organ transplant	
5. Sedentarism		5. Syncope			
6. Outside cardiac rehabilitation (CPR)		6. Stroke			

7. Hypercholesterolemia		7. Angina			
		8. Mental Health			
		9. Alzheimer Disease/dementia			
		10. Delirium			
		11. Coronary artery disease			
Other:		Other:		Other:	

III. Interventions and Procedures Received During Hospitalization. Please check as many as applicable. (√)					
Drugs		**Procedures**		*Other Interventions*	
1. Thrombolysis: TNK, Streptokinase		1.Angiography or Coronary Catheterization		1. Bed rest	

2. ASA (aspirin)		2. PCI or percutaneous coronary angioplasty		2. Intra-aortic balloon pump (IABP)	
3. Heparin		3. Coronary angioplasty (PCI)		3. Cardioversion	
4. Coumadin		4. Coronary artery bypass (CABG)		4.Arterial line	
5. Morphine				5.Central line	
6. Ativan				6.IV tubing	
7. B-blocker: metoprolol, atenolol				7. Mechanical ventilation	
8. ACE Inhibitors: nifedipine, amlopidine, isradipide, verapamil				8. Pacemaker	

9. Nitroglycerin/Nitrates				9.Nasogastric tube	
10. Insulin				10. Swan Ganz	
Others:		Others:		Others:	

IV. Patient Complications During Hospitalization

Complication	**Before CCU**	**In CCU**	**In Ward**	**Complication**	**Before CCU**	**In CCU**	**In Ward**
1.Pulmonary Edema				9. Stroke			
2. Congestive Heart Failure				10. Recurrent Ischemia/or MI			
3. Cardiogenic Shock				11. Depression			

4. Atrial Fibrillation				12. Infection			
5. Atrioventricular Block				13. Sepsis			
6. Ventricular Arrhythmia				14. Death			
7. Bleeding				15. Pain			
8. Renal Insufficiency				Other:			

V. First Walk During Hospitalization

The first walk of the patient was (check only one)		**Date**	**Hour (in 24 hours system)**
1. Independent		Day/_____ Month/_____ Year/_____	
2. Assisted		Day/_____ Month/_____ Year/_____	

3. Supervised		Day/_____ Month/_____ Year/_____	
4. With walker		Day/_____ Month/_____ Year/_____	
5. Other		Day/_____Month/_____Year/_____	
6. ND			

The information about the first walk of the patient was obtained from nursing notes?	**Yes**		**No**	
Was the information clear to be read?	**Yes**		**No**	
Was the information about patient's first walk recorded by	**Hand**		**Typed**	

APPENDIX F

Codification of Terms

	Group	Variable	Name	Data type	Size	Description	Categories/continuous
1							
2	I	Hosp	Hospital	Number	Byte	Hamilton Health Science Centres	1:Henderson 2:McMaster 3:General
3	**Hospital**	Initials	Pat_Ini	Text	50	Patient´s name, initials	
4		Chart number	Pat_Id	Text	20	Chart number identification by centre	
5	**Admission**	DateH	Date_AMI	Date		Hospitalization date. Admission date	dd/mm/yy
6	**and**	Gen	Gender	Number	Byte	Gender	1: Male 2: Female
7	**Demog-Raphics**	D_Birth	Birth	Date		Date of birth	dd/mm/yy
8		Age	Age	Number	Byte	Age (years)	
9		Marital Status	Marit_Status	Number	Byte	Marital Status	1:Single 2: Widowed 3: Married 4: Divorced 5: ND (No data)
10		Employed	Employed	Number	Byte	Patient job	1: Yes 2: No 3: ND (no data)
11		Type of job	Empl_Time	Number	Byte	Job definition	1: Works part-time 2: Retired 3: Works full-time 4: On disability 5: ND (No data)
12		Occup	Occupation	Text	30	Patient's occupation	
13		English	English	Number	Byte	English language	1: Yes 2: No
14		Language	Lang_Home	text	10	Different languages spoken at home	1: Spanish 2: Chinese 3: Russian

						4: Czech 5: Italian 6: Greek 7: Polish 8: Portuguese
15	Came	Came_from	Number	Byte	Patient come to Hospital from	1: Home 2: Other Hospital 3: Physician 4: Worksplace 5: Other
16	Other place different described?	Other_came	text	20	Other	
17	Arrived	Arrived_by	Number	Byte	How does each patient arrive to Emergency department	1: By Walking 2: By Ambulance 3: By Car 4: Air Ambulance
18	Pat_arriving health status	Patient_arrived	Number	Byte	Health status at admission time	1: Oriented or alert 2: Confused 3: Unconscious
19	Serv_1	Emer Room	Number		Emergency Room	1.Yes 2.No
20	Serv_1_Date	Serv_1_Date	Date		Date of admission	dd/mm/yy
21	Serv_1_LOS	Serv_1_LOS	Number		LOS on this service	days
23	Serv_2_Date	Surgical	Date		Date of admission	dd/mm/yy
24	Serv_2_LOS	Serv_2_LOS	Number		LOS on this service	days
26	Serv_3_Date	Intensive care unit	Date		Date of admission	dd/mm/yy
27	Serv_3_LOS	Serv_3_LOS	Number		LOS on this service	days
29	Serv_4_Date	coronary care unit	Date		Date of admission	dd/mm/yy
30	Serv_4_LO	Serv_4_LOS	Number		LOS on this service	days

	S					
32	Serv_5_Date	medical ward	Date		Date of admission	dd/mm/yy
33	Serv_5_LOS	Serv_5_LOS	Number		LOS on this service	days
57	**Total**	**Total_LOS**	Number		Total Length of stay in days	Number
58	Discharge	Discharge	Number	Byte	Patient´s status for discharge	1: Alive 2: Dead
59	Date_death	Date_Dead	Date		Date of death	dd/mm/yy
60	HR_D	Heart_Des	Number	Byte	Heart rate at discharge (mmHg) Last service	
61	SAP_D	SAP_Des	Number	Number	Systolic blood pressure at discharge	
62	DAP_D	DAP_Des	Number	Number	Diastolic blood pression at discharge	
63	Emergency Departmen	Emer Depart	Number	Byte	Reason for hospitalization	1: QMI (STEMI) 2: Non QMI (NSTEMI) 3: Unstable Angina
64	AMI:Loc1	AMI_Ant	Number	Byte	Acute Myocardial Infarction Localization Anterior	1: Yes 2: No
65	AMI_Loc2	AMI_Lat	Number	Byte	AMI lateral	1: Yes 2: No
66	AMI_Loc3	AMI_Inf	Number	Byte	AMI inferior	1: Yes 2: No
67	Troponin	vr_troponin	Number		Troponin value (Normal: 0.0-0.15 ng/ml)	
68	Creatinin	vr_creatin	Number		Creatinin value (normal 60-400U/L)	
69	HR_Entrance	Heart_Ent	Number		Heart rate entrance (Emergency Department)	
70	SAP_Entrance	SAP_Ent	Number		Systolic blood pressure (entrance mmHg)	
71	DAP_Entrance	DAP_Ent	Number		Dyastolic blood pressure (entrance mmHg)	
72	Date_Pain	Pain_began	Date		Date of heart pain beginning	dd/mm/yy
73	Time_Trigger	Time_Trigger	Date		Hour of trigger of pain	hour

74		Activity and trigger of pain	Activity_pain	Number		Activity doing at time of pain trigger	1: Exercise 2: Sleeping 3: Having Sex 4: Eating 5: Emotion 6: Daytime nap 7: Resting 8: Working 9: ND (no data on chart) 10: Other
75		Other_acti	Other_activity	Text	20	Oher activity different to # 74 (1 to 8)	
76		Symptome_1	Chest	Number	Byte	Symptom referred	1: Yes 2: No
77		Symptome_2	Irradiated	Number	Byte	Symptom referred	1: Yes 2: No
78		Symptome_3	Irradi_arms	Number	Byte	Symptom referred	1: Yes 2: No
79		Symptome_4	Irradi_jaw	Number	Byte	Symptom referred	1: Yes 2: No
80		Symptome_5	Nausea	Number	Byte	Symptom referred	1: Yes 2: No
81		Symptome_6	Vomiting	Number	Byte	Symptom referred	1: Yes 2: No
82		Symptome_7	SOB	Number	Byte	Symptom referred	1: Yes 2: No
83		Symptome_8	Symptoms8	Number	Byte	Symptom referred	1: Yes 2: No
84	**II**	RF1	Former_Smoker	Number	Byte	Former smoker	1: Yes 2: No
85	**Past**	RF2	Current_Smok	Number	Byte	Current smoker	1: Yes 2: No
86	**Medical**	RF3	HTA	Number	Byte	Hypertension	1: Yes 2: No
87	**History**	RF4	HyperLipi	Number	Byte	Hyperlipidemia	1: Yes 2: No

88	RF5	HyperCol	Number	Byte	Hypercholesterolemia	1: Yes 2: No
89	RF6	Sedent	Number	Byte	Sedentarism	1: Yes 2: No
90	RF7	CPR	Number	Byte	Outside cardiac rehabilitation (CPR)	1: Yes 2: No
91	RF8	FH_CVD	Number	Byte	Family history of CVD	1: Yes 2: No
92	RF9	Other1_RF	Number	Byte	Other risk factor (1)	1: Yes 2: No
93	RF10	Other2_RF	Number	Byte	Other risk factor (2)	1: Yes 2: No
94	Diag1	MI	Number	Byte	myocardial infarction	1: Yes 2: No
95	Diag2	DiabII	Number	Byte	Diabetes Type II	1: Yes 2: No
96	Diag3	HF	Number	Byte	Heart failure	1: Yes 2: No
97	Diag4	TIA/CVA	Number	Byte	Arrhythmia (TIA / CVA)	1: Yes 2: No
98	Diag5	Coro_Artery	Number	Byte	coronary artery disease	1: Yes 2: No
99	Diag6	Syncope	Number	Byte	Syncope	1: Yes 2: No
100	Diag7	Stroke	Number	Byte	Stroke	1: Yes 2: No
101	Diag8	Angina	Number	Byte	Angina	1: Yes 2: No
102	Diag9	Mental_Health	Number	Byte	Mental health problems	1: Yes 2: No
103	Diag10	Alzheimer	Number	Byte	Alzheimer disease / dementia	1: Yes 2: No
104	Diag11	Delirium	Number	Byte	Delirium	1: Yes 2: No
105	Diag12	Other1_Diag	Number	Byte	Other diagnosed (1)	1: Yes 2: No

106		Diag13	pulm_dis	Number	Byte	Pulmonary disease	1: Yes 2: No
107		Diag14	Card_dis	Number	Byte	Cardiac disease	1: Yes 2: No
108		Diag15	org_fail	Number	Byte	Organic failure	1: Yes 2: No
109		Diag16	gastrop	Number	Byte	Gastric problems	1: Yes 2: No
110		Diag17	emotpr	Number	Byte	Emotional problems	1: Yes 2: No
111		Diag18	osteo	Number	Byte	Osteorthritis	1: Yes 2: No
112		Diag19	cancer	Number	Byte	Cancer	1: Yes 2: No
113		Diag20	subt_abu	Number	Byte	Substance abuse	1: Yes 2: No
114		Diag21	reinter	Number	Byte	Re-interventions	1: Yes 2: No
115		Diag22	vascular	Number	Byte	Vascular	1: Yes 2: No
116		Diag23	neurol	Number	Byte	Neurologic	1: Yes 2: No
117		COP1	CABG	Number	Byte	Coronary artery bypass graft (CABG)	1: Yes 2: No
118		COP2	PCI_CA	Number	Byte	PCI or coronary angioplasty	1: Yes 2: No
119		COP3	Abd_surgery	Number	Byte	Abdominal surgery	1: Yes 2: No
120		COP4	Organ_Trasp	Number	Byte	Organ transplant	1: Yes 2: No
121		COP5	other1	Number	Byte	Other diagnosed (1)	1: Yes 2: No
122		COP6	Other2	Number	Byte	Other diagnosed (2)	1: Yes 2: No
12	III	Drug1	TNK	Number	Byte	Thrombolysis: TNK, Streptokinase	1: Yes

3							2: No
124	**Hospital**	Drug2	ASA	Number	Byte	ASA (aspirin)	1: Yes 2: No
125	**Treat**	Drug3	Heparin	Number	Byte	Heparin	1: Yes 2: No
126		Drug4	Coumadin	Number	Byte	Coumadin	1: Yes 2: No
127		Drug5	Morphine	Number	Byte	Morphine	1: Yes 2: No
128		Drug6	Ativan	Number	Byte	Ativan	1: Yes 2: No
129		Drug7	B-blocker	Number	Byte	B-blocker: metoprolol, atenolol (others)	1: Yes 2: No
130		Drug8	ACE	Number	Byte	ACE inhibitors: mifedipine, amlopidini, isradipide, verapamil	1: Yes 2: No
131		Drug9	Nitrogly	Number	Byte	Nitroglycerin/Nitrates	1: Yes 2: No
132		Drug10	Insulin	Number	Byte	Insulin	1: Yes 2: No
133		Drug11	Inotrop	Number	Byte	Inotropics (e.g., dopamine,dobutamine)	1: Yes 2: No
134		Drug12	antiarrit	Number	Byte	Antiarrhythmics	1: Yes 2: No
135		Drug13	Antiacid	Number	Byte	Antiacid	1: Yes 2: No
136		Drug14	CCblocker	Number	Byte	Calcium channel blockers	1: Yes 2: No
137		Drug15	AntPlaq	Number	Byte	Antiplatelet and anticoagulant agents	1: Yes 2: No
138		Drug16	Sedantives	Number	Byte	Sedatives	1: Yes 2: No
139		Drug17	Analges	Number	Byte	Analgesics	1: Yes 2: No
140		Drug18	cholest_low	Number	Byte	Cholesterol lowering	1: Yes 2: No

141	Drug19	Diurect	Number	Byte	Diuretics	1: Yes 2: No
142	Drug20	Laxative	Number	Byte	Laxative	1: Yes 2: No
143	Drug21	Antib	Number	Byte	Antibiotics	1: Yes 2: No
145	Drug22	Other_drug	Number	Byte	Other drug	1: Yes 2: No
146	Proc1	Ang_coronary	Number	Byte	Angiography or coronary catheterization	1: Yes 2: No
147	EF	EF	Number	Byte	Is there any Ejection fraction data?	%
148	EFvr	ValueEF	Number	Byte	Ejection fraction	%
149	Proc2	PCI_pca	Number	Byte	PCI or percutaneous coronary angioplasty	1: Yes 2: No
150	Proc3	Proc_CABG	Number	Byte	Coronary artery bypass (CABG)	1: Yes 2: No
151	Proc4	Dialysis	Number	Byte	Dialysis	1: Yes 2: No
153	Proc6	chemoth	Number	Byte	Chemotherapy	1: Yes 2: No
154	Proc7	Otherproc	Number	Byte	Other procedure	1: Yes 2: No
155	OI1	Bed_rest	Number	Byte	Bed rest (prescription)	1: Yes 2: No
156	OI2	AAT	Number	Byte	AAT (activity as tolerated precription)	1: Yes 2: No
157	OI3	Mobiliza	Number	Byte	Mobilization	1: Yes 2: No
158	OI4	IABP	Number	Byte	Intra aortic balloon pump (IABP)	1: Yes 2: No
159	OI5	Cardio	Number	Byte	Cardioversion	1: Yes 2: No
16	OI6	Art_line	Number	Byte	Arterial line	1: Yes

0							2: No
161		OI7	Central_line	Number	Byte	Central line	1: Yes 2: No
163		OI9	Mech_Venti	Number	Byte	Mechanical ventilation	1: Yes 2: No
164		OI10	Pacemaker	Number	Byte	Pacemaker	1: Yes 2: No
165		OI11	Nasogastric	Number	Byte	Nasogastric tube	1: Yes 2: No
166		OI12	Swan	Number	Byte	Swan Ganz	1: Yes 2: No
167		OI13	Foley	Number	Byte	Foley tube	1: Yes 2: No
168		OI14	Other1_Interv	Number	Byte	Other interventions (1)	1: Yes 2: No
169	**IV**	Compl1	Pulm_edema	Number	Byte	Pulmonary edema	1: Before CCU 2: In CCU 3: In Ward
170	**Compli**	Compl2	Cong_heart	Number	Byte	Congestive heart failure	1: Before CCU 2: In CCU 3: In Ward
171	**cations**	Compl3	Cardio_shock	Number	Byte	Cardiogenic shock	1: Before CCU 2: In CCU 3: In Ward
172		Compl4	Atrial_Fibri	Number	Byte	Atrial fibrillation	1: Before CCU 2: In CCU 3: In Ward
173		Compl5	Atrio_block	Number	Byte	Atrioventricular block	1: Before CCU 2: In CCU 3: In Ward
174		Compl6	Ventr_arrhyt	Number	Byte	Ventricular arrhythmia	1: Before CCU 2: In CCU 3: In Ward
175		Compl7	Bleeding	Number	Byte	Bleeding	1: Before CCU 2: In CCU 3: In Ward

176	Compl8	Renal_insuf	Number	Byte	Renal insufficiency	1: Before CCU 2: In CCU 3: In Ward
177	Compl9	Stroke(IV)	Number	Byte	Stroke (patient complications during Hospitalization)	1: Before CCU 2: In CCU 3: In Ward
178	Compl10	Rec_isch	Number	Byte	Recurrent ischemia / or MI	1: Before CCU 2: In CCU 3: In Ward
179	Compl11	Depression	Number	Byte	Depression	1: Before CCU 2: In CCU 3: In Ward
180	Compl12	Infection	Number	Byte	Infection	1: Before CCU 2: In CCU 3: In Ward
181	Compl13	Sepsis	Number	Byte	Sepsis	1: Before CCU 2: In CCU 3: In Ward
182	Compl14	Pain	Number	Byte	Pain	1: Before CCU 2: In CCU 3: In Ward
183	Compl15	Death	Number	Byte	Death	1: Before CCU 2: In CCU 3: In Ward
184	Compl16	hypert	Number	Byte	Hypertension	1: Before CCU 2: In CCU 3: In Ward
185	Compl17	Bradycar	Number	Byte	Bradycardia	1: Before CCU 2: In CCU 3: In Ward
186	Compl18	GI_bleeding	Number	Byte	Gastric Bleeding	1: Before CCU 2: In CCU 3: In Ward
187	Compl19	Renal_Fail	Number	Byte	Kidney failure	1: Before CCU 2: In CCU 3: In Ward

188		Compl20	copd	Number	Byte	COPD:Obstructive Pulmonary Disease	1: Before CCU 2: In CCU 3: In Ward
189		Compl21	pericard	Number	Byte	Pericarditis	1: Before CCU 2: In CCU 3: In Ward
190		Compl22	MI_infrac	Number	Byte	MI new, ischemic event	1: Before CCU 2: In CCU 3: In Ward
191		Compl23	stent_trombo	Number	Byte	Stent thrombosis	1: Before CCU 2: In CCU 3: In Ward
192		Compl24	post_MI_angi	Number	Byte	Post MI angina	1: Before CCU 2: In CCU 3: In Ward
193		Compl25	Hypo_shock	Number	Byte	Hypovolemic schock	1: Before CCU 2: In CCU 3: In Ward
194		Compl26	isch_col	Number	Byte	Ischemic colitis	1: Befor eCCU 2: In CCU 3: In Ward
195		Compl27	aort_agita	Number	Byte	Aorta aneurism / agitation	1: Before CCU 2: In CCU 3: In Ward
196		Compl28	AB_damage	Number	Byte	Anoxic brain damage	1: Before CCU 2: In CCU 3: In Ward
197		Compl29	pneumonia	Number	Byte	Pneumonia	1: Before CCU 2: In CCU 3: In Ward
198		Compl30	coagul	Number	Byte	Coagulopathy	1: Before CCU 2: In CCU 3: In Ward
199	V	Walk	walk	Number	Byte	Did the patient walk?	1: Yes 2: No

200	**First**	firstwalk	Firts_walk	Number	Byte	The patient's first walk was independent, assisted, supervised	1: Indep_CCU 2: Indep_CRCU 3: Indep_ICU 4: Indep_Medical Ward 5: Assis_CCU 6: Assis_CRCU 7: Assis_ICU 8: Assis_Medical Ward 9: Super_CCU 10: Super_CRCU 11: Super_ICU 12: Super_Medical Ward 13: With_CCU 14: With_CRCU 15: With_ICU 16: With_Medical Ward 17: Other_CCU 18: Other_CRCU 19: Other_ICU 20: Other_Medical Ward 21: ND 22: No Walk
201	**Walk**	DateWalk	Date_Walk	Date		Date and hour found of the first walk	dd/mm/yy
202		Information	Inf_notes	Number	Byte	The information about the patient's first walk was obtained from nursing notes	1: Yes 2: No
203		Clear	Inf_clare	Number	Byte	Was this information clear?	1: Yes 2: No
204		recorded	Recorded	Number	Byte	Was the information about the patient's first walk recorded by	1: Hand 2: Typed