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Risk Prediction In Older Adults After Acute Myocardial Infarction: The Silver-Ami Study

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RISK PREDICTION IN OLDER ADULTS AFTER ACUTE MYOCARDIAL INFARCTION: THE SILVER-AMI STUDY

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine

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Abstract:

Older adults are at risk for functional decline after hospitalization for acute myocardial infarction (AMI). Our goal with this thesis is to explore two outcomes relevant to maintenance of physical function, falls and cardiac rehabilitation (CR) utilization in a cohort of adults over the age of 75 hospitalized with acute myocardial infarction. We aim to describe the risk of falls within six months of discharge and the rates of CR use, and to identify factors associated with these outcomes.

Our project uses data from the SILVER-AMI study, a prospectively designed cohort study which enrolled 3000 patients over the age of 75 hospitalized with acute myocardial infarction and followed them for six months after discharge. Extensive baseline data was collected on demographics, clinical and psychosocial factors, and geriatric impairments. Outcome data on falls was collected at six months via medical record adjudication and survey, and on CR use by survey.

557 (21.6%) of 2584 participants reported at least one fall within six months of discharge. Independent predictors after logistic regression analysis included: impaired functional mobility (OR 1.5 [1.07-2.11]), recent fall history (OR 2.97 [2.37-3.74]), longer length of stay (OR 1.04 [1.02-1.07] per day, visual impairment (OR 1.33 [1.08-1.64]), and weak grip strength (OR 1.28 [1.02-1.60]).

192 (6.4%) of 3006 participants were found to have a medically serious fall within six months of discharge. Independent predictors of medically serious falls after logistic regression analysis included: impaired functional mobility (OR 1.85 [1.11-3.09]), recent fall history (OR 1.73 [1.23-2.42]), longer length of stay (OR 1.03 [1.01-1.06] per day, living alone (OR 1.37 [1.00-1.87, p = 0.048]), and impairment in the bathing ADL (OR 1.74 [1.06-2.86]).

943 (39.5%) of 2387 participants reported participating in CR within six months of discharge. Independent predictors of CR use after logistic regression analysis included: older age (OR 0.97 [0.95-0.99] per year), non-white race (OR 0.69 [0.50-0.97]), having less than 12 years of education (OR 0.71 [0.59-0.85]), receiving percutaneous (OR 2.07 [1.66-2.57]) or surgical (OR 4.70 [3.32-6.67]) revascularization, cognitive impairment (OR 0.58 [0.43-0.78]), and living alone (OR 0.77 [0.64-0.93]).

From these results, we conclude that falls and CR underutilization are important problems facing older adults after AMI. The comprehensive geriatric assessment performed in SILVER-AMI highlighted independent robust predictors of both functional outcomes. This indicates that there is a role for assessing geriatric impairments during an AMI hospitalization, as identifying patients at risk for poor functional outcomes can lead to steps toward improving their care. High fall risk could be a reason to avoid anticoagulant therapy. Identifying patients less likely to attend CR can allow development of interventions to close this gap in care.

Acknowledgments:

I would like to humbly thank my advisor, Sarwat Chaudhry, for her patience, generosity, and dedication to mentorship throughout this process. She is a role model for me as a researcher, clinician, and person. She has taught me the skills required to design a research question, manage a team, and follow a project through to completion, and she has left me the room to develop independence in those skills. She has been a remarkable resource since we first met, and I could not imagine a better mentor and advisor for me.

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I. INTRODUCTION:

Demographic shifts in the United States have led to radical changes in the population's healthcare needs and utilization. The number of older adults has grown rapidly, as has the incidence of cardiovascular disease in this group, particularly acute myocardial infarction. Over recent decades, a new field of medicine, geriatric cardiology, has blossomed to care for older adults with cardiovascular disease(1). These older patients differ from their younger counterparts in a number of dimensions, and their care requires a thoughtful understanding of their unique needs. Older adults' increased burden of comorbid diseases and aging-specific impairments in cognition and physical function, combined with their limited physiologic reserve, mean that they are a group that is exceptionally vulnerable to poor outcomes after AMI. While older age itself is a known risk factor for unfavorable outcomes, this risk is not distributed evenly across the geriatric population. Older adults are extremely heterogeneous, and the various impairments and comorbidities exist to varying degrees that may or may not correspond with age. Not all older adults exhibit the aging phenotype, and their physiologic age may not always correspond with chronologic age.

Despite the broad interest in better understanding the unique aspects of older adults that impact their cardiovascular care and outcome, few studies have utilized direct observation to develop new risk-prediction tools in this population, and most have relied on administrative datasets. Administrative studies, while useful, lack some of the granular data that may provide a richer understanding of the ways in which geriatric issues impact cardiac care and outcomes. The

Comprehensive Evaluation of Risk Factors in Older Patients with AMI (SILVER-AMI) is a recently completed study designed to address these issues and add new context to risk-prediction in older adults after acute MI. The study enrolled 3000 adults over 75 years old hospitalized with AMI throughout their hospitalization and followed each for 6 months after discharge. As a large, national study of patients hospitalized for AMI, one of the unique aspects of SILVER was its inclusion of a thorough geriatric assessment. This assessment includes gait speed, vision, hearing, cognition, and strength. Such geriatric impairments are not available in large administrative data sets, and while their importance in the field of geriatrics has been well established, neither their prevalence in post-AMI patients nor their significance for risk-prediction in that population is well understood. SILVER-AMI is primarily designed to test the associations of these geriatric-associated variables, along with a host of clinical, demographic, and psychosocial factors, with outcomes including readmission, mortality, and decline in health status. The study has generated far more information, and the sub-studies included in this thesis are focused on using the rich data from SILVER-AMI to investigate associations with outcomes that are uniquely important to patients and practitioners of geriatric cardiology.

Older adults consistently identify maintaining physical function as a top priority(2), and while quality improvement efforts and evolving knowledge have made great strides in improving readmission and mortality after AMI, less attention has been paid to functional outcomes. This thesis utilizes the rich data of the SILVER-AMI study to discover risk factors for outcomes that are more relevant to maintenance of functional status. These outcomes include one adverse event, falls, and one healthcare utilization outcome, cardiac rehabilitation (CR) use. Falls are devastating for older adults, and can have significant impacts on quality of life and functional status. Though they are widely studied, the risk factors after hospitalization are not well described. Cardiac rehabilitation is an important part of post-AMI care, and can reduce mortality and readmission, along with many geriatric specific benefits. Despite this, it is dramatically underused, especially in older adults, and the specific factors associated with underutilization in older adults are unknown. These outcomes have not received adequate attention in the population of older adults following AMI, and this project enhances our ability to identify patients at risk, and to begin the process of improving care delivery.

a. STATEMENT OF PURPOSE:

This thesis will investigate risk factors for outcomes of functional importance to older adults following acute myocardial infarction. This will be accomplished using data generated by the SILVER-AMI study to test associations between baseline variables and outcomes evaluated six months after discharge.

Aim 1: To identify demographic, clinical, geriatric, and psychosocial factors associated with falls within six months of discharge in adults over 75 hospitalized with acute myocardial infarction.

Aim 2: To identify demographic, clinical, geriatric, and psychosocial factors associated with non-utilization of cardiac rehabilitation within six months of discharge in adults over 75 hospitalized with acute myocardial infarction.

Aim 3: To describe the rates of self-reported falls, medically serious falls, and cardiac rehabilitation utilization within six months of discharge in adults over 75 hospitalized with acute myocardial infarction.

II. METHODS OF THE SILVER-AMI STUDY:

SILVER-AMI is a prospective, multi-center longitudinal cohort study approved by the Yale Institutional Review Board and registered at www.clinicaltrials.gov (NCT01755052). Recruitment and enrollment was performed at a network of 90 hospital sites. Sites were roughly half in urban areas, and half in rural areas. At each site, a research coordinator was trained in informed consent, recruitment of older, hospitalized patients, and use of the data capture system, and this individual was responsible for screening and enrolling patients. The research coordinator reviewed daily hospital admissions to screen for potentially eligible patients. Eligibility criteria included: Age >= 75, diagnosis of acute MI by Third Universal Definition of Myocardial Infarction (troponin I or troponin T above upper limit of normal AND either ischemic ECG findings, angina symptoms, imaging evidence of loss of myocardium or new wall motion abnormality or identification of an intracoronary thrombus on angiography)(3). Exclusion criteria included: initial troponin elevation occurring >24 hours after hospital admission, AMI secondary to inpatient procedure or surgery, transfer from another hospital after a stay exceeding 24 hours, incarceration, and inability to provide informed consent with no available proxy.

Upon enrollment, patients were evaluated using a standardized interview and physical assessment by the research coordinator. Data were generated from the following sources and validated instruments.

Demographic:

Demographic data were collected via survey. Participants were asked about race, marital status, education, and income and healthcare finances.

Clinical:

Clinical data were collected from a combination of surveys and medical record abstraction. Patients were asked about their symptoms and presentation the hospital. Baseline health status was queried using the Short Form 12 (SF-12)(4), and their recent symptoms were rated using the Edmonton Symptom Assessment Scale(5) and the abbreviated Seattle Angina Questionnaire (SAQ-7)(6). The research coordinator also performed a detailed medical record abstraction for further clinical data, collecting information about patient presentation, vital signs, laboratory results, past medical history, comorbidities, adverse events in the hospital, and disposition for discharge. The participant's medical records were also provided to the Yale Coordinating Center where a research nurse reviewed them for information about medications, in-hospital cardiac procedures, and discharge instructions.

Geriatric:

Data on geriatric impairments were assessed through a detailed geriatric assessment. Cognitive impairment was evaluated using the Telephone Interview of Cognitive Status (TICS)(7) a validated instrument chosen because it is sensitive to mild cognitive impairment, can be administered quickly, does not require writing, and is not protected by copyright. A cut point of <27 on the TICS was used to indicate cognitive impairment (equivalent to a score of <24 on the Folstein MMSE(8)). Vision was assessed using items from the Visual Functioning Questionnaire (VFQ-25(9)). A composite variable was created to indicate visual impairment based on responses to three questions from this questionnaire. Hearing impairment was assessed with a single global question, "do you have a hearing problem now?" which has shown good sensitivity and specificity compared to audiography(10). Functional mobility was measured with the Timed Get Up and Go (TUG) test, which involves rising from a seated position, walking three meters, and returning to the chair to sit down(11). Strength was measured using a handheld dynamometer (B&L Engineering, Santa Ana, CA), as grip strength is considered a good estimate of overall muscle strength(12). Participants were asked about ability to perform activities of daily living (ADLs) at home(13), as well as recent weight loss, ability to walk a quarter mile, and recent falls.

Psychosocial:

Psychosocial data were gathered through the baseline interview. Participants were asked alcohol and tobacco use. Social support was was evaluated using a shortened version of the Medical Outcomes Study Social Support Scale (MOS-SSS)(14). Participants were evaluated for depression using the PHQ-8(15). Finally, the interviewer indicated their confidence in the answers provided by the participant, and whether any help was required, and assessed whether there was any noticeable change in the participant's mental status during the interview.

Outcome assessment:

At six months from discharge, a telephone interview was conducted by staff at Yale with the participant (or the participant and proxy, for those whose decision-making was deemed impaired at baseline). The interview repeats the SF-12, SAQ-7, ESAS, PHQ-8, ADLs, and specifically asks about occurrence of falls since discharge, as well as asking about the use of cardiac rehabilitation. Participants were also asked if they have been re-hospitalized, and are asked if they have had any symptoms that they attribute to their medications, including upset stomach/nausea, bleeding, bruising, fatigue, muscle weakness, allergic reaction, sadness/depression, confusion or inattention, dizziness, falls, kidney problems, and liver problems. If they had such symptoms, they are asked which to which medication they attribute the symptom, and if any action has been taken to address the adverse effect. At the same time as the follow up interview, medical records were collected for any hospital admissions, outpatient cardiac procedures, ED visits, and deaths. Physicians performed adjudication of all medical records to determine the cause of readmission or ED visits. All data was transmitted from the study site to the Yale Coordinating Center within 3 days, where it was managed using REDCap, an NIH-supported, HIPAA-compliant data capture system(16).

III. CHAPTER I: PREDICTORS OF FALLS AFTER ACUTE MYOCARDIAL INFARCTION

IIIa. BACKGROUND:

A fall is one of the most dangerous events that can happen to an older person. Morbidity associated with falls in older adults includes hip or other bone fracture, head injury, emergency department visits, hospitalization, restriction in mobility, decreased ability to perform activities of daily living, and increased nursing home placement(17). The rate of falls is estimated at one in three each year those over the age of 65 and one in five each year in those over the age of 80(18).

Prior studies have focused on risk prediction during the inpatient period, among community-dwelling older adults, and among institutionalized older adults. In-hospital fall risk is a well-studied topic due to the importance of fall prevention as a hospital quality metric. There are three main risk-prediction tools for in-hospital fall risk: STRATIFY, HFRM II, and MFS, which have been studied extensively. STRATIFY incorporates five criteria: presentation with fall or prior fall on current admission, agitation, frequent need of toileting, visual impairment, low mobility/transfer score(19). HFRM II incorporates eight criteria: confusion/disorientation, depression, elimination, dizziness/vertigo, gender, any prescribed antiepileptics, any prescribed benzodiazepines, timed get-up-and-go test(20). The Morse Fall Scale (MFS) incorporates 6 criteria: history of falling, secondary diagnosis, ambulatory aid, IV therapy, gait, and mental status(21). A systematic review and meta-analysis found that STRATIFY performed best in the inpatient population(22).

Risk factors are different for inpatient and outpatient older adults. Community dwelling older adults are the most extensively studied population with regards to falls, and many risk factors have been identified. Demographic risk factors in community-dwelling older adults include age and gender(23), with women more likely to fall, but men more likely to suffer serious injury from fall. Clinical risk factors include, comorbidities, polypharmacy(18), use of antihypertensives(24), (25). Geriatric risk factors for falls among community-dwelling older adults include prior fall history, impaired functional mobility, visual impairment(26), impaired cognitive function(27) (particularly executive function)(28), use of an assistive device(23), and frailty(29). Frailty is an important concept in geriatrics, and is generally clinically established by the presence of three of the following five criteria: unintentional weight loss, exhaustion, slow gait, weak grip strength, and low physical activity(30). Though the connection is intuitive, it has been difficult to demonstrate an association between orthostatic hypotension and falls, though in the presence of uncontrolled hypertension it is a strong risk factor(31). The major psychosocial risk factor for falls in this population is depression, which has been shown to independently predict fall risk, and this effect is magnified in individuals with comorbid medical conditions(32, 33). The risk factors for falls in an institutionalized population are largely similar to those in community-dwelling older adult, with additional factors including urinary incontinence(34, 35), vasodilator use(35).

While there have been many studies on fall risk, there is still a great deal that is unknown or poorly understood. Few studies have examined period immediately following hospitalization, i.e. the post-discharge period. Limited evidence suggests that the post-discharge period is a time of elevated fall risk, but the it is not well established how risk factors are modified during this time(36). We posit AMI hospitalization will increase fall risk in the post-discharge period, given the direct insult to homeostasis that led to the hospitalization as well as the effect of the hospitalization itself. Older adults admitted to the hospital with AMI are often frail and poorly equipped to respond to the physiologic insult of an MI or a revascularization procedure. Their activity is limited while in the hospital, they experience disturbed sleep and emotional stress, and their medication regimens are often dramatically altered. This all contributes to a phenomenon known as "post-hospitalization syndrome(37)," a catch-all term for the increased risk of adverse events after hospitalization.

AMI itself has not been tied to increased risk of falls in older adults, and it may seem counterintuitive at first to examine a post-AMI cohort for factors associated with falls, but there are numerous aspects of post-AMI care that make this an ideal group to examine for fall risk. For those older adults already at a significant risk of fall, we can hypothesize that an AMI hospitalization may dramatically alter that risk, and that the factors associated with a post-discharge fall may be unique in this population. This study will be the first to focus on falls after an

AMI hospitalization, which will provide valuable context to our understanding of how to deliver optimal care.

Understanding risk factors for falls after discharge from the hospital is essential because of the devastating consequences of falls in older adults, and the steps that can be taken to minimize the risks and harms of falls at the time of discharge. Important treatment decisions are made at discharge that can certainly impact fall risk; beta-blockers could increase fall risk in vulnerable individuals, and anticoagulation could dramatically increase the danger associated with a fall. Understanding the links between cardiovascular disease and fall risk could better inform the risk-benefit calculus that goes into such clinical decisions. Identifying individuals at higher risk for post-discharge falls will allow for future efforts to minimize this risk.

IIIb. METHODS:

Data collection:

SILVER-AMI was a prospective, multi-center longitudinal cohort study (n=3041) whose methods have been published previously(38) and described in detail above. Briefly, recruitment and enrollment is performed at a network of 90 clinical sites. Eligibility criteria include: Age >= 75, diagnosis of acute MI by Third Universal Definition of Myocardial Infarction(3). Exclusion criteria include: initial troponin elevation occurring >24 hours after hospital admission, AMI secondary to inpatient procedure or surgery, transfer from another hospital after a stay exceeding 24 hours, incarceration, and inability to provide informed consent with no available proxy.

Baseline assessment:

Upon enrollment, a research coordinator performed a detailed baseline evaluation including demographic information, symptomatology, measures of health status(4-6), social support(14) and information on geriatric impairments such as ADLs(13), orthostasis, cognitive impairment(7, 39), depression(15), vision(9) or hearing(10) impairment, grip strength(40), functional mobility(41) and prior falls. Baseline information was also generated from a medical record abstraction including details of presentation, vital signs, laboratory results, past medical history, comorbidities, treatments, adverse events in the hospital, and disposition for discharge. Polypharmacy in this analysis was defined as greater than or equal to six medications reported at discharge.

Outcome measurement- self-reported falls:

Six months after discharge from the index hospitalization, the participant (or proxy) was interviewed over the phone by study staff. The interview repeats the SF-12, SAQ-7, ESAS, PHQ-8, ADL, abbreviated CAM, and specifically asks about occurrence of falls. Patients were asked how many falls they have had since discharge, if they had an injury, and if they sought medical care. Patients were excluded if they died during the index hospitalization.

Outcome measurement- medically serious falls:

At the time of the six-month follow up interview, medical records for each participant were reviewed for hospital admissions, outpatient procedures, ED visits, and deaths. Records were adjudicated by physicians involved with the study, and a determination was made whether any hospitalization or ED visit was the result of a fall. Any fall that led to such an ED visit or hospitalization was deemed a "medically serious fall." Patients were excluded if they are completely disabled at baseline or if they die during the index hospitalization.

Data analysis:

Patients without outcome data were excluded from analysis. This included patients who died during the index hospitalization or prior to the six-month follow up, as well as patients who did not complete the study. Two outcomes will be used for this study: self-reported falls at six months, and falls leading to ED visits or hospitalizations. Participants will be classified into two groups for each outcome: those with the outcome and those without. A list of hypothesized predictor variables was generated based on literature review and clinical reasoning to analyze likely demographic, clinical, geriatric, and psychosocial risk factors. Missingness of the data was analyzed, and multiple imputation used in the case of missing data, generating twenty imputed datasets. A table was generated showing the means and proportions of each variable among those with and without self reported falls and adjudicated falls. Each variable was evaluated for its association with falls using a chi-squared test for categorical variables or a Student-t test for continuous variables to compare the groups with falls and without falls for each outcome measure.

Multivariate analysis was performed (for both outcome measurements) using logistic regression to generate adjusted odds ratios. Covariates to be included in the multivariate model were selected using a pre-specified protocol as follows. Backward selection was applied to a pooled sample consisting of all twenty imputed datasets with a p value threshold of 0.001 to account for the artificially inflated sample size. This corrects for the fact that the unimputed dataset may be biased by missingness, and that the twenty imputations may not align with one unique model. A small subset of variables was "forced" into the final logistic regression model, bypassing backward selection because of their previously demonstrated association with falls and broad clinical reference. This group of variables was: age, sex, race, prior fall history, timed-up-and-go (proxy for gait speed), and polypharmacy. Using the covariates generated by this process, Tables 3 and 4 demonstrates the unadjusted and adjusted odds ratios of the predictor variables.

Work performed by student researcher and others:

David Goldstein was responsible for generating the research question for this substudy, determining the relevant outcome variables and generating the list of hypothesized predictor variables. He also designed the analytic plan

Participants were enrolled and data were collected by paid study staff of the SILVER-AMI study under the supervision of the principal investigator, Sarwat Chaudhry, and the project director, Mary Geda.

Imputation of missing data was performed by the SILVER-AMI biostatistician, Terry Murphy, and lead data manager, Sui Tsang. Analysis was performed in the SAS statistical suite by an analyst from the Yale Center for Analytical Sciences (YCAS), Xuemei Song, under the supervision of David Goldstein.

IIIc. RESULTS:

Univariate and Bivariate analysis:

Of the 3041 patients enrolled in the SILVER-AMI study, 2584 (85%) had outcome data on self-reported falls, while 3006 (98.9%) had outcome data on falls leading to an ED visit or hospitalization.

Of the 2584 participants included in the analysis of self-reported falls, 557 (21.6%) reported a fall within six months of discharge. Baseline differences between those who reported a fall and those who did not are reported in Table 1. To summarize the unadjusted bivariate analysis, those who reported a fall were older, had a lower physical component score and mental component score of the SF12, a higher Charlson score, a longer length of stay, a lower social support score, were more likely to have been unable to walk ¼ mile one month prior to admission, more likely to need help bathing, dressing, and rising from a chair, less likely to be able to complete the Timed-up-and-go test, more likely to have cognitive impairment, a history of falls in the past year, unintentional weight loss, weak grip strength, lower activity level, and a positive PHQ screen for depression, though many of these between group differences did not have clinical significance.

Table 1: Baseline characteristics of participants with and without self-reported falls

Variable		No self-reported fall at 6 months N= 2027		Self-reported fall at 6 months N= 557		P value
			Missing		Missing	
Mean Age (SD)		81.1 (4.78)	0	81.9 (5.07)	0	<0.001
Sex (male)		1161 (57.3%)	0	297 (53.3%)	0	0.10
Race (non-white)		204 (10.0%)	29 (1.4%)	46 (8.2%)	15 (2.7%)	0.23
Education ≤ 12 years		1127 (55.6%)	15 (0.7%)	326 (58.5%)	7 (1.2%)	0.17
SF12 Physical Component Score		42.4 (9.96)	8 (0.4%)	39.9 (9.69)	1 (0.2%)	<0.001
SF12 Mental Component Score		53.4 (9.29)	7 (0.4%)	51.4 (10.59)	1 (0.2%)	<0.001
Mean Charlson Score (SD)		3.29 (2.48)	1 (0%)	3.68 (2.68)	1 (0.2%)	0.002
Mean Length of Stay (SD)		5.44 (4.61)	0	6.31 (5.90)	0	0.001
Mean Social Support Score (SD)		21.9 (4.22)	38 (1.9%)	21.10 (4.96)	11 (2.0%)	0.001
Live alone		732 (36.1%)	2 (0.1%)	224 (40.2%)	0	0.08
MI diagnosis	STEMI	565 (27.8%)	0	144 (25.9%)	0	0.34
	NSTEMI	1462 (72.1%)		413 (74.2%)		
Left ventricular EF category	>= 50%	1090 (53.8%)	181 (8.9%)	285 (51.8%)	53 (9.5%)	0.48
	40-50%	384 (18.9%)		120 (21.5%)		
	30-40%	240 (11.8%)		67 (12.0%)		
	<30%	132 (6.5%)		32 (5.8%)		
PCI performed		1229 (60.6%)	0	329 (59.1%)	0	0.50
CABG performed		257 (12.7%)	0	65 (11.7%)	0	0.52
Polypharmacy		1251 (61.7%)	1 (0.1%)	356 (63.9%)	0	0.35
Bleeding complication		504 (24.9%)	0	147 (26.4%)	0	0.46
Acute kidney injury		419 (20.7%)	1 (0.1%)	122 (21.9%)	1 (0.2%)	0.52
Able to walk ¼ mi 1 month prior to admission		1425 (70.3%)	7 (0.4%)	345 (61.9%)	0	<0.001
Needs assistance bathing		103 (5.1%)	0	53 (9.5%)	0	<0.001
Needs assistance dressing		102 (5.0%)	0	47 (8.4%)	0	0.002
Needs assistance rising from chair		89 (4.39%)	3 (0.2%)	38 (6.8%)	0	0.019
Needs assistance walking around		53 (2.6%)	3 (0.2%)	21 (3.8%)	1 (0.2%)	0.15
Timed-up-and-go category	<=15 seconds	678 (33.5%)	321 (15.8%)	121 (21.7%)	96 (17.2%)	<0.001
	16-25 seconds	441 (21.8%)		122 (21.9%)		
	>25 seconds	327 (16.1%)		88 (15.8%)		
	Incomplete due to impairment	260 (12.8%)		130 (23.3%)		
Hearing impairment		1068 (52.7%)	1 (0.1%)	298 (53.5%)	0	<0.001
Visual impairment		670 (33.1%)	1 (0.1%)	250 (44.9%)	0	<0.001
Cognitive impairment		267 (13.2%)	30 (1.5%)	106 (19.0%)	11 (2.0%)	<0.001
Unintentional weight loss		377 (18.6%)	7 (0.4%)	137 (24.6%)	4 (0.7%)	0.001
>= Two falls in past year		281 (13.9%)	4 (0.2%)	200 (35.9%)	2 (0.36%)	<0.001
Weak grip		1138 (56.1%)	71 (3.5%)	367 (65.9%)	29 (5.2%)	<0.001
Activity level vs. same age peers	More active	1106 (54.6%)	10 (0.5%)	262 (47.0%)	6 (1.1%)	0.003
	About as active	640 (31.6%)		189 (33.9%)		
	Less active	271 (13.4%)		100 (18.0%)		
PHQ screen positive		239 (11.8%)	60 (3.0%)	98 (17.6%)	14 (2.5%)	<0.001
Problematic alcohol use		106 (5.2%)	14 (0.7%)	32 (5.8%)	4 (0.7%)	0.63

Of the 3006 patients included in the medically serious falls analysis, 192 (6.4%) had a fall leading to an ED visit or hospitalization. Baseline differences between those who reported a fall and those who did not are reported in Table 2. To summarize the unadjusted bivariate analysis, those who had a fall leading to an ED visit or hospitalization were older, had a lower physical component score of the SF12, longer length of stay, had a higher Charlson score, a lower social support score, were more likely to be living alone, more likely to have polypharmacy, to have had an AKI during their hospitalization, more likely to have been unable to walk ¼ mile prior to admission, less likely to be able to complete the Timed-up-and-go test, more likely to have visual impairment, more likely to need assistance in bathing, dressing, and getting up from a chair, more likely to have a weak grip, a history of two or more falls in the past year, and a positive PHQ screen for depression, though many of these between group differences did not have clinical significance.

Of the 2584 participants with results in both outcome measures, 42 of the 2027 (2.1%) who reported no fall were found to have an ED visit or hospitalization caused by a fall. Of the 557 that reported a fall, 113 (20.3%) had an ED visit or hospitalization resulting from a fall, and the remaining 79.8% did not require medical attention. Of the 422 participants with an adjudicated result but no self-reported data, 37 (8.7%) had an ED visit or hospitalization resulting from a fall. Table 3 contains a simple two-by-two demonstration of both outcome measures.

Table 2: Baseline characteristics of participants with and without medically serious falls

Variable		No medically serious fall at 6 months N = 2814		Medically serious fall at 6 months N =192		P value
			Missing		Missing	
Mean age (SD)		81.47 (4.99)	0	82.81 (5.23)	0	<0.001
Sex (male)		1573 (55.9%)	0	98 (51.0%)	0	0.19
Race (non-white)		300 (10.6%)	44 (1.6%)	17 (8.85%)	4 (2.1%)	0.44
Education ≤ 12 years		1594 (56.7%)	23 (0.8%)	113 (58.9%)	3 (1.6%)	0.47
Mean SF12 Physical Component Score (SD)		41.51 (10.05)	16 (0.1%)	39.31 (10.11)	1 (0.1%)	0.004
Mean SF12 Mental Component Score (SD)		52.76 (9.76)	15 (0.1%)	51.43 (10.25)	1 (0.1%)	0.07
Mean Charlson Score (SD)		3.52 (2.60)	2 (0.1%)	4.08 (2.72)	0	0.004
Mean length of Stay (SD)		5.86 (5.32)	0	7.01 (5.12)	0	0.004
Mean Social Support Score (SD)		21.62 (4.44)	70 (0.3%)	20.85 (4.93)	1 (0.1%)	0.038
Live alone		1053 (37.4%)	2 (0.1%)	91 (47.4%)	0	0.006
MI diagnosis	STEMI	749 (26.6%)	0	42 (21.9%)	0	0.15
	NSTEMI	2065 (73.4%)		150 (78.1%)		
Left ventricular EF category	>= 50%	1439 (51.1%)	258 (9.2%)	88 (45.8%)	19 (9.9%)	0.06
	40-50%	564 (20.0%)		33 (17.2%)		
	30-40%	357 (12.7%)		36 (18.8%)		
	<30%	196 (7.0%)		16 (8.3%)		
PCI performed		1628 (57.9%)	0	101 (52.6%)	0	0.15
CABG performed		338 (12.0%)	0	16 (8.3%)	0	0.13
Polypharmacy		1727 (61.4%)	1 (0%)	132 (68.8%)	0	0.042
Bleeding complication		726 (25.8%)	2 (0.1%)	47 (24.5%)	0	0.69
Acute kidney injury		635 (22.6%)	2 (0.1%)	57 (29.7%)	0	0.024
Able to walk ¼ mi. one month before admission		1868 (66.4%)	9 (0.3%)	113 (58.9%)	0	0.028
Needs assistance bathing		205 (7.3%)	1 (0%)	29 (15.1%)	0	<0.001
Needs assistance dressing		195 (6.9%)	1 (0%)	21 (10.9%)	0	0.038
Needs assistance rising from chair		164 (5.8%)	4 (0.1%)	18 (9.4%)	0	0.047
Needs assistance walking around		113 (4.0%)	4 (0.1%)	9 (4.7%)	1 (0.5%)	0.64
Timed-up-and-go category	<=15 seconds	829 (29.5%)	442 (15.7%)	36 (18.8%)	37 (19.3%)	<0.001
	16-25 seconds	597 (21.2%)		22 (11.5%)		
	>25 seconds	448 (15.9%)		35 (18.2%)		
	Incomplete due to impairment	498 (17.7%)		62 (32.2%)		
Hearing impairment		1511 (53.7%)	2 (0.1%)	101 (52.6%)	0	0.76
Visual impairment		1027 (36.5%)	3 (0.1%)	87 (45.3%)	0	0.015
Cognitive impairment		466 (16.6%)	46 (1.6%)	40 (20.8	3 (1.6%)	0.13
Unintentional weight loss		621 (22.1%)	17 (0.6%)	50 (26.0%)	0	0.22
2 or more falls in past year		530 (18.8%)	12 (0.4%)	63 (32.8%)	0	<0.001
Weak grip		1679 (59.7%)	111 (3.9%)	128 (66.7%)	18 (8.9%)	0.003
Activity level vs. same age peers	More active	1445 (51.35%)	24 (0.9%)	89 (46.35%)	1 (0.5%)	0.38
	About as active	903 (32.09%)		69 (35.94%)		
	Less active	442 (15.71%)		33 (17.19%)		
PHQ screen positive		382 (13.6%)	93 (3.3%)	40 (20.8%)	6 (3.1%)	0.005
Problematic alcohol use		135 (4.8%)	23 (0.8%)	12 (6.3%)	1 (0.5%)	0.37

Table 3: Comparison of self-reported and medically serious falls

N = 2584		Self reported falls	
		Yes	No
Medically serious falls	Yes	113 (4.3%)	42 (1.6%)
	No	444 (17.2%)	1985 (76.8%)

Multivariate analysis:

All variables in tables 1 were included in the backward selection process. Using a pooled sample of all 20 imputed datasets and a threshold for inclusion of 0.001, 20 variables were selected for inclusion in the logistic regression model for self-reported falls. These variables are: age, sex, race, polypharmacy, timed-up-and-go, greater than or equal to two falls in the past year, physical component score of SF12, mental component score of SF12, length of stay, living alone, in-hospital ejection fraction, CABG performed, acute kidney injury, hearing impairment, visual impairment, and impaired grip strength. Table 4 contains the results of the logistic regression model for self-reported falls.

There were five independent predictors of self-reported falls: inability to complete TUG (OR 1.5 [1.07-2.11] relative to completing TUG in less than or equal to 15 seconds), having two or more falls in the year prior to admission (OR 2.97 [2.37-3.74]), longer length of stay (OR 1.04 [1.02-1.07] for each additional day), visual impairment (OR 1.33 [1.08-1.64]), and weak grip strength (OR 1.28 [1.02-1.60]).

Table 4: Results of logistic regression analysis for self-reported falls

Predictor Variable		Odds Ratio for self reported falls (95% CI)	p value
Age (continuous)		1.02 (1.00-1.04)	0.07
Male sex (binary)		1.02 (0.82-1.26)	0.89
Non-white race (binary)		0.74 (0.52-1.06)	0.10
Polypharmacy (binary)		1.09 (0.89-1.35)	0.40
Timed up and go (categorical)	≤ 15 seconds	Reference	n/a
	16-25 seconds	1.29 (0.97-1.71)	0.09
	>25 seconds	1.08 (0.78-1.50)	0.64
	Did not complete due to impairment	1.5 (1.07-2.11)	0.018
Two or more falls in past year (binary)		2.97 (2.37-3.74)	<0.0001
SF12 Physical component score (continuous)		0.99 (0.98-1.00)	0.08
SF12 Mental component score (continuous)		0.99 (0.98-1.00)	0.056
Live alone (binary)		1.14 (0.93-1.41)	0.21
Length of stay, days (continuous)		1.04 (1.02-1.07)	0.0005
In hospital LV ejection fraction (categorical)	<30%	0.69 (0.45-1.07)	0.09
	30-39%	0.86 (0.62-1.18)	0.35
	40-49%	1.11 (0.45-1.07)	0.41
	>= 50%	Reference	n/a
CABG performed (binary)		0.79 (0.55-1.13)	0.20
AKI in hospital (binary)		0.85 (0.65-1.10)	0.21
Hearing impairment (binary)		0.86 (0.70-1.06)	0.15
Visual impairment (binary)		1.33 (1.08-1.64)	0.008
Weak grip strength		1.28 (1.02-1.60)	0.030

In the analysis of medically serious falls, all variables in Table 2 were included. Using a pooled sample of all 20 imputed datasets and a threshold for inclusion of 0.001, 20 variables were selected for inclusion in the logistic regression model for adjudicated falls. These variables are age, sex, race, polypharmacy, timed-up-and-go, two or more falls in the past year, length of stay, living alone, in hospital ejection fraction, CABG performed, impairment in bathing ADL, impairment in walking around ADL, visual impairment, comparison of activity level to peers, and problematic alcohol use. Table 5 contains the results of the logistic regression model for medically serious falls.

There were five independent predictors of medically serious falls: inability to complete TUG (OR 1.85 [1.11-3.09] relative to completion in less than or equal to fifteen seconds), two or more falls in the year prior to admission (OR 1.73 [1.23-2.42]), length of stay (OR 1.03 [1.01-1.06] for each additional day), living alone (OR 1.37 [1.00-1.87, p = 0.048]), and impairment in the bathing ADL (OR 1.74 [1.06-2.86]).

Table 5: Results of logistic regression analysis for medically serious falls

Predictor Variable		Odds Ratio for medically serious falls (95% CI)	p value
Age (continuous)		1.02 (0.99-1.06)	0.12
Male sex (binary)		1.01 (0.73-1.39)	0.96
Non-white race (binary)		0.73 (0.43-1.24)	0.24
Polypharmacy (binary)		1.38 (0.99-1.91)	0.055
Timed up and go (categorical)	≤ 15 seconds	Reference	n/a
	16-25 seconds	0.85 (0.50-1.44)	0.54
	>25 seconds	1.50 (0.91-2.48)	0.11
	Did not complete due to impairment	1.85 (1.11-3.09)	0.018
Two or more falls in past year (binary)		1.73 (1.23-2.42)	0.001
Length of stay, days (continuous)		1.03 (1.01-1.06)	0.013
Live alone (binary)		1.37 (1.00-1.87)	0.048
In hospital LV ejection fraction (categorical)	<30%	1.08 (0.60-1.92)	0.80
	30-39%	1.24 (0.82-1.88)	0.30
	40-49%	0.88 (0.58-1.33)	0.54
	>= 50%	Reference	n/a
CABG performed (binary)		0.58 (0.32-1.06)	0.08
Needs assistance bathing (binary)		1.74 (1.06-2.86)	0.030
Needs assistance walking around (binary)		0.58 (0.27-1.27)	0.18
Visual impairment (binary)		1.23 (0.90-1.68)	0.19
Activity vs. same age peers (categorical)	About as active	1.12 (0.80-1.58)	0.51
	Less active	0.78 (0.5-1.24)	0.30
	More active	Reference	n/a
Problematic alcohol use (binary)		1.48 (0.79-2.78)	0.22

IIId. DISCUSSION:

In this study of fall risk among adults over 75 within six months of discharge following an acute MI hospitalization, 21.6% of participants reported a fall and 6.4% had an ED visit or hospitalization caused by a fall. Self-reported falls were associated with a recent history of prior falls, geriatric impairments in gait speed, grip strength, and vision, and length of stay during their AMI hospitalization. ED visits and hospitalizations secondary to falls were similarly associated with recent history of prior falls, impaired gait speed, and length of stay, and were additionally associated with impairment in the bathing ADL and with living alone.

The high prevalence of falls in this cohort underscores the necessity of considering falls as a possible adverse event after discharge. While the specific population of older adults after AMI had not previously been examined for fall risk, the prevalence we report is similar to other studies of fall risk in community dwelling older adults. More than simply confirming that the fall rate is high among older adults, our univariate analysis grants a novel insight as well, primarily in the use of two separate outcome measures. Self-report has been widely used in prior studies of fall rates and fall risk(18), as have various methods of extrapolating falls from medical records or administrative datasets. No studies have yet used both methods, however, and the ability to compare both gives additional context to the literature on fall risk. The rate of false negatives (participants with a documented medically serious fall who did not report it) via self-report was impressively low, lending further credence to its use as a metric for falls.

We had expected that self-reported falls would be more common than falls leading to ED visits or hospitalizations, as not every fall is necessarily serious enough to require medical attention. It was striking, however, that self-reported falls were over three times more common among our cohort. The difference between these two rates indicates a subset of "subclinical" falls. The scope of the problem, when referring to falls, is frequently framed around serious injuries and deaths, but it is also important to address the impact of falls that do not cause these devastating sequelae. Even in the absence of serious injury, falls can cause a vicious cycle in which increased fear of falling causes a decrease in physical activity, leading to development of frailty, loss of independence, and even future falls(42). While our data cannot address whether any of these consequences arose from the self-reported falls in this cohort, these less medically serious falls should still be treated as an important adverse event in older adults.

In our investigation of factors associated with falls, we found both similarities and differences between our two outcome measures. There were key predictors that were associated with both outcomes, independently predicting a higher rate of falls as well as healthcare utilization resulting from falls. That fall history is associated with falls in our study is unsurprising, as it is a risk factor in nearly every study. Though this result is not novel, it cannot be overstated how important a detailed fall history can be in predicting fall risk, and this holds true when in the post-discharge period. Similarly, the impairment in functional mobility reflected by an inability to complete the timed-up-and-go test is consistent with prior literature, but it is an important result. These associations demonstrate that some of the known risk factors of falls in a community-dwelling population are still independent predictors in this cohort of recently discharged patients following AMI. Obtaining information on fall history and gait speed is simple, and this result points to its importance in the inpatient setting.

The most novel result of these analyses was the association between length of stay with both measurements of falls. There are multiple possible explanations for this effect. Longer hospital stays are likely the result of more complicated inpatient courses. Though individual complications like AKI were not independently predictive in this cohort, length of stay could serve as an important proxy for a more complicated hospitalization in general, or for a worse initial presentation. Alternatively, there could be a more directly causal link between length of stay and falls. The time after hospital discharge is well known to be a high-risk period for many adverse events, a phenomenon known as “post-hospitalization syndrome”(43). While in the hospital, patients are frequently in bed for the vast majority of the day. Immobilization such as this can lead to reduction in physical function in healthy older adults(44), and it would not be surprising to see a similar effect in patients recovering from an MI. Hospitalization as a risk factor for adverse outcomes is Further research is necessary to clarify this association further, but it is important for clinicians to recognize that those patients discharged after a long hospital stay may be more likely to fall.

The two outcomes each yielded some independent associations. These are useful for generating new hypotheses about fall risk and may be helpful in guiding future research, but it is more difficult to draw conclusions from these associations.

The factors that predicted self-reported falls but not medically serious falls included weaker grip strength and visual impairment. It is difficult to confidently explain an association of these variables with self-reported falls but not with adjudicated falls, but both are previously established risk factors for falls(26, 29), and should be taken into consideration as such. Medically serious falls were predicted uniquely by living alone and needing assistance with bathing. One reasonable hypothesis for the association of living alone with medically serious falls, but not with an increase in self-reported falls, is that these individuals may fall at the same rate as others, but may spend more time down after falling because they are alone, and may require the use of emergency services as a result, leading to more healthcare utilization from falls.

This study has numerous strengths supporting its findings. The inclusion of a thorough geriatric assessment is a key component of any examination of risk factors for falls, and the nature of the SILVER-AMI evaluation allowed larger, more comprehensive set of possible predictor variables. Similarly, SILVER-AMI's impressive follow-up rate and thorough data collection meant that missingness was relatively low, and few variables were extensively imputed. The use of two outcome measures grants this study a unique insight into the prevalence of falls and of medically serious falls in this population. We are reassured by the low rate of false negatives on self-report, and the association of some predictors with both outcomes adds extra weight to these specific results.

Limitations of this study include the binary nature of each outcome measure. Some patients may have fallen more than once, information that would not be captured through either outcome in this study. The observational nature of this study places clear limitations on our ability to interpret causality. In contrast to a randomized controlled trial, indication biases can exist which skew associations between treatments and adverse events like falls. For example, beta-blockers are a key component of post-AMI secondary prevention, and are prescribed nearly universally in these patients(45). Those few patients who are not prescribed beta-blockers are likely quite different from the majority who receive them, and this makes it nearly impossible to tease out the effect of this drug on falls, despite its known association with orthostatic hypotension and lightheadedness. For this reason, individual medications were not examined in this analysis.

This study raises important questions for future research directions. The association of longer hospital stays with increased fall risk is a striking result, and further study can clarify the mechanism of the association. Furthermore, there may be interventions to attenuate this increased risk. Increasing mobility while in the hospital could prevent deconditioning. This study was limited to patients discharged after AMI, but it is important to perform similar research after other types of hospitalizations. Do similar factors predict falls after a pneumonia hospitalization, or after a GI bleed?

This study also has important implications for how clinicians should approach older adults leaving the hospital after an acute MI. Clearly, falls are a significant threat to this population, and should be treated as such. Aside from the hospitalizations resulting from injurious falls, there is an even larger subset of the cohort that reports falling after discharge. Treatment decisions including medications, discharge location, or rehabilitation choices can modify fall risk. Similarly, use of anticoagulants can increase the risk of bleeding after falls. To identify those patients at particularly high risk of fall prior to discharge can allow the clinician to modify the care plan. Our results indicate careful attention should be given to those with a history of falls, with extended hospital stays, and with impaired functional mobility, and these factors should be evaluated during the hospitalization.

IV. CHAPTER II: PREDICTORS OF CARDIAC REHABILITATION USE AFTER ACUTE MYOCARDIAL INFARCTION

IVa. BACKGROUND:

Cardiac rehabilitation (CR) is a multifaceted intervention consisting of exercise training, as well as nutritional, psychosocial, vocational, and risk factor counseling. From its advent, CR was primarily focused on patients with coronary heart disease- first those who were recovering from acute myocardial infarctions, and later those who had been surgically revascularized (with or without AMI). In the early days of CR, the patients referred were typically younger, middle-aged males, but as life expectancy has increased, the population with CHD has increasingly become older and more female. These older adults face worse prognoses and face more severe disability and functional impairment than their younger counterparts.

Benefits of CR:

The widespread recommendations for CR use in patients with CHD are based on reduction in mortality and hospital readmission. The most recent Cochrane review on CR for coronary heart disease demonstrated a significant reduction in cardiovascular mortality and all-cause readmission in a meta-analysis of 63 studies(46). The studies contributing to this review were performed in patients of all ages, and so the specific benefits in the geriatric population are still an open research question. While not directly comparing older to younger patients, a propensity study in over 600,000 Medicare beneficiaries also showed a significant mortality benefit similar to other studies of younger cohorts(47).

In addition to benefits on mortality and readmission, CR may offer potential for improvement in numerous geriatric-specific impairments. Possible benefits in functional capacity, cognition, mood, and frailty are summarized here. Further research is certainly necessary to quantify and explain these benefits, but there is already reason to believe that geriatric post-AMI patients may have the most to gain from CR use.

One of the key outcome measures of CR in all age groups is physical function and exercise capacity. This bears particular relevance to older adults because of the typical decline in functional capacity associated with aging, the progressive nature of disability in older adults, and the acute impact to function and exercise capacity of CVD and hospitalization. As part of the normal process of aging, individuals will experience changes on a cellular, muscular, and physiologic level that can impair exercise or functional capacity. Even absent cardiovascular disease, older adults experience a decline in peak oxygen uptake (VO2peak) with every decade, and this decline accelerates in older age(48). Muscle mass decreases with aging as well(49), and there are numerous cellular and molecular changes associated with aging that diminish ability to deliver energy to tissues(50). These changes are even more pronounced in the population that is eligible for cardiac rehabilitation. Deconditioning is a known complication of hospitalization in the geriatric population(51). In a small 2014 study, DiMaria-Ghalili et al. demonstrated that after cardiac surgery, older adults experience continued weight loss in the context of elevated inflammatory markers.

In both coronary heart disease and congestive heart failure, cardiac rehabilitation has been demonstrated to increase functional capacity or its markers in older adults. Studies of patients with ischemic heart disease showed that effects on exercise capacity were just as great in older adults as in younger patients(52, 53). A recent observational study by Baldasseroni et al. found that those older adults with the worst baseline function after AMI or surgical revascularization showed the most improvement of physical performance associated with CR(54).

Physical frailty is a key concept in the field of geriatrics(55) and is a known prognostic factor for many outcomes in geriatric patients. Recent studies have started to look at frailty as a possibly therapeutic target of CR. A recent meta-analysis found that exercise training improved markers of frailty(56).

Cognitive impairment in older adults has been associated previously with CVD(57). There is increasing evidence that CR improves cognition in older adults. In patients with both heart failure(58) and other forms of CVD, participation in exercise therapy has been shown to increase cognitive functioning in multiple domains(59, 60). The molecular and physiologic mechanisms underpinning the link between cognition and cardiovascular disease are not fully explained as of yet, but recent studies have suggested possible causal links, including white matter changes(61) or alterations in perfusion(59) which may be altered by CR.

In those older adults with CVD, there is increased risk of depression, and, through behavioral factors, depression can be associated with adverse cardiovascular events(62). Decreased functional capacity and ability to exercise is thought to be a mediator of increased depression, and so working to alleviate this limitation has been a target to improve mood symptoms in this population. A 2012 meta-analysis on the effect of CR on depression showed that both community-based and in-home CR caused significant improvement in depression outcomes in older adults(63). Part of the positive impact on patients' mood symptoms may be connected to the social aspect of CR. In a survey of adults participating in cardiac rehabilitation, many highlighted socialization as a key benefit(64).

Underuse of CR

Despite the evidence of CR's major benefits, rates of participation are remarkably low(65, 66), particularly in older adults(67, 68). This has led to calls from national organizations, including the AHA, to increase rates of CR utilization in older adults after AMI. Many factors have been implicated in the underuse of cardiac rehabilitation, and older age has consistently been shown to correlate with lower rates of utilization, but few studies have investigated CR use in older adults. This is a key gap in knowledge that this thesis aims to fill, as the specific factors associated with non-utilization of CR among older adults are not yet known.

Qualitative studies have identified barriers to participation including transportation issues, patients' unwillingness, and financial constraints(69, 70). Studies that have quantitatively investigated factors associated with non-utilization have been incorporated into a recent meta-analysis by Ruano-Ravina et al. This study highlighted that older age is one of a number of factors that predicts lower rates of utilization, including female gender, lower educational attainment, lower income, and comorbidities(66). One study of Medicare claims found that among adults over 65, those eligible for CR who did not participate were older, more likely to be female, and had more comorbidities than those who did participate(71). While the patient characteristics that contribute to lower referral rates in older patients are not clearly established, clinicians' actions have an impact. One such survey by Buttery et al. found that older adults were just as likely to desire cardiac rehabilitation as younger adults, but that they were much less likely to be referred(72). Lack of encouragement by a physician was specifically cited as a barrier to participation among older adults in a qualitative study(73). This demonstrates the importance of identifying patients at risk of non-utilization, as this encouragement can be more effectively targeted.

A thorough understanding of factors associated with non-utilization is a key next step in working towards improving utilization rates. It is yet to be shown whether older adults have different factors associated with non-utilization than their younger counterparts. This knowledge is key to developing quality improvement work towards closing the utilization gap that exists among older adults. This study will use the thorough clinical, geriatric, demographic, and psychosocial data generated by the SILVER-AMI study to evaluate risk factors for CR non-utilization. This will allow practitioners to identify which older patients may be least likely to attend, and to focus their efforts on ensuring that those patients can attend CR.

IVb. METHODS:

Data source:

SILVER-AMI was a prospective, multi-center cohort study that enrolled 3041 patients from 90 sites across the United States; detailed methods have been published previously(38) and described in more detail above. Briefly, adults 75 years and older, who were hospitalized with AMI underwent a baseline assessment during their hospitalization and completed a follow-up telephone interview 6 months later.

Study population:

Eligibility criteria included: Age >= 75 and hospitalization for AMI, according to the Third Universal Definition of Myocardial Infarction(3). Exclusion criteria included: initial troponin elevation occurring >24 hours after hospital admission (to exclude AMI secondary to surgery or procedure), and inability to provide informed consent with no available proxy.

Baseline assessment:

Upon enrollment, a research coordinator performed an evaluation of demographic, clinical, geriatric, and psychosocial information. Demographic information gathered included age, sex, and race, as well as socio-economic data. Clinical information included measures of health status(4-6). A thorough geriatric assessment was performed on each participant, gathering information on activities of daily living(13), cognitive impairment(7, 39), vision(9) or hearing(10) impairment, and functional mobility(41). Psychosocial evaluation included information on social support(14) and depression(15). Electronic medical records were abstracted to collect information diagnosis, procedures, and hospital course.

Outcome assessment:

Six months after hospital discharge, participants participated in a telephone survey administered by study staff at Yale. As a part of this interview, they were asked, "did you participate in cardiac rehabilitation?"

Statistical analysis:

A list of hypothesized predictor variables was generated based on prior literature and clinical reasoning. Multiple imputation was performed for missing values of predictor variables, generating twenty imputed datasets. The outcome variable (participation in cardiac rehabilitation) was analyzed for completeness, and participants with no value for the outcome variable were removed from this study, thus a complete case analysis was performed.

Each variable was evaluated for its association with CR use using a chi-squared test for categorical variables or a Student-t test for continuous variables to compare the groups who did and did not attend CR. Bivariate analysis was used to compare those who attended CR and those who did not with respect to each variable, generating unadjusted odds ratios. Multivariate analysis was performed using logistic regression to generate adjusted odds ratios. Covariates to be included in the multivariate model were selected using a pre-specified protocol as follows

Backward selection was applied to a pooled sample consisting of twenty imputed datasets with a p value threshold of 0.001 to account for the artificially inflated sample size. This corrects for the fact that the unimputed dataset may be biased by missingness, and that the twenty imputations may not align with one unique model. Using the covariates generated by this process, Table 7 demonstrates the adjusted odds ratios of the predictor variables included in the model.

Work performed by student researcher and others:

David Goldstein was responsible for generating the research question for this substudy, determining the relevant outcome variables and generating the list of hypothesized predictor variables. He also designed the analytic plan

Participants were enrolled and data were collected by paid study staff of the SILVER-AMI study under the supervision of the principal investigator, Sarwat Chaudhry, and the project director, Mary Geda.

Imputation of missing data was performed by the SILVER-AMI biostatistician, Terry Murphy, and lead data manager, Sui Tsang. Analysis was performed in the SAS statistical suite by an analyst from the Yale Center for Analytical Sciences (YCAS), Xuemei Song, under the supervision of David Goldstein.

IVc. RESULTS:

Univariate and bivariate analysis:

Of the 3041 participants enrolled in SILVER-AMI, 2387 (78.5%) had follow up data on CR use available. Of these 2387, 943 (39.5%) reported that they had attended CR since leaving the hospital. Of those without follow up data on CR use, 188 (5.5%) completed an early version of the interview, which did not ask about CR attendance. Of the 2853 eligible to be have follow up data, 152 (5.3%) did not complete the follow up interview, 190 (6.7%) completed a partial or "panic" interview, which did not ask about CR attendance.

Baseline characteristics and differences between those who attended CR and those who did not are reported in Table 6. When compared with those who attended, those who did not attend CR were statistically significantly more likely to be older, non-white, female, have a higher Charlson score, to have a diagnosis of NSTEMI vs. STEMI, have <= 12 years education, living alone, unable to walk ¼ mile prior to admission, to have cognitive impairment, visual impairment, impaired functional mobility, recent falls, depression, low activity level, unintentional weight loss, and less likely to have had PCI or CABG during their admission though many of these differences between groups were not clinically significant.

Table 6: Baseline characteristics of participants who did and did not attend CR

Variable		Did not attend CR N= 1444	Missing	Attended CR N= 943	Missing	P value
Mean age (SD)		81.63 (5.02)	0	80.51 (4.41)	0	<0.001
Sex (male)		768 (53.2%)	0	582 (61.7%)	0	<0.001
Race (non-white)		159 (11.0%)	27 (1.8%)	62 (6.6%)	14 (1.5%)	<0.001
Education ≤ 12 years		865 (59.9%)	17 (1.2%)	467 (49.5%)	3 (0.3%)	<0.001
Mean Charlson Score (SD)		3.47 (2.54)	2 (0%)	3.11(2.44)	0	<0.001
Mean length of Stay, days (SD)		5.51 (4.72)	0	5.64 (5.02)	0	0.55
Mean Social Support Score (SD)		21.66 (4.44)	32 (2.2%)	21.95 (4.15)	15 (1.6%)	0.11
Live alone		568 (39.3%)	1 (0.1%)	295 (31.3%)	0	<0.001
MI diagnosis	STEMI	369 (25.5%)	0	647 (68.6%)	0	0.002
	NSTEMI	1075 (74.5%)		296 (31.4%)		
Patient finances at the end of the month	Some money left	886 (61.4%)	68 (4.7%)	650 (68.9%)	34 (3.6%)	0.002
	Enough to make ends meet	402 (27.8%)		208 (22%)		
	Not enough to make ends meet	88 (6.1%)		51 (5.4%)		
Avoided healthcare because of cost		133 (9.2%)	11 (0.8%)	77 (8.2%)	3 (0.3%)	0.36
PCI performed		824 (5.0%)	0	630 (66.8%)	0	<0.001
CABG performed		120 (8.3%)	0	174 (18.4%)	0	<0.001
Timed-up-and-go category	≤15 seconds	430 (29.8%)	243 (16.8%)	332 (35.2%)	139 (14.7%)	<0.001
	16-25 seconds	293 (20.3%)		229 (24.3%)		
	>25 seconds	248 (17.2%)		134 (14.2%)		
	Incomplete due to impairment	230 (15.9%)		109 (11.6%)		
Hearing impairment		738 (51.1%)	0	515 (54.1%)	1 (0.1%)	0.09
Visual impairment		540 (37.4%)	0	301 (31.9%)	1 (0.1%)	0.007
Cognitive impairment		254 (17.6%)	19 (1.3%)	78 (8.8%)	18 (1.9%)	<0.001
Unintentional weight loss		306 (21.2%)	7 (0.5%)	164 (17.4%)	3 (0.3%)	0.021
>= Two falls in past year		292 (20.2%)	4 (0.3%)	153 (16.2%)	2 (0.2%)	0.014
Able to walk ¼ mile one month before admission		945 (65.4%)	6 (0.4%)	689 (73.1%)	1 (0.1%)	
Activity level vs. peers	More active	747 (51.7%)	11 (0.8%)	528 (56.0%)	4 (0.4%)	0.018
	About as active	460 (31.9%)		300 (31.8%)		
	Less active	226 (15.7%)		111 (11.8%)		
PHQ screen positive		207 (14.3%)	44 (3.0%)	103 (10.9%)	23 (2.4%)	0.013
Problematic alcohol use		75 (5.2%)	12 (0.8%)	58 (6.2%)	4 (0.4%)	0.33
Current or past smoker		792 (54.9%)	10 (0.7%)	519 (55.0%)	5 (0.5%)	0.96

Multivariate analysis:

All of the variables in Table 6 were included in backward selection. Using a pooled sample of all 20 imputed datasets and a threshold for inclusion of 0.001, 19 variables were selected for inclusion in the logistic regression model. These variables are: age, length of stay, race, education <=12 years, end of month finances (categorical), PCI, CABG, MI diagnosis, ability to walk ¼ mile 1 month prior to admission, Timed-Up-and-Go (Categorical), hearing impairment, visual impairment, cognitive impairment, activity level compared to peers (categorical, and living alone. In the logistic regression analysis, the following variables were independently predictive of CR utilization: older age (OR 0.97 [0.95-0.99] per year), non-white race (OR 0.69 [0.50-0.97]), having less than 12 years of education (OR 0.71 [0.59-0.85]), receiving percutaneous (OR 2.07 [1.66-2.57]) or surgical (OR 4.70 [3.32-6.67]) revascularization, cognitive impairment (OR 0.58 [0.43-0.78]), and living alone (OR 0.77 [0.64-0.93]). The results of the logistic regression analysis are presented in Table 7.

Table 7: Results of logistic regression analysis for cardiac rehabilitation attendance

Predictor Variable		Odds Ratio for attending CR (95% CI)	p value
Age (continuous)		0.97 (0.95-0.99)	0.001
Length of stay (continuous)		0.98 (0.95-1.00)	0.05
Non-white race (binary)		0.69 (0.50-0.97)	0.03
Education ≤ 12 years (binary)		0.71 (0.59-0.85)	0.0002
End of month finances (categorical)	Just enough to make ends meet	0.86 (0.69-1.06)	0.16
	Not enough to make ends meet	1.02 (0.69-1.50)	0.93
	Some money left	Reference	n/a
Percutaneous coronary intervention performed (binary)		2.07 (1.66-2.57)	<0.0001
Coronary artery bypass graft performed (binary)		4.70 (3.32-6.67)	<0.0001
STEMI (vs NSTEMI) (binary)		1.16 (0.94-1.41)	0.16
Able to walk ¼ mile one month prior to admission (binary)		1.09 (0.88-1.34)	0.43
Timed up and go (categorical)	≤ 15 seconds	Reference	n/a
	16-25 seconds	1.21 (0.95-1.53)	0.12
	>25 seconds	0.93 (0.70-1.22)	0.58
	Did not complete due to impairment	0.99 (0.72-1.36)	0.96
Hearing impairment (binary)		1.18 (0.99-1.41)	0.06
Visual impairment (binary)		0.91 (0.75-1.10)	0.31
Cognitive impairment (binary)		0.58 (0.42-0.78)	0.0002
Activity compared to same-age peers (categorical)	About as active	1.04 (0.85-1.27)	0.69
	Less active	0.91 (0.67-1.22)	0.51
	More active	Reference	n/a
Live alone (binary)		0.77 (0.64-0.93)	0.006

IVd. DISCUSSION:

In this study of adults over 75 hospitalized with AMI, 39.5% of participants utilized CR within six months of hospital discharge. On its face, this is a strikingly low proportion, as all patients were eligible for CR following their acute MI. While it is certainly lower than would be ideal, this proportion of CR utilization is actually substantially higher than other contemporary studies into CR utilization. Prior studies in older adults have found participation rates ranging from 18.7%(67) to 20.3%(71). Both studies were performed on large administrative datasets focusing on time periods from seven to twenty years ago. The difference in participation rates is likely reflective of both differences in methodology and a temporal trend towards improving rates of participation. A recent meta-analysis compared coded AMI diagnoses with those confirmed by chart review and found that the positive predictive values of coded diagnoses ranged from 73-96.7%, indicating that dataset based studies could include a large number of patients without AMI(74).

Our analysis found that older age, non-white race, having less than 12 years of education, not receiving percutaneous or surgical revascularization, cognitive impairment, and living alone were robust, independent predictors of failure to utilize CR within 6 months of discharge. In this analysis, we chose not to force any predictor variables into the final model, as the literature on predictors of CR use are not clearly established by prior work, especially in this population of older adults following acute MI.

This study has numerous strengths supporting the findings presented above. First, the strengths of the SILVER-AMI study. The inclusion of direct patient assessment, especially with regards to the comprehensive geriatric assessment, allowed for a much richer set of possible predictor variables. As utilization of CR is a complex, multifactorial outcome, the inclusion of data on factors impacting functional ability gives this study a unique angle in identifying individuals who may not participate. In contrast to prior investigations of factors associated with non-utilization of CR, this study was based on a prospectively designed cohort study, rather than a retrospective study of Medicare codes or some other large database. Every AMI diagnosis was confirmed by use of the Third Universal definition of Myocardial Infarction, rather than by a billing code, which can lead to false positives(74).

Weaknesses include the use of self-report for the outcome variable of CR utilization. Though studies based on billing codes are limited in their own way, use of self-report relies on the participant's memory, which may not be perfectly accurate, especially in a cohort with high rates of cognitive impairment. Importantly, the self-reported outcome measure was binary. Participants were asked whether they participated in CR at all, not whether they completed the full CR program. This leads to a loss of some granularity of the information, as some barriers to participation may cause lower rates of program completion even without lowering the rate of participation. An additional limitation is that the location of CR facilities was not able to be included in the analysis. It has been shown that distance to the nearest CR facility can be an important driver of utilization(74), and this information would have provided additional context to this study.

Many of our findings confirmed prior work in the field, especially with regards to the socio-demographic predictors of non-utilization. Older age has been repeatedly associated with non-utilization in other studies. This study was limited to adults over 75, so it is significant that even within this restricted cohort, older age was one of the most significant predictors. Non-white race has also been associated repeatedly with lower rates of CR utilization(65, 71, 74), as has lower educational attainment(75, 76).

Interestingly, the economic indicators included in this study did not contribute independently to the odds of non-utilization, though this has been an important predictor in prior work(66). The vast majority of the cohort was insured by Medicare, which covers CR, which could remove some economic barriers to participation. Additionally, as this is an older cohort, very few participants needed to miss work to attend CR. Given that there are still costs associated with attendance- namely transportation, it is reassuring that healthcare finances were not predictive of lower attendance rates.

This study's most novel contribution was the comprehensive geriatric assessment. Prior work has largely focused on retrospective analyses of large administrative datasets, and the inclusion of direct assessment of geriatric impairments allowed this study to identify cognitive impairment as an independent predictor of CR non-utilization. In this study, the TICS scores were not corrected for education level, despite the known effect of education on most cognitive screening tools(77). Nevertheless, the effect of low scores on the cognitive screen was independent of the effect of lower educational attainment. Whether cognitive impairment is a barrier preventing patients who were referred from participating in CR or it is a factor leading to lower rates of referral cannot be determined from this study, but the revelation that individuals with cognitive impairment are less likely to participate in CR highlights an important missed opportunity, especially given the benefits that CR has in the domain of cognitive impairment (59, 60).

Another interesting result of the geriatric assessment was the failure of frailty markers, most notably the timed-up-and-go test, to predict non-utilization of CR. A reasonable hypothesis for the association of older age with lower rates of utilization would be that because CR is an exercise-based intervention, those with impaired functional mobility, recent falls, or decreased activity may be less likely to be referred to, attend, or complete programs. While this study did not examine completion rates or referrals, we show here that there was no independent effect of impaired functional mobility, recent falls, or decreased activity level.

Clinically, the only factors associated with non-utilization were not having a revascularization procedure (percutaneous or surgical). Undergoing CABG was the strongest independent predictor of higher CR utilization. This association between more invasive procedures and higher utilization of CR is an interesting result, and there are a few potential explanations for this finding. First, there may be an indication bias for the revascularization procedures: the hardiest or healthiest geriatric patients are likely to be the ones referred for CABG, as they are the only patients who are likely to tolerate the procedure. Though they may need time to recover from their intervention, these are the patients with the highest baseline level of function, and they are therefore most able to successfully complete a challenging rehabilitation program. An alternative hypothesis is that there is an indication bias for the rehabilitation itself. Those who are receiving CABG or PCI may be thought to be “sicker” than those who do not, and therefore more likely to benefit from CR. Those who are not revascularized may be under the care of hospitalists rather than cardiologists, and there may be less impetus for referral to CR at the time of hospital discharge.

There are numerous implications to the findings of this study. Overall, the study demonstrates that there are many factors associated with low rates of CR utilization among older adults. Identifying individuals at risk for missing this important intervention requires consolidation of multiple pieces of information, including demographic, geriatric, and clinical assessment. Socio-demographic differences in CR utilization reveal important disparities in the delivery of care within this population. There are several possible explanations for the observed racial disparity in CR utilization. Black patients are less likely than white counterparts to be referred to CR(78), possibly due to provider biases(79). There may also be barriers preventing non-white individuals who are referred from participating. Historically, minority populations in the US have had fraught relations with medical providers(80), and distrust of physician recommendations may contribute to lower levels of attendance. While the effect of race was independent of finance or education level, inequities in these realms almost certainly contributes to differences in outcomes between whites and non-white patients.

Given the known benefits of CR, especially in older adults, increasing participation rates must become a priority. Despite calls from professional organizations to expand access to CR, many programs are failing to utilize best practices in reducing their referral gap(81). Providers must explore the most effective ways to increase utilization of CR among older adults, and this study provides meaningful information that can guide future research towards that goal. Are there more effective recruitment strategies that could be utilized specifically for non-white populations? What tools could increase understanding of the benefits of CR among those with lower educational attainment? With regards to cognitive impairment, further research could clarify whether there are alterations to CR programs that could better suit the needs of cognitively impaired older adults. Further research is necessary on innovations in the delivery of CR that could be instrumental in delivering the intervention to older adults.

A recent trend in CR has been the advent of home-based programs for delivery. Given the unique needs of the geriatric population, this could be a boon to increasing CR utilization among older adults. The most recent Cochrane review on home-based vs. facility based CR found that there was no difference in outcomes between the two modes of delivery(82), but further research could clarify whether it home-based delivery could increase utilization rates among older adults, especially those who have been identified by this study as less likely to participate.

V. CONCLUSIONS

The SILVER-AMI study is an innovative approach to risk prediction in older adults with an acute hospitalization; the insights it provides into geriatric risk prediction and care are significant and innovative. Few studies of older adults incorporate the direct assessment of aging-specific impairments, and the results of this project demonstrate how impactful this assessment can be. Hospital discharge after an event like an MI can be complicated, especially for older adults. New medications, changes in functional status and other demands on patients make this time a perfect storm of change, and the impairments in mobility, cognition, vision, and strength that are associated with normal and pathologic aging can prevent patients from navigating this period successfully.

While the direct observation involved in the geriatric assessment grants this study a unique lens, there are important limitations. Observational studies require careful consideration, as the associations that arise may not have a clear causal direction. This is particularly true with regards to associations between treatments and outcomes. Because of indication biases, it can be difficult to tease out treatment effects and side effects. The example of beta-blockers and falls is particularly salient, but the same issue impacts our understanding of why patients with more invasive revascularization procedures were more likely to participate in CR.

Together, these studies provide clear examples of effective observational research tailored for the geriatric population. The research questions of each chapter, though markedly different, both focus on outcomes that are clearly tied to maintenance or improvement of functional status. Falls are uniquely relevant to older adults, and any information that allows clinicians to identify and minimize their risk is crucial for delivering the best care. Cardiac rehabilitation has benefits that apply specifically to older adults, yet these same patients are among the least likely to utilize the intervention. In both studies, the results demonstrated clearly that geriatric impairments are highly associated with poorer outcomes, which is a key takeaway from this project. Assessment of such impairments should be a consideration during hospitalization for AMI, as they provide much-needed context to the care of older adults.

The results from this project can be powerful in guiding both patient-care and future research. Identifying patients at risk for falls can help guide decisions about risky medications, or ensure that appropriate anti-fall precautions are taken for the individuals at highest risk. Similarly, identifying which groups of patients are least likely to attend CR allows physicians to target their recommendations most effectively, and allows researchers to test quality improvement projects to improve utilization rates among those groups.

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Cardiac Rehabilitation in Older Persons with Cardiovascular Disease

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Abstract

Purpose of Review Despite widespread recommendations, cardiac rehabilitation (CR) is not well utilized in older adults. This review explores the valuable benefits of CR in geriatric patients as well as strategies to improve utilization.

Recent Findings Eligibility for CR has long included coronary heart disease and has recently expanded to include heart failure, valvular disease, and peripheral artery disease, all which particularly impact older adults. New research has demonstrated unique functional and geriatric-specific benefits in older adults who participate in CR.

Summary Though few studies have specifically focused on geriatric populations, these patients have similar benefits to CR in various types of cardiovascular disease in respect to improved morbidity, rehospitalization, and mortality. Furthermore, older adults participating in CR commonly derive unique benefits in respect to frailty, mood, and functional status. Nonetheless, utilization rates are low in the general population, and even lower in older adults. Increasing use of home-based programs may help increase utilization and benefits among older CR candidates.

Keywords Cardiac rehabilitation · Geriatrics · Cardiovascular disease · Coronary heart disease

Introduction

Cardiac rehabilitation (CR) is a multimodal intervention consisting of exercise therapy along with risk factor modification, education, and psychosocial support. While CR has been a standard part of cardiovascular management since the 1990s, its application is at a critical crossroads. Initially designed as a form of post-acute myocardial infarction (AMI) exercise training for middle-aged men in outpatient hospital-based programs, this model of CR has been typically expensive to run and poorly reimbursed. Moreover, its perceived value has been additionally eroded by advances in revascularization and medically stabilizing therapies that are often interpreted as much more impactful than exercise and lifestyle modification. However, the perceived utility of CR has simultaneously expanded with greater insights about the value of exercise and wellness behaviors, new indications (e.g., valvular heart disease, heart failure [HF]), greater application to women, and greater outreach to a full spectrum of ages. Furthermore, CR has evolved into a much more extensive intervention than the exercise therapy that was offered in its inception. Exercise training is still emphasized, but CR also now incorporates education, risk factor modification, and counseling. The goals have evolved to include greater emphasis on healthy lifestyle patterns, moderating symptoms, increasing exercise tolerance, and optimizing outpatient management of CVD, including medication review, and clarifying goals of care. Furthermore, while most CR is still delivered in the outpatient site-based (hospital or office) settings, it is also now increasingly available as a home-based model.

The use of CR in the geriatric population has become a particularly topical consideration. The population of older adults is growing rapidly, and aging physiology is fundamentally conducive to development of CVD. The relative benefits of CR in this older vulnerable population are particularly important, particularly in respect to achieving functional and qualitative gains that are typically jeopardized by high incidence of disease and disease events.

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Indications for Cardiac Rehabilitation in Older Adults

Coronary Heart Disease

From its advent, CR was primarily focused on patients with coronary heart disease (CHD)—first those who were recovering from AMI, and later those who had been surgically revascularized. In the early days of CR, the patients referred were typically younger males, but as life expectancy has increased, the population with CHD has increasingly become older and more female. These older adults face worse prognoses and face more severe disability and functional impairment than their younger counterparts.

While randomized controlled trials have not definitively shown a mortality benefit of CR for CHD, there have been many meta-analyses and elegant propensity analyses. The most recent Cochrane review on CR for CHD demonstrated a significant reduction in cardiovascular mortality and all-cause readmission in a meta-analysis of 63 studies [1]. The studies contributing to this review were performed in patients of all ages, and so the specific benefits in the geriatric population are still an open research question. While not directly comparing older to younger patients, a propensity study by Suaya in over 600,000 Medicare beneficiaries also showed a significant mortality benefit similar to other studies of younger cohorts [2•].

Heart Failure

Heart failure is a disease that primarily impacts older adults. Heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) both occur at markedly higher rates in older adults than in their younger counterparts [3–5]. It is a disease that can dramatically impact functional decline and cause profound disability, especially in older patients that may otherwise be frail or have comorbid conditions.

Heart failure is a more recently approved indication for CR [6] and data from trials has shown promising benefit, though much of the evidence is limited. The most robust study of CR in patients with HF was the Heart Failure: A Controlled Trial Investigating Outcomes in exercise training (HF-ACTION) study. This study of 2331 adults (median age 59, 28% women) with systolic HF (23% with NYHA class III or IV) showed significant improvements of mortality or hospitalization (RR = 0.89 [0.81–0.99]) after adjusting for comorbidities [7]. Within this study, patients aged over 70 years saw no significant decrease in all-cause mortality or all-cause hospitalization, though this was not adjusted for comorbidities in the same way as the primary analysis.

The most recent Cochrane review [8] on CR for HF also showed a non-significant reduction in mortality (RR = 0.88 [0.75–1.02]) and a statistically significant reduction in hospitalizations (0.75 [0.62–0.92]) among studies with > 1 year of follow-up. Meta-regression analysis showed that these benefits were independent of age, but no studies included were dedicated to the geriatric population. A small randomized controlled trial focusing on older adults with HF found a significant increase in functional status and health-related quality of life [9]. The body of evidence around CR's benefit in HF is slightly more equivocal, and less proven in the geriatric population, but overall promising.

Valve Repair

Adults recovering from aortic valve replacement are recently eligible for CR. Aortic stenosis is primarily a disease of the geriatric population, especially disease severe enough to require valve replacement. Transcatheter aortic valve replacement (TAVR) is the intervention of choice in patients with severe AS who may not tolerate a more invasive surgical intervention—and has included high proportions of older patients who are often regarded as too sick for CR by their providers or families.

The evidence for exercise-based rehabilitation after valve repair is quite limited, with a recent Cochrane review only able to include two small trials [10] that showed benefits from exercise capacity, but called for further trials to establish other benefits. After TAVR, there are a few observational studies that show benefits in functional status and quality of life [11, 12]. A recent small pilot study of 30 patients after TAVR by Pressler et al. showed benefits in exercise capacity, strength, and quality of life [13]. Of note, the studies of CR in TAVR all had a mean age above 80 years, so while there is limited evidence of the benefits in this population, the studies have focused on older adults.

Peripheral Arterial Disease

Peripheral arterial disease (PAD) has seen a recent rise in prevalence, with the majority of this growth in geriatric patients. It can be considered a disease of aging and contributes substantially to the disability and impairment in physical function. Supervised exercise therapy (SET) was just recently approved for Medicare reimbursement as an intervention for symptomatic (PAD) [14]. While exercise is only a single part of a more comprehensive CR program, it still plays a potentially decisive role in increasing CR referral and utilization. This decision was based on evidence that SET has benefits in quality of life and symptoms of claudication [15]. A recent Cochrane review highlighted increased walking distance and walking time, with some studies showing improvements in patient-reported quality of life, though no effects on mortality, cardiac events, or ankle-brachial index were reported [16]. While no studies of more comprehensive CR programs in PAD have been published, there is a current trial underway (NCT03251391).

Age-Specific Benefits

The rationale that led to CR's widespread use as secondary prevention for AMI and after revascularization primarily focused on easily measured and broadly applicable outcomes such as mortality and readmission. These benefits have been difficult to demonstrate clearly in CHD and HF, but have not been shown in valvular disease or PAD. While these types of outcomes are extremely compelling, in older adults a broader definition of benefit provides a more nuanced view of the effects of CR. As the indications for CR have expanded, so too has the field's acknowledgement of broader CR benefits. Functional capacity has become an important metric for CR's efficacy and has been an important determinant of the expansion of CR use to HF, TAVR, and PAD.

Functional capacity is an especially important criterion for older adults, and it is one of a few ways in which CR may benefit older adults differently than their younger counterparts. Geriatric impairments in cognition or mobility can have large effects on quality of life, and any effect of CR on these impairments would be extremely meaningful. These potential benefits can be lost in studies of CR that include younger patients, and so research on CR on older adults is essential to understanding how it can best be utilized in this population.

Functional Capacity

One of the key outcome measures of CR in all age groups is physical function and exercise capacity. This bears particular relevance to older adults because of the typical decline in functional capacity associated with aging, the progressive nature of disability in older adults, and the acute impact to function and exercise capacity of CVD and hospitalization. As part of the normal process of aging, individuals will experience changes on a cellular, muscular, and physiologic level that can impair exercise or functional capacity. Even absent cardiovascular disease, older adults experience a decline in peak oxygen uptake (VO_2 peak) with every decade, and this decline accelerates in older age [17]. Muscle mass decreases with aging as well [18], and there are numerous cellular and molecular changes associated with aging that diminish ability to deliver oxygen (O_2) to tissues as well as its utilization [19].

These changes are even more pronounced in the population that is eligible for CR. Deconditioning is a known complication of hospitalization in the geriatric population [20]. In a small 2014 study, DiMaria-Ghalili et al. demonstrated that after cardiac surgery, older adults experience continued weight loss in the context of elevated inflammatory markers. The transient deconditioning and general period of increased risk after hospitalization has become known as “post-hospitalization syndrome [21],” pointing to how important interventions to improve functional capacity after hospitalization can be in this population.

In both CHD and HF, CR has been demonstrated to increase functional capacity or its markers in older adults. Studies of patients with ischemic heart disease showed that effects on exercise capacity were just as great in older adults as in younger patients [22, 23]. A recent observational study by Baldasseroni et al. found that those older adults with the worst baseline function after AMI or surgical revascularization showed the most improvement of physical performance associated with CR [24•]. Similarly in HF, older adults had gains in functional capacity similar to younger adults [25]. A recent study by Pandey et al. contextualized this finding and showed that older adults with HFpEF showed more improvement in exercise capacity than those with HFrEF, despite the current policy excluding HFpEF from reimbursement for CR [26].

Frailty

Physical frailty is a key concept in the field of geriatrics. It can be defined in multiple ways, but is essentially an indicator of overall weakening and increased fatigability [27]. Frailty is a known prognostic factor for many outcomes in geriatric patients. Recent studies have started to look at frailty as a possibly therapeutic target. A meta-analysis by Bibas et al. found 13 randomized controlled trials investigating exercise training on measures of frailty, and found that in most studies (12/13), exercise training improved one or more markers of frailty, although many of these studies did not specifically look at patients with cardiovascular disease [28].

While exercise may help diminish frailty, it is possible that such benefit could be compounded by specifically tailoring the exercise regimen for older adults. A study by Molino-Lova et al. specifically investigated older adults exhibiting frailty after participating in acute rehabilitation following cardiac surgery. They found a significant improvement in the Short Physical Performance Battery with a structured physical activity intervention focused on strength, flexibility, balance, and coordination, and posit such an intervention could delay or prevent the onset of disability.

Cognition [29, 30]

Cognitive impairment in older adults has been associated previously with CVD [30]. There is increasing evidence that CR improves cognition in older adults. In patients with both HF [29] and other forms of CVD, participation in exercise therapy has been shown to increase cognitive functioning in multiple domains [31, 32].

The molecular and physiologic mechanisms underpinning the link between cognition and CVD are not fully explained as of yet, but recent studies have suggested possible causal links, including white matter changes [33] or alterations in perfusion [31] which may be altered by CR. Furthermore, CR provides opportunity to modify medical regimens, potentially deprescribing drugs that may inadvertently contribute to risks of confusion as well as greater fatigability [34].

Mood

In those older adults with CVD, there is increased risk of depression, and, through behavioral factors, depression can be associated with adverse cardiovascular events [35]. Decreased functional capacity and ability to exercise is thought to be a mediator of increased depression, and so working to alleviate this limitation has been a target to improve mood symptoms in this population. A 2012 meta-analysis on the effect of CR on depression showed that both community-based and in-home CR caused significant improvement in depression outcomes in older adults [36]. Part of the positive impact on patients' mood symptoms may be connected to the social aspect of CR. In a survey of adults participating in CR, many highlighted socialization as a key benefit [37].

Risks Associated with Cardiac Rehabilitation in Geriatric Patients

CV Events

An early concern in CR was that initiating exercise too soon after a cardiac event could cause another ischemic injury. As CR has been studied, it has become clear that this is not the case, and that the exercise performed as part of structured CR programs is safe, with an exceedingly small risk of cardiac events. The incidence of a coronary event, cardiac death, or AMI has been estimated to be 1 every 60–80,000 patient hours of supervised exercise. Whether this risk is different in older patients participating in CR has not been specifically studied, but the expert consensus is that CR is safe for all eligible patients, and that no special considerations should be taken for geriatric patients from this perspective.

Falls

One of the major concerns with initiating CR in the geriatric population is that increased exercise could expose these patients to an increased risk of injurious falls. Unintentional falls in older adults cause significant morbidity, increased healthcare utilization, and mortality. The base rate of falls in adults over 65 is roughly 30% per year [38], and those patients eligible for CR may be at an even higher risk. These patients could experience deconditioning while in the hospital, may have increased likelihood of polypharmacy, and are more likely to have cognitive impairment or frailty than other older adults. The time after hospital discharge is a period of increased fall risk [39], and so it is not surprising that providers are concerned about initiating exercise therapy in these older adults.

Despite these concerns, there is a strong body of evidence that CR can improve some of the risk factors for falls, such as strength and balance [40]. Exercise training has been shown in a systematic review and meta-analysis to be one of the most effective interventions to prevent falls in older adults [41]. No study has yet specifically investigated the rate of falls in CR programs, and so it is important for programs to be aware of this risk, and to modify exercises in ways that might minimize the risk of falls in vulnerable older adults. Careful assessment of hemodynamics and steps to adjust medications to mitigate excessive hypotension and confusion also help to reduce falling risks [34].

Underuse

Despite the evidence of CR's major benefits, rates of participation are remarkably low [42, 43•], particularly in candidates who are older [44, 45]. This has led to calls from national organizations, including the AHA, to increase rates of CR utilization in older adults after AMI. Many factors have been implicated in the underuse of CR, and older age has consistently been shown to correlate with lower rates of utilization, but few studies have investigated CR use in older adults.

Qualitative studies have identified barriers to participation including transportation issues, patients' unwillingness, and financial constraints [46, 47]. Studies that have quantitatively investigated factors associated with non-utilization have been incorporated into a recent meta-analysis by Ruano-Ravina et al. This study highlighted that older age is one of a number of factors that predicts lower rates of utilization, including female gender, lower educational attainment, lower income, and comorbidities [43•]. One study of Medicare claims found that among adults over 65, those eligible for CR who did not participate were older, were more likely to be female, and had more comorbidities than those who did participate [48].

While the patient characteristics that contribute to lower referral rates in older patients are not clearly established, clinicians' actions have an impact. One such survey by Buttery et al. found that older adults were just as likely to desire CR as younger adults, but that they were much less likely to be referred [49]. Lack of encouragement by a physician was specifically cited as a barrier to participation among older adults in a qualitative study [50].

Special Considerations in Older Adults

Older adults have unique risks and benefits of CR participation, and they also have unique needs that require careful consideration for CR implementation. Barriers to participation including lack of transportation, and cost, may be more difficult to overcome for older adults. Cognitive or sensory impairments may require modification of the CR protocols. As many older adults are discharged to skilled nursing facilities there may be a role for incorporating elements of CR into care at these facilities [51].

Home vs. Facility CR

A more recent trend in CR has been the advent of home-based programs for delivery. Given the unique needs of the geriatric population, this could be a boon to increasing CR utilization among older adults, and is part of the AHA recommendations to increase CR referral [52], but careful review of the evidence around these types of programs is important. The most recent Cochrane review on home-based vs. facility-based CR analyzed 17 trials including 2172 patients with AMI, revascularization, or HF and found that there was no difference in outcomes between the two modes of delivery. Importantly, this review did not address the impact of older age on these findings, nor did it comment on any differences in safety between home- and facility-based CR. One small study did focus on patients with CHD over the age of 65 years and found that there was no difference in peak VO_2 or 6-min walk test [53].

A recent study evaluated a smartphone-based delivery of CR and found that it was effective in increasing CR utilization and improving health outcomes, but importantly it was a small study with a mean age of 55, and it is reasonable to worry that these results may not translate to an older cohort less comfortably with such technology [54].

Conclusions

CR is clearly here to stay as an important tool in the cardiologist's armamentarium. As the population ages, and the number of older adults eligible for CR grows, a nuanced understanding of the risks, benefits, and indications for CR that are unique to the geriatric population will be an essential aspect of care. The belief that CR has a mortality benefit, especially in the geriatric population, is based primarily on propensity analyses and meta-analyses rather than straightforward RCTs. This is a relatively weak foundation, but the supporting rationale can be buttressed by future work on the functional and geriatric-specific benefits of CR in older adults. These benefits in cognition, frailty, and especially functional status are difficult to research, and a keen geriatric lens must be applied. Considerations of frailty and disability must account for both the acute post-hospitalization decline in function and the individual's baseline capabilities. Those who undergo invasive cardiac procedures may be more disabled in the short term, but may have a higher level of baseline function, and may in fact be the patients who can benefit most from an intervention like CR.

More study is clearly necessary in this field and can shine a clearer light on the ways in which aging impacts CR. Questions remain about the interplay between multimorbidity and CR. More research can clarify how the calculus about home vs. facility CR is affected by geriatric impairments that may make delivery more complex. What interventions can be taken to promote more use among older adults, who are utilizing CR at a lower rate than their younger counterparts despite their unique benefits? While questions remain, it is clear that CR is an important tool for secondary prevention and improvement of physical function for older adults with CVD.

Compliance with Ethical Standards

Conflict of Interest The authors have nothing to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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P17 Student Presentation

A risk model for falls in older patients after hospitalization for acute myocardial infarction: the SILVER-AMI study

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Background: Discharge after hospitalization for acute myocardial infarction (AMI) is typically marked by functional decline and other changes that modify the risk for falls. Prior research on falls has focused on hospitalized, community dwelling, and institutionalized populations, but the post-discharge period has been understudied, especially after AMI. This study uses the expansive demographic, clinical, geriatric, and psychosocial data of the "ComprehenSIVe Evaluation of Risk Factors in Older Patients with AMI " (SILVER-AMI) cohort to build a risk model for falls in the 6 months after hospitalization for AMI.

Methods: SILVER-AMI is a prospective, multi-center longitudinal cohort study of 3000 adults age 75 years or older hospitalized for AMI. Detailed baseline assessments and medical record abstractions were performed to collect demographic, clinical, geriatric, and psychosocial data. Falls were self-reported in a telephone interview six months after discharge, and analysis was performed on the first 1700 patients enrolled. After multiple imputation for missing data, 85 hypothesized predictors were narrowed to 26 using backward selection. Bayesian model averaging was applied to the combination of these 26 variables and four established predictors (age, gender, race, prior falls) to develop a final risk model for falls.

Results: 23% of patients reported ≥1 fall at 6 months post-discharge. Our model identified the following fall risk factors: prior falls [OR 2.35 (95%CI 1.85-2.98)], cognitive impairment [OR 1.42 (1.03-1.96)], slow gait [OR 1.13 (1.00-1.28)], and visual impairment [OR 1.46 (1.15-1.86)]. Living with a partner [OR 0.67 (0.53-0.85)] and non-white race [OR 0.59 (0.38-0.93)] were shown to be protective. Traditional cardiovascular risk factors for post-AMI outcomes, such as blood pressure and renal function, were not predictive.

Conclusions: This risk model allows the identification of adults over 75 at increased risk for falls following hospital discharge after AMI. This risk stratification could inform clinical decisions at the time of hospital discharge and increase use of preventive interventions such as exercise programs or home hazard reduction. In older patients, geriatric impairments were strongly predictive of falls but traditional cardiovascular risk factors for post-AMI outcomes were not.

P18 Student Presentation

Comparative Safety of Dipeptidyl Peptidase-4 Inhibitors and Sulfonylureas in Older Nursing Home Residents

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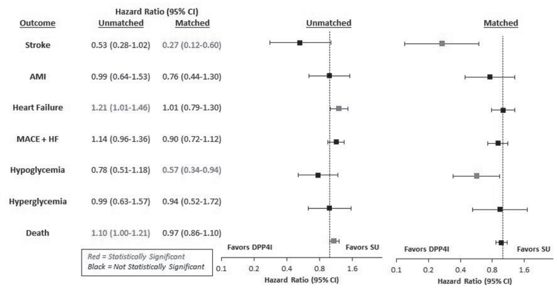
Background: The comparative safety profiles of dipeptidyl peptidase-4 inhibitors (DPP4Is) and sulfonylureas (SUs) have not been studied for older nursing home (NH) residents with type 2 diabetes. We evaluated the risk of major adverse cardiovascular events (MACE), glycemic events, and all-cause mortality in NH residents aged ≧65 who were newly prescribed DPP4Is versus SUs.

Methods: We conducted a retrospective cohort study of 7,885 U.S. NH residents using 2007-2010 national data from the Minimum Data Set and Medicare Parts A, B, and D. Follow-up began at the initial dispensing of a DPP4I or SU and continued until each study outcome (evaluated separately), insurance disenrollment, death (for non-death outcomes), one-year follow-up, or study end, which ever occurred first. Outcomes were hospitalizations and emergency department visits for heart failure (HF), acute myocardial infarction (AMI), stroke, hypoglycemia, hyperglycemia, and death. We propensity score-matched new DPP4I users to an equal number of SU users. Cox models were used to determine hazard ratios (HR) with 95% CIs of each outcome. We used competing risk regressions and nonparametric propensity scores in sensitivity analyses.

Results: Propensity score-matching yielded a cohort of 2,016 residents. Mean age was 81 years. DPP4I users were less likely than SU users to experience hypoglycemia (HR=0.57, 95%CI 0.34-0.95) and stroke (HR=0.27, 95%CI 0.12-0.59), but had a similar risk of HF, AMI, hyperglycemia, and death (Figure). Results from the sensitivity analyses were similar.

Conclusions: NH residents who initiated DPP4Is instead of SUs had a lower risk of hypoglycemia and stroke. Since avoidance of hypoglycemia is a key diabetes treatment goal in the NH, our findings suggest that DPP4Is are the preferred therapy.



P19

Chronic Pain Predicts Accelerated Memory Decline and Dementia in a Longitudinal Cohort of Elders

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Background: Chronic pain is highly prevalent among the elderly and is associated with cognitive deficits in cross sectional studies. Using data from the Health and Retirement Study (HRS), we modeled the association between chronic pain at cohort inception and longitudinal measures of memory and dementia probability over the following 12 years.

Methods: We studied 10,065 HRS participants who were at least 62 in 2000 and answered pain and cognition questions by self-report in both 1998 and 2000. "Chronic pain" was defined as a participant reporting he/she was often troubled with moderate or severe pain in both the 1998 and 2000 HRS interviews. Composite memory score and dementia probability estimated by combining neuropsychological tests and informant interviews were tracked until the 2012 interview. Demographic and comorbidity covariates were fixed at the 2000 interview. Linear mixed effects models, with random slope and intercept for each participant, were used to estimate the impact of chronic pain on slope of the memory score and dementia probability trajectory, applying sampling weights to represent the 2000 US population age 62+. To contextualize the magnitude of associations, we estimated the impact of memory differences associated with pain on functional independence in managing medications and finances.

Results: Chronic pain affected 10.9% of the weighted cohort. After adjustment for health and demographic factors, chronic pain was associated with 9.2% (95% CI 2.8%-15.0%) more rapid memory decline compared with controls. This memory score decrement translated to a 15.9% relative higher risk of inability to manage medications and 11.8% relative higher risk of inability to manage finances independently at the end of 10 years, compared with peers. Dementia