Functional Disability and Cognitive Impairment After Hospitalization for Myocardial Infarction and Stroke

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Background—We assessed the acute and long-term effect of myocardial infarction (MI) and stroke on postevent functional disability and cognition while controlling for survivors’ changes in functioning over the years before the event.

Methods and Results—Among participants in the nationally representative Health and Retirement Study with linked Medicare data (1998–2010), we determined within-person changes in functional limitations (basic and instrumental activities of daily living) and cognitive impairment after hospitalization for stroke (n=432) and MI (n=450), controlling for premorbid functioning using fixed-effects regression. In persons without baseline impairments, an acute MI yielded a mean acute increase of 0.41 functional limitations (95% confidence interval [CI], 0.18–0.63) with a linear increase of 0.14 limitations/year in the following decade. These increases were 0.65 limitations (95% CI, 0.07–1.23) and 0.27 limitations/year afterward for those with mild-to-moderate impairment at baseline. Stroke resulted in an acute increase of 2.07 (95% CI, 1.51–2.63) limitations because of the acute event and an increase of 0.15 limitations/year afterward for those unimpaired at baseline. There were 2.65 new limitations (95% CI, 1.86–3.44) and 0.19/year afterward for those with baseline mild-to-moderate impairment. Stroke hospitalization was associated with greater odds of moderate-to-severe cognitive impairment (odds ratio, 3.86; 95% CI, 2.10–7.11) at the time of the event, after adjustment for premorbid cognition but MI hospitalization was not.

Conclusions—In this population-based cohort, most MI and stroke hospitalizations were associated with significant increases in functional disability at the time of the event and in the decade afterward. Survivors of MI and stroke warrant screening for functional disability over the long-term.

Key Words: activities of daily living ▪ cognitive impairment ▪ myocardial infarction ▪ stroke

Myocardial infarction (MI) and stroke are the leading vascular contributors to illness and death in the United States, with hundreds of thousands of Americans experiencing one of these events annually. In 2010, 7.6 million US adults were MI survivors and 6.8 million were stroke survivors, and these prevalence rates are predicted to increase by ≤25% over the next 2 decades because of treatment advances and growth of the population aged ≥65. The chronic care of MI and stroke survivors will place huge burdens on families, healthcare systems, and public programs, such as Medicare and Medicaid.

Disability accounts for a substantial amount of the health burden and costs because of MI and stroke. Although both MI and stroke experienced major improvements in acute care (e.g., thrombolysis, organized inpatient care) and secondary cardiovascular disease (CVD) prevention between 1990 and 2010, disability rates for MI fell nearly 15% but disability rates for stroke increased 40% during this period. Yet, few studies have compared acute and long-term changes in disability because of functional or cognitive problems after MI and stroke in a contemporary cohort of survivors. Importantly, declines in premorbid functioning may precede acute medical events and these declines may confound or even modify the effect of these events on functional and cognitive outcomes. Although MI and stroke have been associated with acute increases in functional and cognitive disability, studies conflict on whether acute MI or stroke increase the rate of disability after controlling for individuals’ longitudinal changes in disability over time before the vascular event. Many studies suggest that average yearly changes in disability after MI or stroke are not significantly greater than those before MI or stroke. It is also not established whether premorbid...
functioning modifies the effect of acute MI or stroke on functional outcomes. If MI and stroke contribute to acute functional and cognitive disability and also new impairments in physical and cognitive functioning over the long-term, then clinicians and payers will need to consider interventions that identify and treat these problems beyond the immediate postevent period.

This study used a longitudinal, nationally representative cohort of older Americans to compare the acute and long-term changes in functional disability, cognitive impairment, and depression after MI and stroke in a contemporary cohort of survivors. Our analyses focused on the pivotal role of premorbid functioning by controlling for and also stratifying by individuals’ longitudinal changes in function and cognition over time before the vascular event.

**Methods**

**Data Source and Study Population**

Study subjects were participants of the Health Retirement Study (HRS). The HRS is a nationally representative, longitudinal study of 37,000 US residents aged 51 or older. The HRS uses multistage area probability sampling from all US states and the District of Columbia, with oversampling of Blacks and Hispanics. Every 2 years since 1992, HRS participants have been interviewed regarding physical health and functioning, cognitive functioning, disability, health insurance, and other factors. The HRS uses standardized instruments to collect data on valid, generalizable measures that are applicable to stroke, MI, and a range of health conditions. The HRS achieves a high follow-up rate, ranging 85% to 91% from 1998 to 2010 including proxies.

Data regarding inpatient and outpatient medical services received, including dates of hospitalization were available from the Centers for Medicare and Medicaid Services for those participants who were enrolled in Medicare fee-for-service from 1991 through 2007 and agreed to linkage. Approximately 80% of Medicare-eligible HRS participants consent to this linkage of their Medicare data. The HRS protocol was approved by the University of Michigan Institutional Review Board and all participants provided informed consent.

We identified all subjects hospitalized with a principal discharge diagnosis of MI or stroke during 1998 to 2007 using the linked Medicare data and valid International Classification of Diseases-Ninth Revision-Clinical Modification codes. We required hospitalizations to be ≥ 1 day and subjects to have ≥ 1 functional and cognitive measurement before and after the index MI or stroke hospitalization. To determine the unique effects of the exposures, MI and stroke hospitalization, we excluded hospitalizations in which another vascular event or pneumonia was diagnosed and listed as a secondary discharge diagnosis (ie, the MI group included individuals hospitalized with a principal discharge diagnosis of MI and no secondary diagnosis of stroke or pneumonia and the stroke group included individuals hospitalized with a principal discharge diagnosis of stroke and no secondary diagnosis of MI or pneumonia). Figure 1 shows the derivation of the analytic cohort. All patients were followed through death or the 2010 HRS interview.
Definitions of Outcome Measures

Functional Impairment
To ascertain functional disability, respondents (or their proxies) were asked whether they required assistance with any of 6 activities of daily living (ADLs), such as walking, dressing, bathing, eating, getting in/out of bed, and toileting, and 5 instrumental activities of daily living (IADLs), such as preparing a hot meal, grocery shopping, making telephone calls, taking medicines, and managing money. We categorized the level of functional disability using thresholds used in prior HRS studies, defining baseline mild-to-moderate disability as 1 to 3 impairments in ADLs and IADLs, and baseline moderate-to-severe disability as ≥4 impairments.9

Cognitive Impairment
Cognitive impairment was assessed using versions of the modified Telephone Interview for Cognitive Status.22,23 Proxies completed cognitive impairment assessments for patients who were unable to complete the interview themselves using the Informant Questionnaire on Cognitive Decline in the Elderly.24 Thresholds for mild–moderate and moderate–severe cognitive impairment were based on HRS research and the methods used for the Aging, Demographics, and Memory Study.25,26 and have been validated against neuropsychiatric interviews.27

Depression
As a secondary outcome, we examined trajectories of depression before and after stroke and MI hospitalizations, respectively. Depression was assessed at each HRS interview using an 8-item version of the Center for Epidemiologic Studies Depression Scale30 from patients, not proxies.29 We used a cutoff score of ≥4 to define substantial depressive symptoms because this threshold is comparable with the cutoff score of ≥16 on the full Center for Epidemiologic Studies Depression Scale.29

Demographic and Clinical Characteristics
Information on demographics (eg, age, race/ethnicity, sex, education, and marital/partnered status) and health-risk behaviors (eg, alcohol use and smoking) came from HRS interviews. Baseline Charlson Comorbidity Score31 and hospitalization-related characteristics (length of stay, intensive care unit or coronary care unit admission, and requirements for mechanical ventilation, major surgery, and dialysis) were obtained from Medicare claims.

Statistical Analysis
Multivariable regression analyses examined the adjusted associations between MI or stroke hospitalization and the 3 outcome measures. For analyses of functional status posthospitalization for MI or stroke, our dependent variable was the total number of impairments in ADLs and IADLs. We conducted separate analyses for MI survivors and for stroke survivors. Initially, the change in functional status over time was graphed using piecewise regression models with one knot and one jump to account for the difference in status at the time of the acute event (MI or stroke).31 We used fixed-effects regression to model trajectories of functional impairments over time with control for all stable patient characteristics (see the Data Supplement).32,33 These models used only within-person variation over time to estimate the effect of hospitalization for each of our conditions of interest (ie, patients serve as their own controls). We estimated 3 values with 95% confidence intervals (CI): (1) the average change in functional impairments over time before the MI or stroke hospitalization (the pre-event slope or trajectory), (2) the acute change in functional impairments at the time of the MI or stroke hospitalization, and (3) the average change in functional impairments over time after the MI or stroke hospitalization (the postevent slope). We used all available information on the outcome measure for each participant to calculate these estimates. We also adjusted for posthospitalization cognitive impairment to examine trajectories beyond that associated with cognitive impairment.

Similarly, we used multivariable conditional logistic regression to examine the effect of MI or stroke hospitalization on each outcome, development of moderate-to-severe cognitive impairment or the presence of substantial depressive symptoms. Trajectories reflect the change in the odds of developing each outcome over time before or after the event (eg, the odds of developing cognitive impairment per year before MI). Given that survivors who develop cognitive impairment or new functional impairments after MI or stroke are also more likely to develop substantial depressive symptoms, we added time-dependent variables for incident mild-to-moderate cognitive impairment, moderate-to-severe cognitive impairment, and functional impairments to the model predicting the outcome of substantial depressive symptoms. Multivariable results are reported as adjusted odds ratios and 95% CI.

For the primary analyses, patients were allowed to have one or more hospitalization(s) for the vascular event (MI or stroke).

Sensitivity Analysis
We repeated analyses using only the first MI or stroke hospitalization for each patient. Because 8% of MI survivors and 11% of stroke survivors were missing posthospitalization depression measurements because they required a proxy, we used nonresponse propensity score adjustment in our final depression model to quantify potential biases in our results.34 Analyses were performed with the IBM SPSS Statistics 18 (SPSS Inc, Chicago, IL) and STATA 11.2 (Stata Corporation, College Station, TX) statistical software programs.

Results
There were 391 individuals who experienced 450 hospitalizations for MI but not for stroke and 370 individuals who experienced 432 hospitalizations for stroke though not for MI in which individuals survived to complete ≥1 follow-up outcome assessment. Patients had ≤5 outcome measurements (range, 7.7–9.8 years) before hospitalization and up to 6 outcome measurements (range, 9.9–12.7 years) after hospitalization.

Characteristics of the patients and the hospitalizations have been reported previously.33 MI survivors were younger and more likely to be male, white, married, and former smokers compared with survivors of stroke hospitalization. Functional limitations, cognitive impairments, and depressive symptoms before the hospitalization were less common in survivors of MI hospitalization than in survivors of stroke hospitalization. Hospitalizations for MI more frequently involved major surgery and stays in intensive care units or critical care units compared with hospitalizations for stroke. Survivors of stroke hospitalization had a greater likelihood of switching to proxy respondent status than MI hospitalization survivors (28% versus 8%).

Functional Outcomes
Figure 2 displays the adjusted change in functional status over time for both MI and stroke using fixed-effects regression. Overall, individuals experienced a mean of 0.40 additional limitations shortly after an MI (95% CI, 0.16–0.64), whereas patients who experienced a stroke had gained 1.97 additional limitations (95% CI, 1.56–2.39).

In fixed-effects regression, stratification by baseline functional status indicated that individuals with fewer limitations at baseline were most likely to experience additional limitations (Figure 3). For those without baseline impairment, there was a significant difference in trajectory slopes pre- to postevent for both MI (P<0.001) and stroke (P=0.003). This was also true for those with moderate-to-severe impairment at baseline for MI (P=0.004) and stroke (P<0.001). However,
There was no difference in the pre- versus post-slopes for those with mild-to-moderate impairment at baseline for either MI ($P=0.11$) or stroke ($P=0.49$).

We then performed fixed-effects regression models controlling for pre-event functional impairment. For individuals without baseline functional disability, the effect of an MI yielded a mean of 0.41 (95% CI, 0.18–0.63) new functional limitations, with a significant increase of 0.14 limitations/year in the decade after the MI (Table 1). Individuals with mild-to-moderate baseline disability gained 0.65 (95% CI, 0.07–1.23) new functional limitations with an acute MI, which steadily increased by 0.27 limitations/year in the ensuing decade. Persons with moderate-to-severe impairment at baseline experienced a significant increase in the rate of impairments (0.65/year) before acute MI, which did not appreciably change after the event.

Functional impairment was more acutely affected by a stroke, with an additional 2.07 limitations experienced by those without baseline impairment and 2.65 limitations by those with mild-to-moderate baseline impairment. Furthermore, there was a steady increase for both of these groups in the rate of impairment over the decade after the stroke (0.15/year and 0.19/year, respectively). As found in MI, persons with moderate-to-severe baseline impairment experienced a rapid increase in the rate of functional impairment (0.63/year) before an acute stroke and no significant change in impairments at the time of, and in the decade after, the stroke.

**Cognitive Outcomes**

Stroke hospitalization was associated with worse cognitive outcomes than MI hospitalization. The percentage of survivors with moderate-to-severe cognitive impairment increased from 19.6% at the interview just before stroke hospitalization to 30.2% at the first interview after stroke hospitalization ($P<0.001$), whereas the percentage increased from 9.6% before MI hospitalization to 15.1% after MI hospitalization ($P=0.01$).

In fixed-effects regression controlling for cognitive impairment before the event, the odds of developing moderate-to-severe cognitive impairment at the time of the acute MI was increased but not significantly (adjusted odds ratios, 1.68; 95% CI, 0.91–3.10; $P=0.10$), whereas survivors of acute stroke had significantly greater odds of developing moderate-to-severe cognitive impairment (odds ratio, 3.86; 95% CI, 2.10–7.11; Table 2). In the decade after the MI or the stroke, we did not observe significantly greater odds of developing moderate-to-severe cognitive impairment over the long-term after controlling for the odds of developing cognitive impairment before or acutely after the event. However, before having an MI or stroke, these individuals experienced a significant annual increase in odds of developing moderate-to-severe cognitive impairment (odds ratios=1.23 for MI and odds ratios=1.52 for stroke).

**Depression Outcomes**

In unadjusted analyses, stroke hospitalization was associated with a significant increase in the presence of substantial depressive symptoms but MI hospitalization was not. The percentage of survivors with substantial depressive symptoms increased from 16.4% at the interview just before stroke hospitalization to 22.0% at the first interview after stroke hospitalization.

**Figure 2.** Piecewise fixed-effects regression models of mean predicted functional limitations before and after acute myocardial infarction (AMI) and stroke. Plots are based on the fixed-effects regression model.

**Figure 3.** Piecewise fixed-effects regression models of mean predicted functional limitations before and after acute myocardial infarction and stroke, stratified by baseline functional status. Plots are based on the fixed-effects regression model. AMI indicates acute myocardial infarction.
before MI results were similar except some within-strata contrasts for

In analyses limited to the first hospitalization for MI or stroke, results were similar except some within-strata contrasts for functional impairments were no longer statistically significant and the magnitude of acute moderate-to-severe cognitive impairment after MI and stroke was lower (see the Data Supplement). Results for substantial depressive symptoms were similar after adjusting for nonresponse propensity scores (see the Data Supplement).

### Discussion

In this nationally representative cohort of older Americans, MI hospitalization was associated with significant acute and long-term increases in functional disability. We were able to demonstrate that MI and stroke each increase the rate of additional impairments in the following decade. This emphasizes the extent to which these acute vascular events are potential inflection points in patients’ lives. Clinically, this suggests that clinicians should have an increased index of suspicion that patients may need additional help with ADLs and IADLs over the years after MI and stroke. Scientifically, it suggests an urgent need to disentangle the extent to which this acute and also accelerated disability are the result of incomplete rehabilitation from the initial hospitalization, subsequent vascular events, behavioral changes, or other mechanisms.

Most studies have lacked information on individuals’ changes in disability over time before the MI or stroke hospitalization...
and consequently have controlled for baseline functioning using measures obtained during or soon after the hospitalization. However, many adults experience significant declines in functional disability over time before MI or stroke. Studies assessing changes in functional disability before and after MI and stroke in older adults have yielded mixed results. Some studies observed that MI increased the risk of a decline in physical functioning but that the effect was explained by comorbidity or limited to subjects with recent MI (<1 year). Other studies have found that the average rate of yearly increase in functional disability after MI or stroke did not change or lessened compared with changes in disability before the vascular event. We observed that acute MI is associated with increases in functional impairments years after the event, even after accounting for individuals’ changes in functional disability before the MI and acutely after the event. We likely detected a significant increase in rates of disability after MI and stroke because we had larger sample size, more outcome data before and after the vascular events, and included IADL changes.

We also observed that stroke significantly increased the odds of survivors’ developing moderate-to-severe cognitive impairment acutely at the time of the event with a nonsignificant trend for MI to do so. After accounting for changes in cognitive impairment before and acutely after the vascular events, we did not detect a significant increase in survivors’ subsequent risk of cognitive impairment over the long-term, consistent with previous stroke research. Our results may differ from others because of cohort differences and we studied incident MI and stroke events, used a different measure of cognitive impairment, and controlled for cognitive changes before the event and acutely at the time of the event. It is also possible that our measure of cognitive impairment was not sensitive to more subtle long-term changes in executive functioning, attention, or processing speed present after acute MI or stroke.

We did not detect a significant increase in the presence of substantial depressive symptoms after MI hospitalization when controlling for depressive symptoms before the acute event, similar to previous MI research. Still, we observed that having a higher number of functional impairments after acute MI or stroke was independently associated with substantial depressive symptoms, consistent with studies of other acute medical events, such as pneumonia and sepsis. Taken together, these studies suggest that it is not the acute medical event itself but how disabling the event is that incrementally increases the risk of developing depression.

The key finding of our study—that functional disability mounts after an MI and stroke—has clinical implications. Clinical practice guidelines and quality improvement programs recommend assessments of function, cognition, and depression in stroke patients before discharge and also in the postacute settings. Our results suggest that survivors of MI merit functional assessment before hospital discharge because they may have acutely acquired functional impairments. Moreover, our results suggest that survivors of MI and stroke also warrant monitoring for mounting functional disability over the years after the event. Clinicians can screen survivors for difficulty performing ADLs or IADLs because these were our measures. Those survivors who acquire new functional impairments further warrant screening for depression because, in our study, the odds of developing substantial depressive symptoms increased 20% with each new functional limitation gained after MI and 34% greater per each new functional limitation gained after stroke.

We observed that progression of functional disability is relatively worse in some patients than in others. Survivors with
fewer baseline limitations were most likely to gain functional limitations. These intriguing results should be interpreted with caution. We may not have detected significant changes in physical functioning after MI or stroke in patients with more baseline limitations because acute clinical events have less effect or our measures are relatively insensitive in patients with moderate-to-severe pre-existing functional disability. The patients with moderate-to-severe disability at baseline had steep functional declines over the years before MI or stroke and these trends did not seem to change over the long-term after the events. Those with substantial functional decline before the MI or stroke event likely had CVD or other disabling clinical events before the study period, whereas those with no disability at baseline may have experienced their first event. This vulnerable population warrants further study as to the reasons for, and prevention of, these steep functional declines.

The World Health Organization's International Classification of Functioning, Disability, and Health describes the complex interplay between a health condition, such as MI or stroke, functioning, and disability with contributions by pathophysiological processes, the effect of the health condition on the survivor, and contextual factors, such as each survivor's personal and environmental resources. Although we did not aim to identify the activities, behaviors, or contextual factors that predict long-term functional declines after MI or stroke, studies have shown that having Medicaid or no health insurance, lack of cardiac rehabilitation referral, and moderate-to-high perceived stress increase the risk for functional decline after MI. Conversely, vascular risk factor modification may reduce the long-term risk of cognitive impairment after stroke. Research is needed to better elucidate the mechanisms and risk factors for functional decline over the long-term after MI or stroke.

Because more adults are elderly and surviving MI and stroke, we need to better understand how to best care for an older population with CVD and functional or cognitive impairments. Although much is known about the benefits and risks of rehabilitation, transitions of care, and pharmacological management in patients during the early months after MI or stroke, less is known about the benefits and risks of these interventions in functionally or cognitively disabled patients. How do we best apply or tailor effective CVD interventions to an older survivor population with functional or cognitive impairments? Research to identify efficacious, patient-centered clinical interventions and systems of care for the large and growing population of older adults with CVD and functional or cognitive impairments is urgently needed.

Our study has some potential limitations. Our results are generalizable to older, community-dwelling survivors of MI and stroke, including those who move to nursing homes. Although survivors were sampled from a nationally representative cohort, the small numbers, particularly within functional strata, may limit generalizability. Still, our study was larger than other studies of this topic. Although the HRS-Medicare data do not include the results of testing for cardiac biomarkers, the principal and secondary diagnoses of MI and dates for a hospitalization are highly accurate in Centers for Medicare and Medicaid Services records. Our analysis does not include individuals with out-of-hospital or severe events that do not survive hospitalization. The use of proxies by survivors during longitudinal follow up is a potential limitation. Although 28% of stroke survivors and 8% of MI survivors converted to proxy respondents at some point during follow up, sensitivity analyses with nonresponse propensity score adjustment found similar results for the depression outcome.

Our estimates of declines in physical and cognitive functioning may be underestimated because of survivor bias and outmigration because of death (ie, death of patients with greater disability at baseline or patients with severe deficits after MI or stroke). We were unable to examine the role of clinical variables, such as disease severity, treatments, atrial fibrillation, or revascularization surgery. However, among patients with coronary artery disease, long-term cognitive decline may occur similarly in those who do and do not undergo surgery and physical disability after 1 year may be less in those undergoing surgery compared with percutaneous coronary intervention. Although we did not study disease-specific functional measures, we studied functional and cognitive impairments using standardized, valid instruments that are commonly used in older adults with vascular and nonvascular conditions. Our outcome measures represent clinically meaningful changes in patient-centered outcomes, such as physical and cognitive functioning.

Conclusions
The population of MI and stroke survivors is substantial and growing. Given improved event survival, the increasing number of older adults, and recent disability trends, the chronic care of MI and stroke survivors will prove costly. In this nationally representative cohort of older Americans, we found that hospitalizations for MI and stroke were associated with significant acute and long-term increases in functional disability. Our results suggest that survivors of MI merit functional assessment before hospital discharge because they may have acutely acquired functional impairments. Moreover, our results suggest that survivors of MI and stroke also warrant monitoring for mounting functional disability over the years after the event.

Acknowledgments
We thank Tish Shapiro and Mohammed Kabeto for their excellent programming. The Health and Retirement Study is conducted by the Institute for Social Research at the University of Michigan. The views expressed are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government. Dr Levine, Dr Davydow, and Dr Iwashyna contributed to conception and design. Dr Iwashyna and Dr Langa contributed to acquisition of data. Dr Levine, Dr Davydow, Dr Hough, Dr Langa, Dr Rogers, and Dr Iwashyna contributed to analysis and interpretation of data. Dr Levine and Dr Davydow drafted the manuscript. Dr Levine, Dr Davydow, Dr Hough, Dr Langa, Dr Rogers, and Dr Iwashyna contributed to critical revision of the manuscript for important intellectual content. Dr Levine, Dr Davydow, and Dr Iwashyna carried out the statistical analysis. Dr Rogers contributed to administrative, technical, or material support. Dr Levine, Dr Davydow, Dr Hough, Dr Langa, Dr Rogers, and Dr Iwashyna contributed to supervision.
Sources of Funding

The Health and Retirement Study is sponsored by the National Institute on Aging (U01 AG09740) and the Social Security Administration. Dr Levine received research support from the National Institutes of Health (NIH; P30DK092926 and K23AG040278). Dr Davydow received research support from the NIH (KL2 TR000421). Dr Iwashyna received research support from the NIH (K08, HL091249) and VA Health Services Research and Development (IIR 11–109).

Disclosures

None.

References


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*Circ Cardiovasc Qual Outcomes.* 2014;7:863-871; originally published online November 11, 2014;
doi: 10.1161/HCQ.0000000000000008
*Circulation: Cardiovascular Quality and Outcomes* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/7/6/863

Data Supplement (unedited) at:
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SUPPLEMENTAL MATERIAL

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I. Statistical Methods for Analyses

In models testing the hypothesis that hospitalization for an event (stroke or MI) is associated with a subsequent change in Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) impairments, we used fixed-effects regression. This analysis was implemented using `xtreg, fe` in STATA 11.2 (Stata Corporation, College Station, TX). In this analytic approach, patients served as their own controls. Only within-person variation over time was used to estimate the effect of stroke (or MI) hospitalization on functional limitations. In longitudinal analyses of panel data, this approach is known as a “fixed effects” approach.\(^1,2\) Please note that this definition of “fixed effects” is different from the term “fixed effect” referring to regression seen commonly in the biostatistical literature.\(^3\) We estimated a separate intercept for each hospitalization. This approach controlled for all characteristics of the patient that did not change over time without explicitly measuring these characteristics. The models accounted for repeated observations from each individual through the use of robust standard errors clustered by respondent. The equation for fitting the change in functional limitations over time in patients with MI was:

\[
y_{ij} = \alpha + \beta_1 X_{1,i} + \beta_2 X_{2,ij} + \beta_3 X_{3,ij} + \nu + \varepsilon_{ij}
\]

where \(y\) represents the functional limitations for \(i=1,2,\ldots,n\) occasions nested within \(j=1,2,\ldots,n\) subjects, \(\alpha\) is the intercept, \(\beta_1\) is the coefficient for the pre-MI slope (time prior to hospitalization for MI), \(\beta_2\) is the coefficient for the effect of MI hospitalization (binary coded, 0 prior to hospitalization and 1 after hospitalization), \(\beta_3\) is the coefficient for the post-MI slope (time after hospitalization for MI), and \((\nu_i + \varepsilon_{ij})\) is the residual (error). A similar equation was used for fitting the change in functional limitations over time in patients with stroke. Thus, the rate of change in functional impairments over time was modeled prior to the event (stroke/MI) as well as after the event, with the inclusion of the effect of the event itself at the time of hospital admission.

As an alternative approach, we replicated our analyses using mixed-effects linear regression using `xtmixed` with an exchangeable covariance structure in STATA 11.2. In these models, hospitalization-specific intercepts were estimated, but they are assumed to be drawn from a distribution for which a mean and variance are estimated.\(^2\) When we replicated our analyses as mixed-effects models, we found nearly identical results to our fixed-effects models.

For analyses of the effect of a stroke (or MI) hospitalization on the development of moderate-to-severe cognitive impairment and substantial depressive symptoms, we used conditional logistic regression. These analyses were implemented using `clogit` in STATA 11.2. As for our analyses of ADL/IADL impairments following a stroke hospitalization, these analyses used only within-person variation over time, controlling for all time-invariant patient characteristics. We used the same spline parameterization. In addition, we replicated our analyses of the effect of a stroke (or MI) hospitalization on the development of moderate-to-severe cognitive impairment and substantial depressive symptoms using mixed-effects logistic regression. These analyses were implemented using `xtmelogit` with an exchangeable covariance structure in STATA 11.2. Once again, we found nearly identical results to our conditional models.

REFERENCES

2. Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using STATA. College Station, TX: Stata Press; 2008
II. Sensitivity Analyses

1. ADL/IADL Impairments after a single stroke hospitalization:

Effect of Stroke:
No baseline impairment: beta: 1.71, 95%CI: 1.15, 2.26
Mild-to-moderate baseline impairment: beta: 2.13, 95%CI: 1.27, 2.99
Moderate-to-severe baseline impairment: beta: 1.08, 95%CI: 0.19, 1.96

Trajectory after stroke, per year:
No baseline impairment: beta: 0.16, 95%CI: 0.05, 0.27
Mild-to-moderate baseline impairment: beta: 0.17, 95%CI: 0.00, 0.34 (P=0.05)
Moderate-to-severe baseline impairment: beta: 0.03, 95%CI: -0.20, 0.26

2. ADL/IADL Impairments after a single MI hospitalization:

Effect of MI:
No baseline impairment: beta: 0.49, 95%CI: 0.23, 0.75
Mild-to-moderate baseline impairment: beta: 0.88, 95%CI: 0.19, 1.56
Moderate-to-severe baseline impairment: beta: -0.30, 95%CI: -1.32, 0.73

Trajectory after MI, per year:
No baseline impairment: beta: 0.13, 95%CI: 0.07, 0.19
Mild-to-moderate baseline impairment: beta: 0.13, 95%CI: 0.00, 0.26 (P=0.057)
Moderate-to-severe baseline impairment: beta: 0.03, 95%CI: -0.23, 0.28

3. ADL/IADL Impairments after stroke hospitalization adjusted for cognitive impairment:

Effect of stroke:
No baseline impairment: beta: 1.76, 95%CI: 1.32, 2.21
Mild-to-moderate baseline impairment: beta: 2.00, 95%CI: 1.24, 2.75
Moderate-to-severe baseline impairment: beta: 0.28, 95%CI: -0.66, 1.21

Trajectory after stroke, per year:
No baseline impairment: beta: 0.04, 95%CI: -0.05, 0.13
Mild-to-moderate baseline impairment: beta: 0.18, 95%CI: -0.07, 0.44 (P=0.15)
Moderate-to-severe baseline impairment: beta: -0.01, 95%CI: -0.21, 0.19

4. ADL/IADL Impairments after MI hospitalization adjusted for cognitive impairment:

Effect of MI:
No baseline impairment: beta: 0.47, 95%CI: 0.27, 0.67
Mild-to-moderate baseline impairment: beta: 0.69, 95%CI: 0.09, 1.29
Moderate-to-severe baseline impairment: beta: 0.12, 95%CI: -0.84, 1.08

Trajectory after MI, per year:
No baseline impairment: beta: 0.09, 95%CI: 0.03, 0.14
Mild-to-moderate baseline impairment: beta: 0.17, 95%CI: -0.01, 0.35 (P=0.07)
Moderate-to-severe baseline impairment: beta: 0.04, 95%CI: -0.33, 0.41

5. Adjusted OR of moderate-to-severe cognitive impairment in survivors of a single stroke hospitalization

OR 4.11, 95%CI: 2.10, 8.05

Effect of stroke: OR 2.14, 95%CI: 1.00, 4.58
Trajectory after stroke: OR 0.88, 95%CI: 0.76, 1.01

6. Adjusted OR of moderate-to-severe cognitive impairment in survivors of a single MI hospitalization

OR 1.56, 95%CI: 0.78, 3.12

Effect of MI: OR 1.35, 95%CI: 0.67, 2.70
Trajectory after stroke: OR 0.99, 95%CI: 0.86, 1.14

7. Adjusted OR of substantial depressive symptoms in survivors of a single stroke hospitalization adjusted for post-stroke cognition, functional impairments and non-response propensity scores

Effect of stroke: OR 1.71, 95%CI: 0.83, 3.53
Trajectory after stroke: OR 0.91, 95%CI: 0.76, 1.10

8. Adjusted OR of substantial depressive symptoms in survivors of a single MI hospitalization adjusted for post-stroke cognition, functional impairments and non-response propensity scores

Effect of MI: OR 1.45, 95%CI: 0.84, 2.52
Trajectory after MI: OR 0.98, 95%CI: 0.87, 1.11