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Association of Risk Factors and Comorbidities With Chronic Pain in the Elderly Population.

Neil Mookerjee
Rowan University, mookerjee@rowan.edu

Nicole Schmalbach
Rowan University

Gianna Antinori
Rowan University

Subhadra Thampi
Rowan University

Dylan Windle-Puente
Rowan University

See next page for additional authors

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Authors

Neil Mookerjee, Nicole Schmalbach, Gianna Antinori, Subhadra Thampi, Dylan Windle-Puente, Amy Gilligan, Ha Huy, Megha Andrews, Angela Sun, Roshni Gandhi, William Benedict, Austin Chang, Ben Sanders, Justin Nguyen, Maanika Reddy Keesara, Janet Aliev, Aneri Patel, Isaiah Hughes, Ian Millstein, Krystal Hunter, and Satyajeet Roy

Original Research

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Neil Mookerjee[1], Nicole Schmalbach[1], Gianna Antinori[1], Subhadra Thampi[1], Dylan Windle-Puente[1], Amy Gilligan[1], Ha Huy[1], Megha Andrews[1], Angela Sun[1], Roshni Gandhi[1], William Benedict[1], Austin Chang[1], Ben Sanders[1], Justin Nguyen[1], Maanika Reddy Keesara[1], Janet Aliev[1], Aneri Patel[1], Isaiah Hughes[1], Ian Millstein[1], Krystal Hunter[1], and Satyajeet Roy[1,2]

Abstract

Introduction/Objective: Chronic pain disorders affect about 20% of adults in the United States, and it disproportionately affects individuals living in the neighborhoods of extreme socioeconomic disadvantage. In many instances, chronic pain has been noted to arise from an aggregation of multiple risk factors and events. Therefore, it is of importance to recognize the modifiable risk factors. The aim of this study was to investigate the comorbid medical conditions and risk factors associated with chronic pain disorders in patients aged 65 years and older. **Methods:** Our team retrospectively reviewed medical records of elderly patients (65 years and older) who were evaluated in our outpatient medicine office between July 1, 2020 and June 30, 2021 for acute problems, management of chronic medical problems, or well visits. We divided our patients into a group who suffered from chronic pain disorder, and another group who did not have chronic pain disorder. The association of variables were compared between those groups. **Results:** Of the 2431 patients, 493 (20.3%) had a chronic pain disorder. A higher frequency of females in the group with chronic pain disorder was found compared to the group without a chronic pain disorder (60.6% vs 55.2%; $P = .033$). The mean ages between the two groups were similar in the group with a chronic pain disorder compared to the group without (76.35 ± 7.5 year vs 76.81 ± 7.59 year; $P = .228$). There were significant associations of certain comorbidities in the group with a chronic pain disorder compared to the group without a chronic pain disorder, such as depression (21.9% vs 15.2%; $P < .001$), anxiety (27.0% vs 17.1%; $P < .001$), chronic obstructive pulmonary disease (8.7% vs 6.1%; $P = .036$), obstructive sleep apnea (16.8% vs 11.6%; $P = .002$), gastroesophageal reflux disease (40.8% vs 29.0%; $P < .001$), osteoarthritis (49.3% vs 26.1%; $P < .001$), other rheumatologic diseases (24.9% vs 19.4%; $P = .006$), and peripheral neuropathy (14.4% vs 5.3%; $P < .001$). **Conclusion:** Female sex, depression, anxiety, chronic obstructive pulmonary disease, obstructive sleep apnea, gastroesophageal reflux disease, osteoarthritis, other rheumatologic diseases, and peripheral neuropathy were significantly associated with chronic pain disorder in elderly patients, while BMI was not associated with chronic pain disorder.

Keywords

chronic pain disorder, elderly population, pain disorders in elderly, risk factors of pain, elderly chronic pain

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Introduction

Chronic pain disorders affect about 20% of adults in the United States. This data is based on a study that sought to determine the prevalence of chronic pain by using the National Health Interview Survey.[1] The International Association for the Study of Pain (IASP) defines pain as an

[1]Cooper Medical School of Rowan University, Camden, NJ, USA
[2]Cooper University Health Care, Camden, NJ, USA

Corresponding Author:
Satyajeet Roy, Cooper Medical School of Rowan University, Department of Medicine, Cooper University Health Care, 1103 North Kings Highway, Suite 203, Cherry Hill, NJ 08034, USA.
Email: roy-satyajeet@cooperhealth.edu

"unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described by the patients in terms of such damage."[2] Pain is considered chronic when it has "persisted beyond normal tissue healing time."[2] With this being a vague definition for chronic pain, most clinicians differentiate acute and chronic pain based on the desired therapeutic management. Acute pain management aims to treat the cause of the pain, while chronic pain management aims to treat the function and quality of life of the patient with pain.[2] Chronic pain is also defined as any pain lasting longer than 3 months.[3]

Multiple factors, such as sociodemographic, physiologic, clinical, and biological, play a role in the development of chronic pain. In many instances chronic pain has been noted to arise from an aggregation of multiple events even if there was one event that instigated it.[4] This exemplifies the complex mechanism that one must consider when managing chronic pain. In addition, chronic pain has been linked to multiple co-morbidities and risk factors.[5] For example, women have been found to be at an increased risk for developing a chronic pain disorder for reasons, such as sex-linked differences in the neurobiology of pain and pain perception.[6] This causes them to experience a greater intensity of pain and hence the female gender is considered a risk factor.[6] Depression and cardiovascular disease have been proven to be associated with chronic pain disorders after adjusting for socioeconomic and environmental cofounders.[7,8] Older age has been identified as an important risk factor based on multiple epidemiologic studies.[9] According to the Center for Disease Control and Prevention (CDC) in which the data from the National Health Interview Survey in 2019 was used, individuals who are 65 years old or older, 30.8% have chronic pain, compared to 25.8% in those who are 45 to 64 years old, and 14.6% in those who are 18 to 29 years old.[10] Therefore, a thorough understanding of the various risk factors and comorbidities in those who are 65 years or older is of high importance.[9]

Chronic pain has diverse etiologies, hence the management is multifaceted. Addressing the various etiologies and associated aspects helps design effective management. There are several approaches, such as pharmaceutical, surgical, electrical interventions, as well as lifestyle changes to address the various biomedical aspects of chronic pain. Biopsychosocial approaches and use of management methods, such as physiotherapy and occupational therapy when warranted, further maximize the effectiveness of the treatment plan.[11] Additionally, integrative, inter-professional and other evidenced based chronic pain treatments can also be incorporated.[12] The knowledge of various co-morbidities and risk factors are essential due to their bidirectional relationship with chronic pain.[13] For example, those with depression and chronic pain, emotional support systems and a good mental health state have been exemplified to lead to reduced pain chronicity.[13] Furthermore, adequate treatment of chronic pain has a salutary effect on the mental state for those with depression.[13] Therefore, it is essential to understand the patient as a whole to see how various comorbidities and risk factors may influence those with chronic pain. Understanding the bidirectional relationship can help design the management in a more effective manner.

Overall, the association of risk factors and comorbidities with chronic pain disorders lack consensus.[5,8] There is a need for a better understanding which will lead to higher quality management especially in the elderly population, where this condition is more prevalent than the younger populations. We aimed to examine the association of risk factors and comorbid medical conditions associated with chronic pain in the elderly population.

Materials and Methods

Study Design and Setting

This study was a retrospective cohort study using the electronic medical records of all elderly patients who visited our suburban internal medicine office.

Participants

Patients, 65 years of age or older, who visited our internal medicine office between July 1, 2020 and June 30, 2021 for acute problems, management of chronic medical problems, or well visits, were included in this study. Those excluded were patients younger than 65 years of age.

Variables

The following data on each patient were collected: age, sex, race, tobacco use, recreational drug use, and alcohol use; comorbid medical conditions including diabetes mellitus (DM), hypertension, stroke, transient ischemic attack (TIA), seizure disorder, traumatic brain injury, Parkinson's disease, depression, bipolar disorder, anxiety disorder, schizophrenia, coronary artery disease (CAD), congestive heart failure (CHF), atrial fibrillation, chronic obstructive pulmonary disease (COPD), asthma, obstructive sleep apnea (OSA), gastroesophageal reflux disorder (GERD), liver cirrhosis, chronic kidney disease (CKD), anemia, cancer, hypothyroidism, osteoarthritis, other rheumatologic diseases including polymyalgia rheumatic (PMR), peripheral neuropathy, and chronic pain disorders. Data was also collected on body mass index (BMI), vitamin B12, vitamin D, hemoglobin, mortality; use of medications, such as statin, antidepressants, benzodiazepines, and central nervous system stimulants. The collected data was recorded into a Microsoft Excel (2016, Redmond, Washington, USA) spreadsheet.

Data Source and Access

The Institutional Review Board (IRB) of our healthcare system reviewed and approved this study. We received permission to collect data strictly for research study purposes according to the Health Insurance Portability and Accountability Act (HIPPA) requirements. The IRB granted waivers for the need to receive informed consent. Additionally, our study complied with the ethical standards set forth by the IRB. The electronic medical record data of all patients approved by the medical informatics and stored in Epic healthcare software (Epic Systems Corporation, Wisconsin, USA) was assessable only to the investigators enrolled in the study.

Bias

To address the potential for inappropriate or presumptive diagnosis of chronic pain disorder, we excluded patients who had a musculoskeletal trauma, or a surgical procedure performed within the preceding 3 months.

Study Sample Size

We enrolled 2431 patients in our study.

Statistical Methods

We used SPSS (Statistical Package for the Social Sciences, version 15.01, IBM, Armonk, New York, USA) software for computation of statistical analysis. We divided the patients in a group consisted of patients who had a chronic pain disorder, and in another group consisted of patients who did not have a chronic pain disorder. Patients having chronic pain disorder were identified by reviewing the documentation of persistent pain for more than 3 months in their progress notes, or documentation of ICD-10 codes G89.4 or F45.41 in their problem lists. Data distribution was tested by using a test of skewness for continuous variables. An independent *t*-test was used for analysis for those with a value between 1 and −1 exemplifying normal distribution. A Mann-Whitney *U* test was used for those with skewness that was greater than 1 or less than −1 as this exemplified that the data was non-parametric. We applied Chi square tests to analyze the categorical variables. We used logistic regression to model the outcome of those with chronic pain disorder. We used the quasi-Delphi method. The independent variables used in the model were determined by clinicians' observation in their practice in combination with data elements that were statistically significant in univariable analysis of chronic pain. We placed the data elements into the model in 1 step using the "Enter" method. We verified its ability to appropriately classify data by use of area under the curve (AUC) which showed an acceptable level (AUC = 0.702). We further validated the model by splitting the data where 80% was training data while 20% was in the testing data. The AUC was 0.712 for the training data and 0.721 for the testing data which indicated an acceptable ability to classify data. The statistical significance in this study was defined as a $P < .05$.

Results

In this study, we included 2431 patients, out of which 493 (20.3%) patients had a chronic pain disorder and 1938 (79.7%) did not. In comparing mean ages, we found no statistically significant difference between the group of patients with a chronic pain disorder compared to the group of patients without a chronic pain disorder (76.4 ± 7.5 year vs 76.8 ± 7.5 year; $P = .228$; Table 1). Women were significantly higher in frequency in the group with a chronic pain disorder compared to the group without a chronic pain disorder (60.6% vs 55.2%; $P = .033$; Table 1). We found no significant difference in the race distribution and social factors between the 2 groups. Similarly, we found no significant difference in BMI, levels of vitamin B12, vitamin D, hemoglobin, and mortality between the 2 groups (Table 1).

There were significantly higher frequencies of association of certain comorbid medical conditions in the group with chronic pain disorder compared to the group without chronic pain disorders, which included depression (21.9% vs 15.2%; $P < .001$), anxiety (37.0% vs 17.1%; $P < .001$), COPD (8.7% vs 6.1%; $P = .036$), OSA(16.8% vs 11.6%; $P = .002$), GERD (40.8% vs 29.0%; $P < .001$), osteoarthritis (49.3% vs 26.1%; $P < .001$), other rheumatologic diseases including polymyalgia rheumatica (24.9% vs 19.4%; $P = .006$), and peripheral neuropathy (14.4% vs 5.3%; $P < .001$) (Table 2). We found no significant differences in the frequencies of diabetes mellitus, stroke, TIA, seizure disorder, traumatic brain injury, Parkinson's disease, schizophrenia, bipolar disorder, coronary artery disease, congestive heart failure, atrial fibrillation, asthma, OSA, liver cirrhosis, CKD, anemia, cancer, and hypothyroidism between the 2 groups (Table 2).

Higher frequencies of the usage of certain medications was found when comparing the group with chronic pain disorders to that without chronic pain disorders, which included antidepressants (28.8% vs 21.9%; $P < .001$), benzodiazepines (16.4% vs 12.6%; $P = .028$), and antiepileptic medications (14.0% vs 7.3%; $P < .001$; Table 3). There were no significant differences in patients who used statins, and central nervous system stimulants (Table 3).

We found significantly greater odds of chronic pain in logistic regression analysis in patients who had osteoarthritis (OR = 2.565, 95% CI 2.060-3.194; $P < .001$), obstructive sleep apnea (OR = 1.424, 95% CI 1.063-1.909; $P = .018$), GERD (OR = 1.400, 95% CI 1.100-1.782; $P = .006$), peripheral neuropathy (OR = 2.544, 95% CI 1.787-3.623; $P < .001$),

Table 1. Baseline Characteristics, Laboratory Values, and Mortality.

Variable	Variable	Patients with a chronic pain disorder (n = 493)	Patients without a chronic pain disorder (n = 1938)	*P*
Age	Years, mean (SD)	76.4 (7.5)	76.8 (7.5)	.228
Sex	Male, n (%)	194 (39.4)	868 (44.8)	.033
	Female, n (%)	299 (60.6)	1070 (55.2)	
Race	White, n (%)	372 (75.5)	1506 (77.7)	.237
	Black, n (%)	64 (13.0)	290 (14.9)	
	Hispanic, n (%)	23 (4.7)	74 (3.8)	
	Other, n (%)	34 (6.8)	68 (3.6)	
Social	Tobacco use, n (%)	209 (42.4)	851 (43.9)	.554
	Alcohol use, n (%)	244 (49.5)	1018 (52.5)	.228
	Recreational drug use, n (%)	17 (22.4)	43 (2.2)	.117
Weight	BMI (kg/m^2), mean (SD)	28.4 (6.2)	27.9 (5.9)	.075
Mortality	Dead, n (%)	19 (3.9)	92 (4.7)	.396
Lab values	Vit B_{12} (pg/mL), mean (SD)	729.6 (582.1)	774.6 (597.7)	.225
	Vit D (ng/mL), mean (SD)	40.0 (23.4)	39.0 (15.0)	.327
	Hb (g/dL), mean (SD)	13.0 (2.9)	12.9 (2.6)	.397

Abbreviations: BMI, body mass index; Hb, hemoglobin; n, number of subjects; SD, standard deviation; Vit B_{12}, vitamin B_{12}; Vit D, vitamin D.

Table 2. Comparative Association of the Comorbid Medical Conditions.

Comorbidity	Patients with a chronic pain disorder (n = 493)	Patients without a chronic pain disorder (n = 1938)	*P*
DM, n (%)	141 (28.6)	548 (28.3)	.887
TIA, n (%)	22 (4.5)	65 (3.4)	.237
Stroke, n (%)	30 (6.1)	126 (6.5)	.736
Seizure, n (%)	7 (1.4)	30 (1.5)	.836
TBI, n (%)	4 (0.8)	8 (0.4)	.278
Parkinson's Ds, n (%)	2 (0.4)	19 (1.0)	.284
Depression, n (%)	108 (21.9)	294 (15.2)	<.001
Bipolar Dis, n (%)	6 (1.2)	18 (0.9)	.609
Anxiety Dis, n (%)	133 (37.0)	332 (17.1)	<.001
Schizophrenia, n (%)	0 (0.0)	7 (0.4)	.357
CAD, n (%)	106 (21.5)	396 (20.4)	.601
CHF, n (%)	40 (8.1)	112 (5.8)	.056
Atrial fibrillation, n (%)	68 (13.8)	273 (14.1)	.867
COPD, n (%)	43 (8.7)	118 (6.1)	.036
Asthma, n (%)	66 (13.4)	206 (10.6)	.083
OSA, n (%)	83 (16.8)	224 (11.6)	.002
GERD, n (%)	201 (40.8)	562 (29.0)	<.001
Liver Cirrhosis, n (%)	4 (0.8)	21 (1.1)	.593
CKD, n (%)	57 (11.6)	270 (13.9)	.167
Anemia, n (%)	84 (17.0)	266 (13.7)	.061
Cancer, n (%)	154 (31.2)	553 (28.5)	.238
Hypothyroidism, n (%)	93 (18.9)	340 (17.6)	.497
Osteoarthritis, n (%)	243 (49.3)	505 (26.1)	<.001
Other Rheum Ds, n (%)	123 (24.9)	376 (19.4)	.006
Peripheral neuropathy, n (%)	71 (14.4)	103 (5.3)	<.001

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; GERD, gastroesophageal reflux disorder; n, number of subjects; OSA, obstructive sleep apnea; Other Rheum Ds, other rheumatological disorders; TBI, traumatic brain injury; TIA, transient ischemic attack.

Table 3. Comparative Association of Medications.

Medication	Patients with a chronic pain disorder (n = 493)	Patients without a chronic pain disorder (n = 1938)	*P*
Statin, n (%)	310 (62.9)	1215 (62.7)	.949
Antidepressants, n (%)	142 (28.8)	424 (21.9)	.001
Benzodiazepines, n (%)	81 (16.4)	245 (12.6)	.028
Antiepileptic med, n (%)	69 (14.0)	141 (7.3)	<.001
CNS stimulants, n (%)	9 (1.8)	30 (1.5)	.658

Abbreviations: CNS, central nervous system; n, number of subjects.

Table 4. Influence of Comorbidities and Risk Factors on Chronic Pain Disorders.

Variable	*B*	*P*	Exp(*B*)	95% CI for EXP(*B*) lower	95% CI for EXP(*B*) upper
Age	−0.019	.016	0.981	0.966	0.996
Sex: Male	0.031	.791	1.031	0.821	1.295
Race: White	−0.120	.358	0.887	0.686	1.146
Alcohol use	−0.060	.582	0.941	0.759	1.167
DM	−0.224	.077	0.799	0.623	1.025
CHF	0.415	.062	1.515	0.979	2.344
CKD	−0.251	.150	0.778	0.553	1.095
Cancer	0.066	.575	1.068	0.848	1.344
Osteoarthritis	0.942	<.001	2.565	2.060	3.194
COPD	0.093	.655	1.097	0.730	1.648
OSA	0.354	.018	1.424	1.063	1.909
GERD	0.337	.006	1.400	1.100	1.782
Peri Neuro	0.934	<.001	2.544	1.787	3.623
Other Rhem Ds	0.021	.870	1.021	0.793	1.316
Anxiety	0.442	.002	1.556	1.177	2.057
Depression	0.042	.786	1.043	0.769	1.416

Abbreviations: CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; GERD, gastroesophageal reflux disorder; OSA, obstructive sleep apnea; Other Rheum Ds, other rheumatological disorders; Peri Neuro, peripheral neuropathy.

and anxiety disorder (OR = 1.556, 95% CI 1.177-2.057; *P* = .002) (Table 4). For every unit increase in age in year, there were decreased odds of chronic pain (OR = 0.981, 95% CI 0.966-0.996; *P* = .016) (Table 4).

Discussion

We found that female sex, depression, anxiety, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), gastroesophageal reflux disease (GERD), osteoarthritis (OA), other rheumatologic disease, and peripheral neuropathy had greater association with chronic pain disorders in the elderly patients. Multiple epidemiologic research studies have concluded that chronic pain disorders are more prevalent in females than in males worldwide.[14,15] Our findings align with these findings. Studies specific for chronic pain disorders demonstrated that 50% of chronic pain conditions affected females more often than males, 20% of specific conditions affected more males than females, and the other 30% being equal in both populations.[16] One possible reason for this association of chronic pain disorders and female sex is attributed to the differences in the perception of pain. Studies have illustrated that females are more sensitive and have lower thresholds to experimental pain than males.[17,18] In addition, differences in conditioned pain modulation, which exemplifies how well perceived pain is diminished when applying a stimulus of pain to a different area of the body, might as well contribute to this finding.[19] Additionally, a systematic review has demonstrated that the conditioned pain response is better tolerated in males than in females.[20] Looking into biological mechanisms that can contribute to this, there are some genetic differences when comparing each sex that have been established and is associated with increased pain in females but not in males.[21] Additionally, there has been a link to sex-based difference in the immune system which contributes to females being more susceptible to various chronic pain conditions than males.[22] Furthermore, sex-based differences in hormonal makeup

have been associated with increased chronic pain conditions in females. It is believed that sex hormones in females that are brought out around the time of perimenopause are associated with chronic pain conditions.[23] Since our study reviewed the elderly population, we believe all our patients have passed this stage and have the hormonal differences brought about. Understanding that elderly females are subject to greater risk for chronic pain than males can help design adequate management strategies. With the majority of the published pain management clinical trials for various pharmacological interventions being carried out predominantly in males, we believe that the scientific community likely has less understanding if there are differences in the pharmacokinetics, adverse effects, and efficacy of pain management interventions in females based on sex-based differences.[24,25] Conducting more pharmacological trials in female subjects can help us understand which drugs can lead to different outcomes based on sex to improve patient care.

In our study, we found a significant association of those with chronic pain disorders to have depression. Although, the logistic regression model did not show significantly higher odds, nevertheless, our finding aligns with the existing scientific literature. A cross sectional epidemiologic study in the United States, which included 840 subjects aged 70 years or older, concluded that those with chronic pain were 2.5 times more likely to have depression than those without chronic pain (OR = 2.5, 95% CI = 1.40-4.55).[26] Another study conducted in Germany in those with chronic widespread pain were found to have about a 4 times greater risk of having depression when using confounder-adjusted logistic regression analysis (OR = 4.08, 95% CI 1.90-8.74).[27] A reason for this association could be because of increased neuroinflammation and the subsequent pathologic effects. Multiple studies have established connections between chronic pain disorders and depression based on neurobiological mechanisms and changes in neuroplasticity.[28] For example, neuroinflammation in both peripheral and central nervous system leads to chronic pain due to the sensitization of nociceptive neurons.[29] Additionally, various cellular pathophysiological processes can instigate chronic pain pathologies. This includes increased microglia and mast cell contribution than the normal which contributes to the increased inflammatory process.[30] This inflammation then leads to alterations in pain sensitization which eventually gives rise to chronic pain pathologies.[31] Other researchers have investigated ways depression could influence the central nervous system by causing inflammation through immune dysregulation. One of the mechanism proposed emphasizes on higher than normal corticosterone levels which triggers a positive uncontrolled feedback loop of cytokines through stimulation of microglia and astrocytes.[32,33] This then provokes various neuroinflammation pathology which causes problems in the nervous system such as issues with neurogenesis which can instigate one to have depression.[34] Since both these processes can come about through a similar mechanism, one can postulate that either one can cause the other to amplify due to a possible synergistic effect. Other ways that chronic pain disorders and depression can be linked is through similarities in alterations in monoamine neurotransmitters such as serotonin, dopamine, and norepinephrine, and alterations from the normal in glutamate and its receptor subtypes.[28] These biologic mechanisms can contribute to one having either condition brought about if they have the other or exacerbated based on the changes in pathophysiology. Therefore, a patient's past medical history can help understand the full picture and assess if they have other factors such as depression, in addition to a chronic pain disorder. This can help effective management by prioritizing to treat both conditions than just one for a better outcome for the patient. Additionally, this may help management strategies as one can use medications that can target both depression and chronic pain disorders such as tricyclic antidepressants (TCA), monoamine oxidase inhibitors (MAOi), and opioids to name a few that have been shown in scientific literature to help both conditions.[28] Understanding the biopsychosocial model may also enhance the understanding of the association of chronic pain with depression. The biopsychosocial model of pain emphasizes chronic pain as a dynamic integration of physiological, psychological, and social factors in a multidirectional manner acting as risk or resilience factors, influencing the probability of developing a chronic pain disorder.[35]

In this study, we found a significant association of anxiety with chronic pain disorders (OR = 1.556, 95% CI 1.177-2.057; $P = .002$) which aligns with some of the literature. In a cross sectional epidemiologic study that analyzed the association of chronic pain disorders and depression in the United States also investigated the association of chronic pain disorders and anxiety. The study reported a significantly high association and found that those who had anxiety were 2.3 times likely to have a chronic pain disorder (OR = 2.3, 95% CI 1.22-4.64).[26] A systematic review and meta-analysis studied if there was an association between chronic nonspecific neck-arm pain (NSNAP) in adults and anxiety, and found a strong association.[36]A possible reason of the association suggests that chronic pain disorder can cause anxiety due to an alteration in the reward and anti-reward system.[37] On the contrary, there are some studies that have found limited or no evidence for an association of anxiety and chronic pain disorders. For example, a systematic review and meta-analysis explored if there was an association of anxiety and chronic non-specific low back pain in those who were aged 60 years or older, and found there to be limited evidence of an association.[38] Researchers have questioned the influence of anxiety related to chronic pain

in certain areas on the body. One such study found a correlation with anxiety and chronic pain disorders; however, it was not enough to be significant.[39] Further studies to find what caused the differences in findings of the association can help management such as areas of the chronic pain disorder. Certain chronic pain disorders have been found to be associated with anxiety and knowledge of this can help management if the patient has such a disorder. For example, a significant association of anxiety and burning mouth syndrome, a chronic pain disorder, has been established in multiple studies.[40,41] Burning mouth syndrome is often misdiagnosed and the knowledge that a patient has anxiety and has issues in the mouth such as xerostomia can lead a provider to put burning mouth syndrome higher on the differential which can lead to better control of this syndrome.[42] Additional management strategies include neuroscience education which has been demonstrated to help those with both anxiety and chronic pain disorders.[43]

The patients with chronic pain disorders in our study had higher association with COPD. This association has been increasingly recognized; however, and there is a lack of consensus in such association across multiple studies. A systematic review and meta-analysis found pain conditions to be more prevalent in those with COPD but were likely due to other confounding factors such as comorbidity and nutritional status. The study did not show a significant relationship between lung function and prevalence of pain.[44] Another systematic review found that pain was a clinical complication of COPD in the form that subjects with COPD who had higher pain intensity were related to worse symptoms of COPD, such as dyspnea and fatigue.[45] An additional systematic review investigated those with COPD to see if patients with COPD were at risk for musculoskeletal (MSK) pain conditions. The study reported that many common chronic MSK conditions, such as lumbar pain, cervical pain, and chest pain were highly reported in those who had COPD.[46] This systematic review also discussed the lack of clinical trials studying the relationship of chronic pain disorders and COPD, and illustrated the potential association between COPD and chronic pain conditions.[46] More studies are needed to see if it is due to potential confounders. We found a significant association which can serve as a foundation to build upon for additional studies. This will help patient care by helping providers with appropriate management approaches. Patients with COPD and problems with pain tend to have worse clinical consequences.[45] Therefore, the knowledge of such association with chronic pain condition and COPD may allow clinicians ensure optimal management of each condition for better patient outcome.

There was higher association of patients with OSA and chronic pain disorders. Similar findings were observed in a meta-analysis in which the investigators reported that in patients with chronic pain disorders, 44% had a sleep disorder with OSA being one of the most common.[47] Another meta-analysis showed a small association between those with OSA and chronic pain.[47] On the other hand, a study that looked to see if there was an association between OSA and chronic facial pain found the role of OSA in developing chronic facial pain inconclusive.[48,49] More research is needed to confirm the unidirectional or bidirectional relationship of one of these disorders causing the other as this can help plan optimal management of pain. Another study reported a high comorbidity between chronic head and neck pain and OSA.[50] In one study, it has been reported that in those with chronic headaches and OSA, there were improved pain due to headaches with proper use of the positive airway pressure in addition to helping with pain tolerance.[51] Additionally, clinicians can help manage sleep issues that could worsen OSA symptoms through adequate collaboration between various healthcare subspecialties; and by doing this, the exact sleep breathing issue origin can be determined to subsequently help optimize management.[50] Additionally, whether specific chronic pain conditions, such as chronic headaches, or all chronic pain conditions have an association with OSA needs to be determined.

We found there to be a significant association of GERD with chronic pain disorders. The scientific literature exploring the association between these conditions is limited. However, there are some studies that have studied the specific chronic pain disorders and their association with GERD. In a case control study conducted in China, GERD was found to be associated with temporomandibular pain disorders (OR = 2.74, 95% CI 1.88-3.98).[52] A potential mechanisms for this association includes a hypothesis that increased acid in esophagus from GERD leads to an alteration in CNS perception of pain. This then causes there to be changes in pain pathways which in turn result in decreased pain thresholds in various other parts of the body.[52] However, no study has confirmed this, and studies are needed to build upon our finding of the association of GERD with chronic pain disorders.

A significant association for patients with osteoarthritis (OA) having chronic pain disorders was found in our study. This aligns with the scientific literature and the main reason for this is that chronic pain disorders are a widely known complication of osteoarthritis. According to the American Pharmacists Association foundation of those with chronic pain disorders, 27% stem from complications and progression of osteoarthritis.[53] In those with osteoarthritis, there is a low level of inflammation in the joint. Over a prolonged period, this causes significant damage to the joint. The damage and increased inflammatory mediators lead to chronic pain disorders. In addition to the damage causing pain, mechanical sensitization which can alter sensitivity of joint nociceptors through the increase of inflammatory mediators is what leads to progression of this chronic pain condition.[54]

Management options most commonly include pharmacologic interventions. Other options include physical therapy, cognitive behavioral therapy, mindfulness techniques, and invasive procedures to target the pain receptors which may be used alone or in combination with other therapies.[55] Even with all these options, management for those who have osteoarthritis and chronic pain is complex. Pharmacological interventions are unsuccessful in many instances especially after progression of disease.[54] Investigations into alternative pathways, such as calcitonin gene-related peptide (CGRP), NOD-like receptor family (NLR), and Wnt/B-catenin signaling pathway, etc. may prove to be valuable in the genesis of chronic pain associated with OA.[56]

We found a significant association of other rheumatologic diseases with chronic pain disorders which aligns with previous research.[57] Rheumatologic disease encompasses many pathologic processes, and some are considered as a chronic pain disorder such as fibromyalgia which progresses over time to change from an acute pain management approach to that of chronic pain management.[57] Systemic lupus erythematosus (SLE) can also be considered a chronic pain disorder once progressed. Of the many presenting symptoms of SLE, pain is a common first complaint. During the initial stages of the disease the pain can come and go away when the SLE flare recedes. However, if uncontrolled and advanced, the pain can be present for a long period of time and can then be considered a chronic pain disorder.[58] Understanding the pathophysiology and how certain rheumatologic diseases can progress to chronic pain is essential in targeting therapies to modify disease activity in order to optimize control of chronic pain.

In our study we found a significantly increased association between peripheral neuropathy and chronic pain disorders. Peripheral neuropathy encompasses a wide range of symptoms due to the multitude of function of motor and sensory nerves. Additionally, there are multiple causes of peripheral neuropathy such as diabetic neuropathy, carpal tunnel syndrome, and complex regional pain syndrome to name a few.[59] These conditions can affect the sensory nerves which can lead to neuropathic pain. Due to the definition of chronic pain disorder and the pathogenesis of peripheral neuropathy, our findings can explain why our results exhibited a significant association which aligns with the existing scientific literature. Recent updates in the Internal Classification of Diseases (ICD) classification of chronic neuropathic pain, considers these disorders as chronic pain disorder which is a new change from the previous ICD classification.[60] The knowledge of this updated classification opens avenues in planning for effective management strategies for patients with this condition.

There were some limitations to our study. Retrospective data collection limited our ability to rely solely on the available data entry as entered by the office staff and the physicians, therefore variables, such as socioeconomic status and other social determinants of health, could not be reliably ascertained, which could have influenced the management of underlying comorbidities and symptoms of chronic pain. We also acknowledge that our suburban office setting limits the patient population predominantly to a specific type based on their race distribution, which limits the generalizability. Other factors, such the availability and interpretability of clinical and non-clinical data on socioeconomic inequities and other social determinants of health might have been insufficiently documented in the electronic medical records. The major strength of our study was the entire population of patients who were followed by and received care from their specific physicians in the single office based medical practice for many years. The degree of symptoms, additional medical disorders, and management were meticulously documented by the caring team.

Conclusion

In conclusion, we found that female sex, depression, anxiety, chronic obstructive pulmonary disease, obstructive sleep apnea, gastroesophageal reflux disease, osteoarthritis, other rheumatologic diseases and peripheral neuropathy were significantly associated with chronic pain disorder in the elderly population, while BMI was not associated with chronic pain disorder. Additional studies may build upon our findings and identify similar or additional factors associated with chronic pain in the elderly patients.

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Author Contributions

NM and SR made substantial contributions to the study design, drafting, data acquisition and analysis, and manuscript writing. All authors contributed in data collection and manuscript writing and review. KH analyzed the data. SR contributed in revising the manuscript critically for improved intellectual content, and final approval for the version to be published.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Declaration of Conflicting Interests

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ORCID iDs

Roshni Gandhi https://orcid.org/0000-0002-0517-7118
Ian Millstein https://orcid.org/0000-0002-8253-7412
Krystal Hunter https://orcid.org/0000-0002-8991-2625
Satyajeet Roy https://orcid.org/0000-0002-1536-3678

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