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Pain as a Risk Factor for Disability or Death

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Abstract

OBJECTIVES—To determine whether pain predicts future activity of daily living (ADL) disability or death in individuals aged 60 years and above.

DESIGN—Prospective cohort study

SETTING—The 1998 to 2008 Health and Retirement Study (HRS), a nationally-representative study of older community-living individuals.

PARTICIPANTS—Twelve thousand six hundred and thirty-one participants in the 1998 HRS aged 60 years and older who did not need help in any activity of daily living (ADL).

MEASUREMENTS—Participants reporting that they were troubled by moderate or severe pain most of the time were defined as having significant pain. Our primary outcome was time to development of ADL disability or death over 10 years, assessed in 5 successive 2 year intervals. ADL disability was defined as needing help performing any ADL: bathing, dressing, transferring, toileting, eating, or walking across a room. We used a discrete hazards survival model to examine the relationship between pain and incident disability over each two year interval using only participants who started the interval with no ADL disability. We adjusted for several potential confounders at the start of each interval: demographic factors, 7 chronic health conditions, and functional limitations (ADL difficulty, and difficulty with 5 measures of mobility).

RESULTS—At baseline, 2,283 (18%) subjects had significant pain. Subjects with pain were more likely (all $p<0.001$) to be female (65% vs. 54%), have ADL difficulty (eg. transferring 12% vs. 2%, toileting 11% vs. 2%), have difficulty walking several blocks (60% vs. 21%), and have difficulty climbing one flight of stairs (40% vs. 12%). Over 10 years, subjects with pain were more likely to develop ADL disability or death (58% vs43%, unadjusted HR 1.67, 95% confidence interval (1.57 to 1.79)). However, after adjustment for confounders, participants with pain were not at increased risk for ADL disability or death (HR 0.98 (0.91 to 1.07)). The difference between the unadjusted and adjusted results was almost entirely explained by adjustment for functional status.

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Conflicts of Interest

Dr. Andrews and Mrs. Stijacic Cenzer report no conflicts of interest.

Author Contributions:

Andrews, Yelin, Covinsky: study concept and design, analysis and interpretation of data, and preparation of manuscript. StijacicCenzer: concept and design, acquisition of subjects and/or data, analysis and interpretation of data, and preparation of manuscript.

CONCLUSION—While there are strong cross-sectional relationships between pain and functional limitations, individuals with pain are not at higher risk for subsequent disability or death, after accounting for functional limitations. Like many geriatric syndromes, pain and disability may represent interrelated phenomena that occur simultaneously and require unified treatment paradigms.

Keywords

pain; functional limitations; activities of daily living; disability; quality of life

INTRODUCTION

Pain is common among older adults[1, 2] and is one of most important threats to their quality of life. Individuals with severe pain are several times more likely than those with no or only moderate pain to rate their overall health as poor.[3] In addition, elders with pain also commonly suffer from functional limitations.[1, 2, 4, 5]

The ability to perform the activities of daily living (ADL), such as bathing, dressing transferring, toileting, and eating, without assistance largely determines whether an individual can live independently. Those who need the help of another person to perform these ADL, generally referred to as ADL disability, usually need long term care or the assistance of a family caregiver. Moreover, individuals often experience a period of ADL disability prior to death.[6, 7] Thus, in addition to its impact on quality of life, ADL disability strongly predicts health care costs and mortality in the elderly.[8–12]

Cross-sectional studies have demonstrated strong relationships between pain, functional limitations, and ADL disability.[2, 13–16] For example, we demonstrated that individuals with pain resemble pain-free individuals who are three decades older with respect to the severity of functional limitations.[2] Because of the strong relationship between pain and functional limitations, it is often presumed that older adults with pain are more likely to develop poor health outcomes, including ADL disability and death, in the future. However, the evidence supporting the belief that pain predicts increased risk of becoming disabled is scant as few studies examine the extent to which pain predicts development of future ADL disability, and death.

The limited existing data on the longitudinal association between pain and functional limitations suggest that pain may predict future ADL disability. [17–20]However, many of these studies are limited by small sample sizes, not being population-based, and younger study populations. Perhaps most important, many of these studies include limited adjustment for baseline functional impairment. The process of ADL disablement is often an insidious process in which an elder starts with no functional limitations, develops impairments in physical capacity such as slow gait speed, develops limitations in higher levels of functioning such distance walking and stair climbing, perceives difficulty performing ADLs, and finally progresses to the point at which they need the help of another person performing ADL. [21]Since one of the strongest risk factors for developing ADL disability is the presence of functional limitations less severe than ADL disability, rigorous adjustment for baseline limitations is essential if we are to understand whether pain predicts ADL disability.

Therefore, to determine whether older individuals with pain are more likely to become ADL disabled over time, we used data from the nationally representative Health and Retirement Study to examine the longitudinal relationship between pain and disability. The HRS is well suited for this study because it is representative of the US older population and has a long length of follow-up. Further, it also has extensive data on baseline limitations, better

enabling us to differentiate whether future ADL disability in persons with pain is due to the presence of pain, or due to higher rates of baseline impairments in persons with pain.

METHODS

Participants

This was a longitudinal study of participants age 60 years and older in the 1998 HRS. The goal of the HRS is to examine changes in health and wealth as people transition from work to retirement to old age.[22] The HRS is administered every two years. Interviews are administered either by phone or in person, and include modules on chronic conditions, functional status, and financial well being. The 1998 wave of the HRS was designed to be representative of community-living people in the United States age 50 years and older. We limited the study to those at greatest risk for ADL disability, persons 60 year of age or greater. Of the 14,030 subjects in the HRS who were age 60 years and older in 1998, 25 were excluded because they did not provide data on pain and another 16 were excluded because they did not provide data on functional status. Of the remaining 13,989 participants, 1,117 (8.0%) were excluded because they reported being disabled in at least one ADL at baseline, and another 241 participants (1.9%) were lost to follow-up between 1998 and 2008, and therefore have no data available on ADL outcomes. Our final sample included 12,631 participants.

Measures

Pain—Our primary predictor variable was the presence of significant pain as determined by the following two questions. Participants were first asked, “Are you often troubled with pain?” Participants who responded “yes” were then asked, “How bad is the pain most of the time: mild, moderate, or severe?” Participants who responded “moderate” or “severe” were classified as having significant pain. When participants were unavailable, a surrogate was asked to rate the participant’s pain (n=903)). This classification of moderate or severe pain has been applied in previous studies[23] because it reflects the American Geriatrics Society Guidelines for the Pharmacologic Management of Persistent Pain in Older Adults and the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, which both recommend that moderate or severe pain should prompt a clinical response. [24], [25]The SUPPORT study (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) also used this classification to categorize reports of pain at the end of life. [26]Pain was assessed every two years.

Physical Disability

While many definitions of disability exist in the medical literature, we defined disability as the need for help with activities of daily living (ADL). This is the most common definition of disability in the geriatrics literature because it identifies elders who can not live by themselves without formal or informal help. We use the term “functional limitations” to refer to problems less severe than ADL disability, including difficulty performing ADL and higher order mobility functions.

Our primary outcome was time to development of disability in activities of daily living (ADL) or death over 10 years. This combined outcome measure corresponds to active life expectancy.[27] To assess ADL function participants were asked whether they had difficulty performing six ADL: bathing, dressing, transferring, toileting, eating, or walking across a room. Those who reported having difficulty were then asked if they needed help performing the activity. ADL disability was defined as needing help from another person to perform any ADL. For each ADL, participants were asked “Does anyone ever help you [perform that ADL].” The use of assistive devices was not classified as needing help. We combined ADL

disability and death as an outcome because the vast majority of elders have a period of ADL disability before they die.[6, 7] Therefore elders who report ADL independence in one wave, and death in the next wave 2 years later are highly likely to have become ADL disabled, even though this disability was not documented. To test this assumption, we examined exit interviews conducted with next of kin of decedents in this study. Next of kin were asked whether the subject needed help with activities daily living during the last 3 months of life.

Potential Confounders

Several measures that could potentially confound the relationship between pain and physical disability were considered. Demographic characteristics such as age, gender, ethnicity, and marital status were measured according to self-report. Measures of socioeconomic status included years of education, household income, and total net worth. Comorbid conditions, including arthritis, hypertension, diabetes, cancer, chronic lung disease, cardiac disease, and stroke were assessed by asking participants if a physician had ever told them that they had the condition. Symptoms of depression were measured using the eight-item Center for Epidemiologic Studies Depression Scale[28]. Participants were classified as having symptoms consistent with the diagnosis of depression if they reported more than three symptoms. Participants were also asked whether they were current smokers, and whether they consumed alcohol.

The need for help with ADL (ADL disability) results an advanced stage on the continuum of functional status problems. A crucial determinant of ADL disability is one's baseline point on that continuum. Therefore, our adjustment model included well established indicators of position on this continuum. First, we considered whether the subject had difficulty performing any of the activities of daily living. For each ADL and mobility measure, participants were asked, "Because of a health or memory problem, doyou have any difficulty [performing the activity]. Prior findings demonstrate that ADL difficulty and disability represent clinically distinct entities, with ADL difficulty preceding ADL disability. [29]Second, we assessed difficulty in several measures of mobility because of evidence that mobility impairments frequently precede ADL disability. Persons with these mobility impairments are therefore further along the pathway towards ADL disability than those without these impairments. [9]We assessed difficulty in the following non-vigorous mobility measures: walking several blocks, climbing one flight of stairs, extending arms above shoulders, pulling or pushing large objects, lifting a weight heavier than 10 pounds.

Analyses

The analyses used the sampling and design weights provided by the HRS to account for the probability of selection and clustering in the HRS sample. The characteristics of subjects reporting significant pain were compared using chi-square tests for categorical variables and *t*-tests for continuous variables.

To fully account for the longitudinal nature of the data, we used a time-dependent discrete hazard model to examine whether the hazard of developing ADL disability or death differs between participants with and without pain from 1998 to 2008. In a discrete hazards model, each participant contributes multiple observations to our analysis dataset, one for each HRS interview until the participant dies or reports disability. In a discrete hazards model, each subject can potentially contribute an observation for each wave in which they are alive and not disabled at the beginning of the wave. The model then predicts whether they will be dead or disabled by the next wave, dependent on whether they had pain at the beginning of the wave. Subjects continue to add observations to the analysis until they develop the outcome of death or disability. This model accounted for changing reports of pain, comorbid conditions, ADL, and functional status by updating data on each of these measures on each

subsequent interview (every 2 years).To examine the effect of potential confounding factors on the relationship between pain and development of ADL disability, a series of models were conducted for a series of domains of potentially confounding factors. These domains included demographic characteristics, socioeconomic status, comorbid conditions other than arthritis, arthritis, health-related behaviors (smoking and alcohol consumption), depressive symptoms, and baseline functional limitations (ADL difficulty and mobility difficulty). We performed an additional analysis exploring whether there was an age-pain interaction, and this interaction was not statistically significant (p=0.55). We performed descriptive analyses of how the prevalence of pain changed over the 10-year study period. Finally, we performed discrete time survival analyses examining whether participants with arthritis pain or back pain at baseline were more likely than those without arthritis pain or back pain to go on to develop ADL disability or death. Statistical analyses were conducted using Stata software, version 10.1 (StatCorp, College Station, Texas), and SAS software, version 9.2 (SAS Institute, Cary, North Carolina.)

RESULTS

12,631 participants were independent of all ADL in 1998. Of these, 2,283 (18%) subjects reported significant pain. Participants with pain differed markedly from those without pain at baseline. Participants with pain were more likely (all $p<0.05$) to be female (66% vs. 54%), have ADL difficulty (eg. transferring 12% vs. 2%, toileting 11% vs. 2%), have difficulty walking several blocks (60% vs. 21%), and have difficulty climbing one flight of stairs (40% vs. 12%) (Table 1).

Overall, 46% of participants had the outcome of ADL disability or death over 10 years. Of those, 45% first were disabled, and 55% died without reporting disability on one of the biennial HRS interviews. However, among those who died, 66% of next of kin reported in the after-death exit interview that the subject needed help with ADL in the last 3 months of life. Therefore, we estimate that 81% of subjects who had the “ADL disability or death” outcome were first disabled in ADL.

Over 10 years, participants with pain were more likely to develop ADL disability or death (58% vs 43%, HR 1.67, 95% CI 1.57–1.79) (Table 2). However, after adjustment for demographic factors, socioeconomic status, health-related behaviors, comorbidity, arthritis, depression, and functional status in a discrete hazard analysisthat included subjects free of disability at the start of each wave and adjusted for health, functional measures, and pain, participants with pain were not at increased risk for the development of ADL disability or death (HR 0.98 (0.91–1.07). The difference between adjusted and unadjusted analyses was almost entirely explained by adjustment for baseline ADL difficulty and mobility limitations. The relationship between pain and ADL disability or death remained similar with all proxy-reported data (n=903) excluded from the analysis (HR 0.78 (0.71 to 0.86). The results were also similar when we limited our outcome definition to either ADL disability (HR 1.09, 95% CI 0.96–1.24) or death (HR 091, 95% CI 0.82–1.01).

To further examine changes in participants’ pain during the study during the study period, Table 3 compares pain prevalence at the time of the final interview between participants with and without pain at baseline in subgroups defined by the final outcome (death, disability, or survival). For subjects whose outcome was death, we defined pain based on the interview preceding death. While there is frequent resolution of pain and development of new pain among participants, pain status at baseline strongly predicts pain status at time of the final interview. Pain tends to persist, in particular, among participants who go on to develop ADL disability. Among participants without pain at baseline, those who go on to develop ADL disability more frequently develop new pain.

We also examined two specific etiologies of pain, arthritis pain and back pain. The relationships between arthritis pain and future disability and between back pain and future disability were nearly identical to that between overall pain and future disability, (arthritis pain HR 1.04 (0.94 to 1.15; back pain HR 0.94 (0.88 to 1.01)).

Finally, we censored, at time of death, those individuals who died during the study period without a report of disability in one of the HRS waves or a report from the next of kin that they were disabled in the last three months of life (n=1,290). Even after censoring the deceased participants that were not reported disabled, the relationship between pain and risk of development of ADL disability or death remained similar, (HR 1.02 (0.93 to 1.12).

DISCUSSION

We examined the longitudinal relationship between pain and the development of ADL disability or death over ten years of follow-up in a nationally representative cohort of individuals aged 60 years and older who did not need help with ADL at baseline. At baseline, persons with pain were much more likely to have multiple functional limitations. The presence of significant pain predicted an increased risk of future ADL disability or death. However, this relationship was entirely explained by higher levels of baseline functional impairment in persons with pain compared to those without pain. After accounting for existing functional limitations, individuals with pain are not at higher risk for developing future ADL disability than those without pain. This relationship remains similar even when accounting for changes in pain, comorbid health conditions, and functional status during the 10-year follow-up periodin analyses that utilized repeated measures of pain and functional status in each follow-up interview.

The absence of a longitudinal association between pain and ADL disability does not imply that pain lacks a fundamental role in the pathogenesis of disability. Rather, it is likely that pain and disability are interdependent phenomena acting through common underlying mechanisms. From this perspective, pain and disability are similar to many geriatric syndromes such as falls and incontinence which have common underlying risk factors and mechanisms.

An additional reason that pain may not predict future ADL disability is that pain may represent a source of disability that acts more immediately. Prior studies have shown that in cross-sectional analyses pain and ADL disability correlate strongly. [2, 13–16]Our finding that pain does not predict future ADL disability after adjusting for baseline functional impairment may suggest that the effect of pain on disability occurs over a relatively short time that is probably shorter than the 2 year interval between HRS waves. Further research would be needed to clarify this hypothesis. Our observations, though, that participants' pain status frequently remained the same over the study period and that the development of new pain and new ADL disability often occurred in the same participants, may suggest that pain affects functional status in the short term. Another possible explanation is that pain may identify individuals who have a potentially reversible cause of the functional limitations and disability. We could not examine this possibility because we did not have information about whether subjects received treatment for pain. However, the negative association between pain and subsequent disability we observed when adjusting for only baseline functional limitation suggests such a mechanism. The latter hypothesis may again underscore the fundamental importance of active pain treatment among older persons. Lastly, we acknowledge that adjusting for baseline difficulty in ADL and mobility tasks may risk over-adjusting for baseline functional status. However, Table 3 provides the hazard ratios for each step of the step-wise analysis and thus allows readers to evaluate the effect of adjusting for each potential confounder.

Despite this unexpected finding, our data underscore that pain remains a common and important source of morbidity for elders and thus requires prompt identification and management. Indeed, elders in our cohort commonly reported pain. Nearly one in five reported significant persistent pain at baseline, suggesting that there is great epidemiological importance of pain in older populations. Moreover, elders with pain had increased rates of comorbidities and functional limitations at baseline. Indeed, among elders with pain, we observed significantly increased rates of all comorbidities assessed, except cancer, and increased rates of baseline difficulty in every functional activity measured (Table 1). This observation corroborates previous reports of a cross-sectional association between pain and increased risk of ADL difficulty. [2], [13–16]Thus, pain is highly prevalent, carries substantial quality of life and physical well-being implications among elders, and must be treated aggressively.

Our observation that pain does not predict future development of ADL disabilityafter adjusting for baseline functional limitations extends previous findings. We corroborated prior observations that pain may predict the incidence of future ADL impairment when not adjusting for baseline functional limitations.[15], [17–20] Few studies, to our knowledge, have rigorously controlled for baseline functional limitations, which our findings suggest play a crucial role in mediating the relationship between pain and ADL disability. Lastly we were able to include data from a large, nationally-representative cohort of men and women, age 60 years and above, who were followed for 10 years.

Overall, our findings may call into question the traditional view of pain as a predictor of future disability. It may not be correct to view the relationship between pain and older age disability through the typical lens of a risk factor and an outcome. Instead, it may be more accurate to view pain and disability as highly interrelated phenomenon, perhaps precipitated by common underlying processes. To the extent that pain and disability occur concomitantly, pain will not predict future disability because adjustment for baseline disability may adjust for a common mechanism that impacts both pain and disability. The management of both pain and disability may therefore benefit from treatment paradigms that recognize how both problems may occur simultaneously and may have common underlying etiologies. These more unified treatment algorithms, addressing both pain and disability concomitantly, have ramifications on current clinical practice. Interventions focused on improving functional status, for example by providing rehabilitation services, should be included in multidisciplinary pain management approaches. Conversely, adequate management of patients' pain becomes an important component of disability treatment.

Our study has several potential limitations. First, participants in the HRS do not report the specific cause or location of their pain. Thus we considered all types of pain, such as musculoskeletal, arthritis, cancer, and diabetes, as equivalent. Second, we relied on self-reported data that were collected at two-year intervals. The biannual frequency of data collection limits to an extent our ability to precisely quantify trajectories of pain and disability over time. Third, we did not have data on whether or not participants were treated for their pain. Fourth, we are limited by our potential difficulty distinguishing whether a given measure represents a confounder or instead a factor contributing to the underlying causal mechanism. Fifth, adjusting for several measures of baseline functional status, may risk over adjusting the data. Strengths include the community-based national sampling frame representing the population at risk for ADL disability and high rates of retention, crucial to increasing the reliability of longitudinal research.

In conclusion, among a representative cohort of community-dwelling elders over age 60 years, participants with pain had greater baseline rates of ADL difficulty and increased rates of future ADL disability over 10 years. However, after adjusting for baseline functional

limitations, pain no longer predicted future ADL disability. Our results highlight the need to view pain and disability as interrelated phenomena that often occur simultaneously. Treatment paradigms for both pain and disability may need to account for the close linkage between pain and disability.

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The study sponsor had no role in the design, methods, subject recruitment, data collections, analysis or preparation of paper.

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Table 1

Comparison of the Baseline Characteristics of Participants with and without Pain (N=12,631)

Characteristic		Pain (N = 2,283; 17.8%)	No Pain (N = 10,348; 82.2%)	*P*-value
Demographic characteristics	Age (mean, SD)	71.2 ± 7.8	71.1 ± 7.7	0.638
	Age Category, %	46.4	46.3	
	60–64	24.6	24	
	65–69	21.8	22.3	0.897
	70–74	21.3	21.7	
	>=75	32.3	32.0	
	Female, %	65.5	54.2	<0.001
	Ethnicity, %			
	White	85.2	85.0	
	Black	8.2	8.3	
	Hispanic	5.6	4.9	0.006
	Other	1.0	1.8	
	Married or Partnered	57.1	61.7	0.001
SES Measures	<HS education, %	34.6	26.9	<0.001
	Income, median (IQR)	23K (12K–40K)	28K (16K–50K)	<0.001
	Net worth, median (IQR)	103K (24K–266K)	160K (57K–372K)	<0.001
Comorbid Conditions	Hypertension, %	52.8%	44.5	<0.001
	Diabetes, %	15.6	12.5	<0.001
	Cancer, %	13.4	12.2	0.150
	Chronic lung disease, %	11.8	6.6	<0.001
	Heart condition, %	31.5	22.2	<0.001
	Stroke, %	9.5	6.3	<0.001
	Arthritis, %	81.1	46.4	<0.001
ADLs (Difficulty)	Dressing, %	15.0	3.4	<0.001
	Eating, %	2.8	0.7	<0.001
	Bathing, %	10.1	2.2	<0.001
	Transferring to/from Bed, %	12.3	1.6	<0.001
	Walking Across Room,%	11.5	1.9	<0.001
	Using Toilet, %	10.7	1.7	<0.001
Functional Status (Difficulty)	Walking Several Blocks,%	60.0	20.6	<0.001
	Climbing One Flight of Stairs, %	39.9	12.2	<0.001
	Extending Arms Above Shoulders, %	32.5	9.6	<0.001
	Pulling or Pushing Large Objects, %	56.1	22.8	<0.001
	Lifting Weight Heavier then 10 lbs, %	50.3	18.1	<0.001
Other health	Depression[1], %	30.0	10.9	<0.001
	Current smoker, %	15.6	12.7	0.001
	Currently drinks alcohol, %	40.0	49.5	<0.001

[1] Data on depression were collected only on self-respondents (n=11,722).

SES=Socioeconomic Status

Table 2

Relationship between Pain and Activities of Daily Living (ADL) Disability or Death, with and without Adjustment for Groups of Confounders[1] (N=12,631)

	HR for pain	95% CI
Unadjusted	1.67	(1.57, 1.79)
Adjusted for Demographic Characteristics (age, gender, ethnicity, marital status)	1.68	(1.57, 1.80)
Adjusted for SES (education, income, net worth)	1.56	(1.47, 1.66)
Adjusted for Comorbid Conditions (hypertension, diabetes, cancer, lung disease, heart condition, stroke)	1.44	(1.36, 1.54)
Adjusted For Arthritis	1.57	(1.47–1.68)
Adjusted for Health Habits (smoking and drinking)	1.59	(1.49–1.69)
Adjusted for Depression	1.51	(1.28–1.51)
Adjusted for Difficulty with ADL function (dressing, eating, transferring, using toilet, walking across the room, bathing)	1.22	(1.14, 1.31)
Adjusted for Baseline Mobility Measures Difficulty (stairs, walking, lifting, extending arms, pulling/pushing,)	0.85	(0.80, 0.91)
Adjusted for All Functional Measures at Baseline[2]	0.81	(0.76–0.86)
Adjusted for All of the Above[3]	0.98	(0.91–1.07)

[1] Outcome is “Time to first ADL disability or death after 1998 interview”.

[2] All functional measures at baseline includes difficulty with any ADL, or mobility measure.

[3] Measures of age, income, and wealth were treated as continuous variable. Measures of race/ethnicity were treated as categorical variable. Measures of education, comorbid conditions, arthritis, depression, smoking, drinking, ADL difficulty, and mobility difficulty were all treated as dichotomized variables.

SES=Socioeconomic Status

Table 3

Prevalence of Pain at Final Interview among Participants with Different Primary Outcomes, Stratified by Pain at Baseline (n=11,503)

	Prevalence of Pain on Final Interview			
		Subjects Stratified by Final Outcome		
Presence of Pain on Baseline Interview	**All Subjects**	**Death**	**ADL Disability**	**Survival without ADL disability**
Yes (n=2046)	58.4%	53.5%	69.0%	52.9%
No (n=9457)	18.8%	18.1%	30.2%	15.6%