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ORIGINAL RESEARCH

Analyzing Pain Patterns in Stroke Survivors in Outpatient Clinics: A Retrospective, Cross-Sectional, Observational Study

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Background: Pain is one of the most common sequelae after a stroke. Yet it is under-recognized, under-treated, and under-investigated, with no standard care guidelines for management during post-stroke recovery.

Purpose: The primary objective of this study was to capture the prevalence of pain and different pain types in stroke survivors.

Patients and Methods: The study included stroke survivors who completed a pre-visit telehealth review of systems instrument between March 1, 2020, and February 28, 2022. 442 out-patient subjects were identified and matched to their respective electronic health record from the incident stroke. Subjects were divided into pain and no-pain groups based on self-report of post-stroke pain. Bivariate analyses were performed to test the association between the patient's demographic and clinical characteristics and pain using *t*-tests or Wilcoxon rank sum tests for continuous variables and chi-square tests for categorical variables. Random forest imputation was used to address missing values. Multivariable analysis was performed using the logistic regression method.

Results: Of the 442 subjects, 58% (N=258) reported pain, with 56% experiencing multiple pain types. Musculoskeletal pain (36%), Neuropathic pain (22%), and Headaches (17%) were the most common pain types. Only 20% of patients reporting pain used analgesics, with gabapentin (43%) and opioids (11%) being the most common prescriptions. Obstructive sleep apnea (OSA), history of recreational drug use, and gender showed a significant relationship with pain in univariate analysis. In the final logistic regression model, OSA (OR: 3.37, 95% CI: 1.34–9.80, p: 0.015) and history of recreational drug use (OR: 2.05, 95% CI: 1.16–3.83, p: 0.018) remained significant. The model achieved moderate discrimination with an AUC of 0.62.

Conclusion: Over half of stroke survivors experienced pain, with 30% reporting multiple pain types. The low rate of analgesic use (20%) and significant proportion of patients experiencing pain highlight the critical need for evidence-based pain management guidelines in post-stroke care.

Keywords: stroke, post-stroke pain, neuropathic pain, musculoskeletal pain

Introduction

Each year worldwide, 12-plus million people experience an incident stroke.[1] Greater than 50% of the survivors will experience stroke-related pain sometime over their post-stroke lifetime, with those at greater risk being older, having more disability, and experiencing ischemic stroke.[2–4] Often overlooked and under- or untreated, there are no accepted standards of care regarding post-stroke pain assessment and management to guide providers.[2,5,6] Furthermore, pain reporting by stroke survivors often does not occur unless prompted by targeted clinician assessment and questioning.[5,6]

Pain after stroke, including chronic headache, shoulder pain, and central post-stroke pain syndrome, is a common complication but not well-understood.[3–6] The true prevalence of post-stroke pain (PSP) remains unknown, with reports including a wide range of 14–70%, likely a function of the variability in types of stroke and resultant disability.[2,7]

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Mechanisms of pain after stroke are also equally uncertain, with evidence pointing to three physiologic sources either acting separately or in combination:[3,6] musculoskeletal lesions, impaired motor control (muscle tone changes, ie, spasticity, contracture), and altered peripheral and central nervous system activity (central sensitization and central neuronal hyperexcitability).[2,4–6,8]

The lack of high-level evidence from controlled clinical trials creates challenges in PSP treatment, particularly for pain conditions other than central post-stroke pain (such as spasticity and contracture-related pain, hemiplegic shoulder pain, joint pain), which are the most common presenting pain types.[7] Currently, available PSP treatment guidelines solely address central post-stroke pain,[9–11] with recommendations of gabapentin, pregabalin, duloxetine, or amitriptyline, potentially switching agents in the absence of relief. This all occurs in the absence of high-quality evidence and adequately powered randomized trials.[9] Evidence for non-pharmacological treatment is similarly problematic.[12] This evidence vacuum results in under- or untreated pain, compounded by intolerable drug side effects.

Examining both self-report records from stroke survivor telehealth visits and their respective Electronic Health Records (EHR) from the start of the COVID-19 pandemic through the ensuing two years, this retrospective, cross-sectional study investigates pain reporting in a cohort of stroke survivors. Our primary objective in this investigation was to estimate the prevalence of pain and types of pain in stroke survivors and, secondarily, to explore any relationships between reports of pain, type of stroke, and comorbidities and to examine the pain-related medication history of those reporting pain.

Methods

We examined telehealth pre-visit health status questionnaire responses from March 1, 2020, to February 28, 2022, of adult stroke survivors aged 18 and older. The questionnaire included a self-report health status overview with an item related to pain for each body system. The questions pertaining to pain presence by system (ie, eye pain, abdominal pain, extremity pain) were completed by the subject and/or caregiver, with no clinician input. For those patients with communication and/or disability hindrances, surveys were completed by a family member or caregiver. Questionnaire items included one asking if pain is present, and the location and description of the pain. Subjects used descriptive terms such as burning, tingling, aching, joint pain, and muscle pain, from which the types of pain were coded. The records from 1602 outpatient visits were examined, and 732 were manually matched to the EHR from the individual's incident stroke hospitalization from the large, urban, university-based healthcare system at which they were treated for the stroke. From these 732 remaining records, those with stroke mimic, subdural hematoma, or other non-stroke neurologic conditions were excluded, leaving 442 in our sample (Figure 1). The variables captured in our dataset include general reporting of pain, location of pain, all classes of reported prescribed medications, sociodemographic variables including age, gender, race, ethnicity, education, marital status, and employment, comorbidities, such as diabetes, hypertension, high cholesterol, heart disease and heart failure, kidney disease, obstructive sleep apnea (OSA), cancer, previous stroke/transient ischemic attack (TIA), body mass index (BMI), tobacco use, alcohol intake and recreational drug use, stroke type, time since stroke, NIH stroke scale (NIHSS), and hospital length of stay.

Statistical Analyses

Descriptive Statistics

We analyzed the demographic and clinical characteristics of this cohort of stroke survivors. The patient population was divided into two groups: those who reported pain post-stroke and those who did not report pain. Further, bivariate relationships between each characteristic and the outcome were examined using the *t*-test for normal continuous variables, the Wilcoxon rank sum test for non-normal continuous variables, and the chi-square test or Fisher's exact test for categorical variables as appropriate. Similar bivariate analyses were performed for the following subtypes of pain: musculoskeletal, neuropathic, and headache. Simple statistics on pain medication were also completed.

Identifying Potential Predictors

Initially, predictors with extreme missingness (>90%) were excluded. This excluded predictors "Anxiety/Depression/Mental Health", "Cancer", and "Other Cardiovascular History". Among these remaining predictors, "Ethnicity" (10.2%),

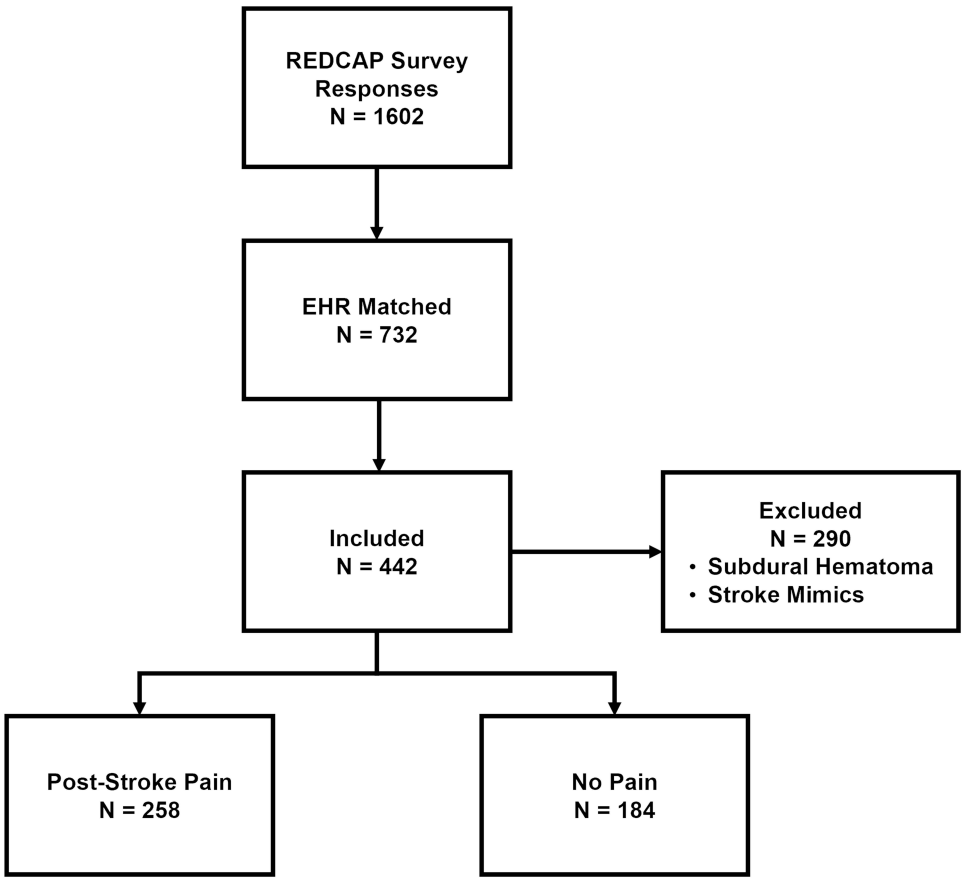

Figure 1 Study Population Selection.

"Hospital Length of Stay" (17.1%), and Stroke Type (22.6%) had the highest missing values. The rest of the variables, on average, had minimal missingness (~1.5%). No missing data were observed in the pain outcome variables. For the missing data in predictors, missing at random (MAR) mechanism was assumed, meaning that the patterns of missingness can be appropriately modeled using information available in the observed data. To address this, a nonparametric Random forest imputation method was employed to account for potentially complex interactions and nonlinear relationships among variables, offering a robust alternative to listwise deletion. This imputation procedure was conducted prior to elastic net regularization to reduce bias, preserve sample size, and enhance model stability.

The data was then split into a training (80%) and test (20%) dataset. Elastic Net regularization was used to select variables entering our final logistic regression model.[13] The elastic net model was tuned on the training set using 10-fold cross-validation (CV) and maximizing the area under the curve (AUC). Optimal values for the alpha and lambda parameters, which govern the penalty function structure and the degree of shrinkage, were searched along a range from 0 to 1. Once tuned, the model with the optimal parameters was refitted to the entire training dataset, and variables with non-zero coefficients were retained. The performance of our final logistic model with the selected variables was evaluated using our test dataset. After selecting predictors using Elastic Net regularization and refitting the final logistic regression model, we assessed multicollinearity using Variance Inflation Factors (VIF). This was done to ensure that retained predictors were not highly correlated and would not lead to unstable coefficient estimates.

Results

Patient Characteristics

The cohort included a total of 442 patients, of whom 258 (58%) reported pain. Of those reporting pain, the median age was 63 years (IQR: [52, 73]). Gender distribution showed a significant difference between those who reported pain and

those who did not (p=0.028), with 57% of the patients reporting pain being female (n = 147). The distribution of marital status also differed significantly between the groups (p=0.027), with 47.9% (n = 123) of those reporting pain being married. Additionally, obstructive sleep apnea (OSA) was significantly more prevalent among patients who reported pain compared to those who did not (12% vs 6%, p=0.029). Lastly, a greater proportion of patients reporting pain had also received pain medications compared to those who did not report pain (20% vs 12%, p=0.035) (Table 1).

Table 1 Descriptive Statistics Stratified by Patients Who Reported Pain Outcome

	No Pain Reported N = 184	**Pain Reported N = 258**	**P-value**
Gender (%) b			**0.028**
Women	84 (45.9)	147 (57.0)	
Men	99 (54.1)	111 (43.0)	
Age (median [IQR]) a	62.00 [50.50, 72.00]	63.00 [52.00, 73.00]	0.381
BMI (median [IQR]) a	28.60 [25.00, 32.80]	28.70 [25.60, 33.78]	0.380
Race (%) c			0.700
American Indian/Alaskan Native	3 (1.7)	2 (0.8)	
Asian	12 (6.8)	14 (5.4)	
Black/African American	56 (31.8)	85 (33.1)	
Other	10 (5.7)	11 (4.3)	
Unknown	0 (0.0)	2 (0.8)	
White/Caucasian	95 (54.0)	143 (55.6)	
Ethnicity (%) b			0.808
Hispanic	32 (18.7)	39 (17.3)	
Non-Hispanic	139 (81.3)	187 (82.7)	
Hypertension (%) b	145 (78.8)	219 (84.9)	0.127
Diabetes (%) b	56 (30.4)	84 (32.6)	0.712
High Cholesterol (%) b	103 (56.0)	167 (64.7)	0.078
Transient Ischemic Attack (TIA) (%) b	32 (17.4)	57 (22.1)	0.274
Atrial Fibrillation (%) b	21 (11.4)	40 (15.5)	0.276
Obstructive Sleep Apnea (%) b	10 (5.4)	31 (12.0)	**0.029**
Heart Attack (%) b	17 (9.2)	37 (14.3)	0.142
Heart Failure (%) b	8 (4.3)	25 (9.7)	0.055
Kidney Disease (%) b	12 (6.5)	17 (6.6)	1
Cancer (%) b	1 (33.3)	0 (0.0)	0.506
Previous Stroke (%) b	68 (37.0)	105 (40.7)	0.487
Anxiety/Depression/mental health (%) c	2 (100.0)	4 (100.0)	>0.999
NIHSS stroke score (median [IQR]) a	4.00 [1.00, 10.00]	3.00 [1.00, 7.00]	0.327

(*Continued*)

Table 1 (Continued).

	No Pain Reported N = 184	Pain Reported N = 258	P-value
Stroke Type (%) b			0.625
Hemorrhagic	41 (28.1)	61 (31.1)	
Ischemic	105 (71.9)	135 (68.9)	
Hospital length of stay (days) (median [IQR]) a	4.00 [2.75, 9.00]	4.00 [3.00, 7.00]	0.52
Marital Status (%) c			**0.03**
Divorced	16 (8.9)	37 (14.4)	
Married	111 (61.7)	123 (47.9)	
Other	2 (1.1)	0 (0.0)	
Separated	2 (1.1)	7 (2.7)	
Single	27 (15.0)	50 (19.5)	
Widowed	22 (12.2)	40 (15.6)	
Employment (%) b			0.25
Disability (prior to stroke)	13 (7.3)	26 (10.2)	
Employed	65 (36.3)	73 (28.5)	
Other	5 (2.8)	15 (5.9)	
Retired	69 (38.5)	98 (38.3)	
Unemployed	27 (15.1)	44 (17.2)	
Education (%) b			0.68
Associate's Degree (2-year College)	13 (7.3)	24 (9.5)	
Bachelor's Degree (4-year College)	33 (18.4)	33 (13.0)	
Did not complete High School	20 (11.2)	33 (13.0)	
Doctorate or Equivalent (MD, PhD, etc)	7 (3.9)	8 (3.2)	
High School Diploma/GED	51 (28.5)	73 (28.9)	
Master's Degree	12 (6.7)	17 (6.7)	
Current/Past History of Tobacco (%) c			0.17
Current Use	18 (10.0)	40 (15.6)	
No History of Tobacco Use	91 (50.6)	130 (50.8)	
Past Use	71 (39.4)	86 (33.6)	
History of Alcohol Use (%) b	54 (30.2)	67 (26.1)	0.41
History of Recreational Drug Use b			0.28
Marijuana	153 (87.9)	212 (83.8)	
Cocaine	18 (10.3)	30 (11.9)	
Methamphetamines	3 (1.7)	11 (4.3)	

(*Continued*)

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Table 1 (Continued).

	No Pain Reported N = 184	Pain Reported N = 258	P-value
Reported Received Pain Medication(s) = 1 (%) b	22 (12.0)	51 (20.0)	**0.04**
Time from stroke (%) b			0.69
<1 month	67 (40.1)	112 (45.7)	
1-3 months	79 (47.3)	102 (41.6)	
3-6 months	9 (5.4)	14 (5.7)	
6+ months	12 (7.2)	17 (6.9)	

Notes: [a]Wilcoxon rank sum test for non-normal continuous variables. [b]Chi-square test of independence. [c]Fisher's exact test. Bolded p-values indicate statistical significance at $p < 0.05$.

Elastic Net Optimization & Final Logistic Regression Model

The optimal parameters that maximized the cross-validation (CV) AUC at 0.59 were determined to be 0.44 for alpha and 0.013 for lambda. The variables that survived to be included in the final logistic regression model were age, gender, race, education, BMI, hypertension, high cholesterol, atrial fibrillation, OSA, heart attack, heart failure, kidney disease, previous TIA, tobacco use, alcohol intake, recreational drug use, stroke type, NIHSS, time since stroke, and whether pain medication was prescribed. All variance inflation factors were below the conservative threshold of 5, indicating the absence of multicollinearity among the selected variables. The final logistic regression showed a significant relationship between OSA and pain reporting. The odds of reporting pain in those with OSA are 3.37 times the odds of reporting pain in those without (OR = 3.37, 95% CI: 1.34, 9.80, p = 0.015) (Table 2). This significance was also seen in the univariate analysis, where 12% of patients with pain had OSA compared to 6% of those without pain (p = 0.029, Table 1). Similarly, a history of recreational drug use was significantly associated with PSP. Those who have a history of recreational drug use have 2.05 times the odds of reporting pain than those who do not have such a history (OR =

Table 2 Logistic Regression for the Overall Cohort

Characteristic	OR a	95% CI b	p-value
Gender	0.66	0.41, 1.05	0.079
Age	1.01	0.99, 1.03	0.4
BMI	1.00	0.97, 1.04	0.8
Race	1.05	0.85, 1.31	0.6
Hypertension	1.08	0.56, 2.10	0.8
High Cholesterol	1.34	0.82, 2.20	0.2
TIA	1.24	0.68, 2.28	0.5
Atrial Fibrillation	1.09	0.53, 2.25	0.8
Obstructive Sleep Apnea	3.37	1.34, 9.80	**0.015**
Heart Attack	1.35	0.65, 2.89	0.4
Heart Failure	2.55	0.95, 7.74	0.076
Kidney Disease	0.72	0.28, 1.92	0.5
NIHSS Stroke Score	0.97	0.94, 1.01	0.13

(*Continued*)

Table 2 (Continued).

Characteristic	OR a	95% CI b	p-value
Stroke Type	0.69	0.38, 1.23	0.2
Education	1.07	0.95, 1.20	0.3
Current/Past History of Tobacco	0.89	0.61, 1.27	0.5
History of Alcohol Use	0.91	0.54, 1.54	0.7
History of Recreational Drug Use	2.05	1.16, 3.83	**0.018**
Reported Received Pain Medication(s)	1.49	0.78, 2.92	0.2
Time From Stroke	0.89	0.66, 1.20	0.4

Notes: [a]OR = Odds Ratio. [b]CI = Confidence Interval. Bolded p-values indicate statistical significance at $p < 0.05$.

2.05, 95% CI: 1.16, 3.83, p = 0.018). Although gender was found to be significant in the univariate analysis, it was not found significant in the multivariable logistic regression analysis (OR = 0.66, 95% CI: [0.41, 1.05], p = 0.079) (Table 2). This odds ratio (0.66) suggests that males had approximately 34% lower odds of reporting pain compared to females. However, because the confidence intervals [0.41, 1.05] include 1.0 and the p-value (0.079) was not significant, we cannot conclude that there is a meaningful difference in pain reporting between genders in this cohort after adjusting for other factors. The model's AUC was 0.62, indicating moderate discrimination between those who report pain and those who do not.

Subtypes of PSP

The most reported pain types were musculoskeletal pain (n = 191, 36%), neuropathic pain (n = 118, 22%), and headaches (n = 92, 17%) (Figure 2). Each subtype demonstrated distinct demographic and clinical patterns.

Musculoskeletal pain reporting was significantly associated with age (p=0.009). Median age of those experiencing musculoskeletal pain was 66 years (IQR: [56, 73]) and 61 years (IQR: [49, 72]) for those without. Additionally, patients

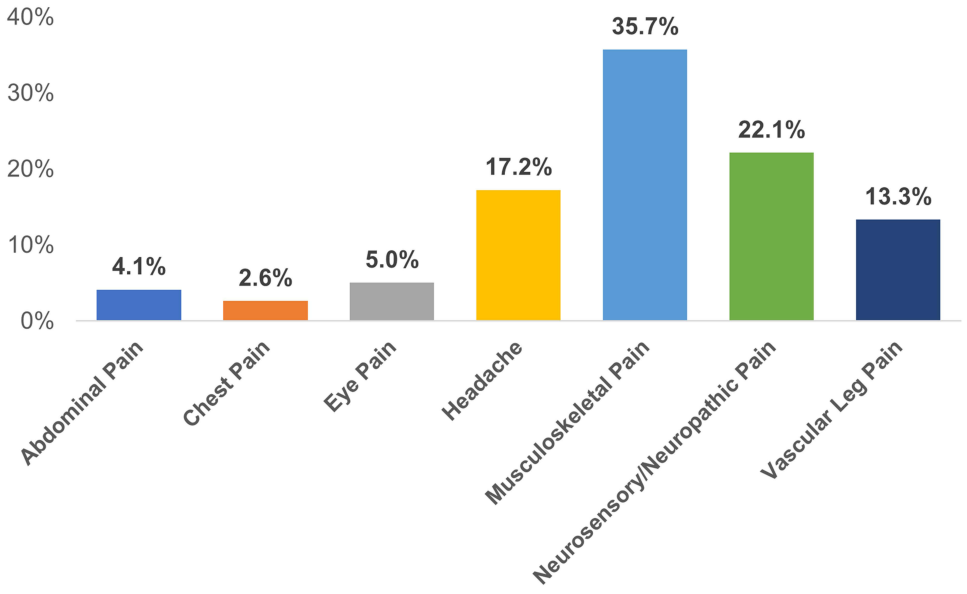

Figure 2 Overall Frequency of Each Pain Type.

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with musculoskeletal pain had a significantly higher prevalence of hypertension (88% vs 78.1%, p = 0.01) and OSA (13.1% vs 6.4%, p = 0.025) compared to those without this pain type. These two groups also differed significantly in tobacco use (p = 0.041) and employment status (p = 0.019). 18% of those who report musculoskeletal pain currently use tobacco, while only 9.7% of those not reporting musculoskeletal pain use tobacco (Table 3).

Neuropathic pain was the second most common type of pain reported, accounting for 22% of all pain types. Patients reporting neuropathic pain were significantly younger (59 years, IQR: 49–70) compared to those who did not report this pain (64 years, IQR: 53–74) (p = 0.005). There was a higher prevalence of OSA in patients with neuropathic pain (16.1% vs 6.8%, p=0.005). Significant differences were also observed between the groups with respect to tobacco use (p = 0.024) and employment status (p = 0.001). History of tobacco use was significantly associated with neuropathic pain, with

Table 3 Descriptive Statistics Stratified by Patients Who Report Musculoskeletal Pain

	No Pain Reported N = 251	**Pain Reported N = 191**	**P-value**
Gender = Male (%) b	128 (51.2)	82 (42.9)	0.104
Age (median [IQR]) a	61.00 [49.00, 72.00]	66.00 [56.00, 73.00]	**0.009**
BMI (median [IQR]) a	28.75 [25.22, 33.15]	28.55 [25.25, 33.52]	0.711
Race (%) b			0.307
American Indian/Alaskan Native	4 (1.6)	1 (0.5)	
Asian	18 (7.4)	8 (4.3)	
Black/African American	72 (29.6)	69 (36.7)	
Other	13 (5.3)	8 (4.3)	
White/Caucasian	136 (56.0)	102 (54.3)	
Ethnicity = Non-Hispanic (%) b	189 (81.1)	137 (83.5)	0.626
Hypertension (%) b	196 (78.1)	168 (88.0)	**0.01**
Diabetes (%) b	74 (29.5)	66 (34.6)	0.302
High Cholesterol (%) b	143 (57.0)	127 (66.5)	0.053
TIA (%) b	42 (16.7)	47 (24.6)	0.054
Atrial Fibrillation (%) b	28 (11.2)	33 (17.3)	0.087
Obstructive Sleep Apnea (%) b	16 (6.4)	25 (13.1)	**0.025**
Heart Attack (%) b	26 (10.4)	28 (14.7)	0.222
Heart Failure (%) b	13 (5.2)	20 (10.5)	0.056
Kidney Disease (%) b	15 (6.0)	14 (7.3)	0.707
Cancer (%) c	1 (20.0)	0 (0.0)	0.805
Previous Stroke (%) b	93 (37.1)	80 (41.9)	0.351
Anxiety/Depression/mental health (%) c	2 (100.0)	4 (100.0)	>0.999
NIHSS stroke score (median [IQR]) a	3.00 [1.00, 9.00]	3.00 [1.00, 7.00]	0.729
Stroke Type = Ischemic (%) b	138 (69.3)	102 (71.3)	0.783
Hospital Length of Stay (Days) (median [IQR]) a	4.00 [3.00, 8.75]	4.00 [3.00, 7.00]	0.451

(*Continued*)

Table 3 (Continued).

	No Pain Reported N = 251	Pain Reported N = 191	P-value
Marital Status (%) c			0.06
Divorced	24 (9.7)	29 (15.3)	
Married	146 (59.1)	88 (46.3)	
Other	2 (0.8)	0 (0.0)	
Separated	4 (1.6)	5 (2.6)	
Single	42 (17.0)	35 (18.4)	
Widowed	29 (11.7)	33 (17.4)	
Employment (%) b			**0.019**
Disability (prior to stroke)	15 (6.1)	24 (12.6)	
Employed	86 (35.1)	52 (27.4)	
Other	9 (3.7)	11 (5.8)	
Retired	88 (35.9)	79 (41.6)	
Unemployed	47 (19.2)	24 (12.6)	
Education (%) b			0.511
Associate's Degree (2-year College)	20 (8.3)	17 (9.5)	
Bachelor's Degree (4-year College)	44 (18.3)	22 (12.3)	
Did not complete High School	29 (12.1)	24 (13.4)	
Doctorate or Equivalent (MD, PhD, etc)	10 (4.2)	5 (2.8)	
High School Diploma/GED	71 (29.6)	53 (29.6)	
Master's Degree	18 (7.5)	11 (6.1)	
Some College	48 (20.0)	47 (26.3)	
Current/Past History of Tobacco (%) b			**0.041**
Current Use	24 (9.7)	34 (18.0)	
No History of Tobacco Use	131 (53.0)	90 (47.6)	
Past Use	92 (37.2)	65 (34.4)	
History of Alcohol Use = Yes (%) b	72 (29.4)	49 (25.7)	0.45
History of Recreational Drug Use (%) b			0.749
Marijuana	207 (86.6)	158 (84.0)	
Cocaine	25 (10.5)	23 (12.2)	
Methamphetamines	7 (2.9)	7 (3.7)	
Reported Received Pain Medication(s) (%) b	34 (13.5)	39 (20.7)	0.061

(*Continued*)

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Table 3 (Continued).

	No Pain Reported N = 251	Pain Reported N = 191	P-value
Time from stroke (%) b			0.671
<1 month	95 (41.3)	84 (46.2)	
1-3 months	107 (46.5)	74 (40.7)	
3-6 months	13 (5.7)	10 (5.5)	
6+ months	15 (6.5)	14 (7.7)	

Notes: [a]Wilcoxon rank sum test for non-normal continuous variables. [b]Chi-square test of independence. [c]Fisher's exact test. Bolded p-values indicate statistical significance at $p < 0.05$.

Table 4 Descriptive Statistics Stratified by Patients Who Reported Neuropathic Pain

	No Pain Reported N = 324	Pain Reported N = 118	P-value
Gender = Male (%) b	163 (50.5)	47 (39.8)	0.061
Age (median [IQR]) a	64.00 [53.00, 74.00]	59.00 [49.00, 70.00]	**0.005**
BMI (median [IQR]) a	28.30 [25.00, 33.00]	29.10 [25.70, 34.30]	0.187
Race (%) c			0.844
American Indian/Alaskan Native	4 (1.3)	1 (0.8)	
Asian	21 (6.7)	5 (4.2)	
Black/African American	102 (32.6)	39 (33.1)	
Other	14 (4.5)	7 (5.9)	
White/Caucasian	172 (55.0)	66 (55.9)	
Ethnicity = Non-Hispanic (%) b	241 (82.0)	85 (82.5)	>0.999
Hypertension (%) b	268 (82.7)	96 (81.4)	0.849
Diabetes (%) b	97 (29.9)	43 (36.4)	0.236
High Cholesterol (%) b	200 (61.7)	70 (59.3)	0.727
TIA (%) b	58 (17.9)	31 (26.3)	0.071
Atrial Fibrillation (%) b	48 (14.8)	13 (11.0)	0.385
Obstructive Sleep Apnea (%) b	22 (6.8)	19 (16.1)	**0.005**
Heart Attack (%) b	41 (12.7)	13 (11.0)	0.764
Heart Failure (%) c	29 (9.0)	4 (3.4)	0.078
Kidney Disease (%) b	22 (6.8)	7 (5.9)	0.916
Cancer (%) c	1 (12.5)	0 (0.0)	>0.999
Previous Stroke (%) b	131 (40.4)	42 (35.6)	0.417
Anxiety/Depression/mental health (%) c	4 (100.0)	2 (100.0)	>0.999
NIHSS stroke score (median [IQR]) a	3.00 [1.00, 9.00]	3.00 [1.00, 6.00]	0.227

(*Continued*)

Table 4 (Continued).

	No Pain Reported N = 324	Pain Reported N = 118	P-value
Stroke Type = Ischemic (%) b	173 (69.2)	67 (72.8)	0.605
Hospital Length of Stay (Days) (median [IQR]) a	4.00 [3.00, 8.00]	4.00 [2.00, 7.00]	0.506
Marital Status (%) c			0.629
Divorced	37 (11.6)	16 (13.6)	
Married	172 (53.9)	62 (52.5)	
Other	2 (0.6)	0 (0.0)	
Separated	7 (2.2)	2 (1.7)	
Single	52 (16.3)	25 (21.2)	
Widowed	49 (15.4)	13 (11.0)	
Employment (%) b			**0.001**
Disability (prior to stroke)	26 (8.2)	13 (11.0)	
Employed	101 (31.9)	37 (31.4)	
Other	14 (4.4)	6 (5.1)	
Retired	137 (43.2)	30 (25.4)	
Unemployed	39 (12.3)	32 (27.1)	
Education (%) c			0.114
Associate's Degree (2-year College)	26 (8.5)	11 (9.7)	
Bachelor's Degree (4-year College)	48 (15.7)	18 (15.9)	
Did not complete High School	35 (11.4)	18 (15.9)	
Doctorate or Equivalent (MD, PhD, etc)	13 (4.2)	2 (1.8)	
High School Diploma/GED	101 (33.0)	23 (20.4)	
Master's Degree	21 (6.9)	8 (7.1)	
Some College	62 (20.3)	33 (29.2)	
Current/Past History of Tobacco (%) b			**0.024**
Current Use	34 (10.7)	24 (20.3)	
No History of Tobacco Use	163 (51.3)	58 (49.2)	
Past Use	121 (38.1)	36 (30.5)	
History of Alcohol Use = Yes (%) b	86 (27.0)	35 (29.9)	0.624
History of Recreational Drug Use (%) b			0.765
Marijuana	267 (85.9)	98 (84.5)	
Cocaine	35 (11.3)	13 (11.2)	
Methamphetamines	9 (2.9)	5 (4.3)	

(*Continued*)

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Table 4 (Continued).

	No Pain Reported N = 324	Pain Reported N = 118	P-value
Reported Received Pain Medication(s) (%) b	48 (14.9)	25 (21.4)	0.144
Time from stroke (%) b			0.058
<1 month	127 (42.1)	52 (47.3)	
1-3 months	143 (47.4)	38 (34.5)	
3-6 months	15 (5.0)	8 (7.3)	
6+ months	17 (5.6)	12 (10.9)	

Notes: [a]Wilcoxon rank sum test for non-normal continuous variables. [b]Chi-square test of independence. [c]Fisher's exact test. Bolded p-values indicate statistical significance at $p < 0.05$.

a notably higher prevalence of current tobacco use (20.3%) among those reporting pain compared to those who did not (10.7%) (Table 4).

Headache accounted for 17% of all pain types reported. Gender distribution was significantly different in patients reporting headache compared to those who did not (p = 0.001). A majority of those experiencing headache were female (68.5%). The median age of patients reporting headache (Median = 58, IQR: [45, 69]) was also significantly lower than the median age of patients without headache (Median = 64, IQR: [54, 73]) (p = 0.001). Baseline NIHSS (p=0.042) and

Table 5 Descriptive Statistics Stratified by Patients Who Reported Headache Pain

	No Pain Reported N = 350	Pain Reported N = 92	P-value
Gender = Male (%) b	**181 (51.9)**	**29 (31.5)**	**0.001**
Age (median [IQR]) a	**64.00 [53.50, 73.00]**	**58.00 [44.75, 68.50]**	**0.001**
BMI (median [IQR]) a	28.45 [25.08, 33.00]	29.80 [25.83, 34.65]	0.118
Race (%) c			0.282
American Indian/Alaskan Native	4 (1.2)	1 (1.1)	
Asian	22 (6.5)	4 (4.4)	
Black/African American	106 (31.2)	35 (38.5)	
Other	20 (5.9)	1 (1.1)	
White/Caucasian	188 (55.3)	50 (54.9)	
Ethnicity = Non-Hispanic (%) b	258 (82.4)	68 (81.0)	0.878
Hypertension (%) b	290 (82.9)	74 (80.4)	0.698
Diabetes (%) b	112 (32.0)	28 (30.4)	0.872
High Cholesterol (%) b	**224 (64.0)**	**46 (50.0)**	**0.02**
TIA (%) b	72 (20.6)	17 (18.5)	0.765
Atrial Fibrillation (%) b	53 (15.1)	8 (8.7)	0.154
Obstructive Sleep Apnea (%) b	29 (8.3)	12 (13.0)	0.231
Heart Attack (%) b	46 (13.1)	8 (8.7)	0.327

(*Continued*)

Table 5 (Continued).

	No Pain Reported N = 350	Pain Reported N = 92	P-value
Heart Failure (%) c	29 (8.3)	4 (4.3)	0.291
Kidney Disease (%) b	24 (6.9)	5 (5.4)	0.8
Cancer (%) c	0 (0.0)	1 (16.7)	0.936
Previous Stroke (%) b	145 (41.4)	28 (30.4)	0.071
Anxiety/Depression/mental health (%) c	4 (100.0)	2 (100.0)	>0.999
NIHSS stroke score (median [IQR]) [a]	3.00 [1.00, 9.00]	2.00 [1.00, 5.00]	0.042
Stroke Type = Ischemic (%) b	191 (71.0)	49 (67.1)	0.618
Hospital Length of Stay (Days) (median [IQR]) a	4.00 [3.00, 8.00]	4.00 [2.00, 7.00]	0.304
Marital Status (%) c			0.373
Divorced	43 (12.5)	10 (10.9)	
Married	187 (54.2)	47 (51.1)	
Other	2 (0.6)	0 (0.0)	
Separated	8 (2.3)	1 (1.1)	
Single	54 (15.7)	23 (25.0)	
Widowed	51 (14.8)	11 (12.0)	
Employment (%) c			0.154
Disability (prior to stroke)	33 (9.5)	6 (6.7)	
Employed	105 (30.3)	33 (37.1)	
Other	16 (4.6)	4 (4.5)	
Retired	141 (40.8)	26 (29.2)	
Unemployed	51 (14.7)	20 (22.5)	
Education (%) c			0.312
Associate's Degree (2-year College)	25 (7.6)	12 (13.6)	
Bachelor's Degree (4-year College)	51 (15.4)	15 (17.0)	
Did not complete High School	40 (12.1)	13 (14.8)	
Doctorate or Equivalent (MD, PhD, etc)	12 (3.6)	3 (3.4)	
High School Diploma/GED	106 (32.0)	18 (20.5)	
Master's Degree	24 (7.3)	5 (5.7)	
Some College	73 (22.1)	22 (25.0)	
Current/Past History of Tobacco (%) b			0.115
Current Use	42 (12.2)	16 (17.6)	
No History of Tobacco Use	171 (49.6)	50 (54.9)	
Past Use	132 (38.3)	25 (27.5)	

(*Continued*)

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Table 5 (Continued).

	No Pain Reported N = 350	Pain Reported N = 92	P-value
History of Alcohol Use = Yes (%) b	100 (29.1)	21 (22.8)	0.291
History of Recreational Drug Use (%) b			0.393
Marijuana	290 (86.1)	75 (83.3)	
Cocaine	38 (11.3)	10 (11.1)	
Methamphetamines	9 (2.7)	5 (5.6)	
Reported Received Pain Medication(s) (%) b	56 (16.1)	17 (18.5)	0.705
Time from stroke (%) c			0.197
<1 month	135 (41.4)	44 (51.2)	
1-3 months	150 (46.0)	31 (36.0)	
3-6 months	20 (6.1)	3 (3.5)	
6+ months	21 (6.4)	8 (9.3)	

Notes: [a]Wilcoxon rank sum test for non-normal continuous variables. [b]Chi-square test of independence. [c]Fisher's exact test. Bolded p-values indicate statistical significance at $p < 0.05$.

the prevalence of cholesterol (p=0.02) also differed between groups. Patients without headache had higher median baseline NIHSS (3, IQR: [1, 9] vs 2, IQR: [1, 5]) and higher cholesterol prevalence (64% vs 50%) (Table 5).

Reported Pain Treatment

Among patients reporting post-stroke pain, only 20% (n = 51) disclosed pain medication (Table 1). Of those on analgesics, 71% (n=36) were prescribed a single medication. Gabapentin was the most common single analgesic prescribed (43%, n = 15), followed by opioids (11%, n = 4). Patients taking multiple analgesics (n = 15) were most likely to receive gabapentin with non-opioid medications (47%, n = 7), followed by opioids in combination with other analgesics (27%, n = 4) and opioids with gabapentin (20%, n = 3). There were no non-pharmacological pain management strategies reported in the patient medical records or self-reported outpatient history questionnaires from which the data for this study were collected.

Discussion

In the cohort of 442 stroke survivors, nearly 60% reported pain, and among them, 56% disclosed more than one type of pain. Though women comprised more of the group that reported pain in the descriptive analysis, when adjusting for other variables, the regression analysis suggested that there was no significant difference in pain reporting between men and women. The regression analysis also demonstrated that those with OSA and a history of recreational drug use were more than three times more likely to report pain. As echoed in current evidence, the most frequently reported pain types were musculoskeletal (36%), neuropathic (22%), and headache (17%).[7,8,14] Despite a high prevalence of patients reporting pain, only 20% disclosed analgesics in listing of prescribed medications. Interestingly, 22% were prescribed opioids, and 27% of this subgroup disclosed both gabapentin and opioid use.

Chronic pain evidence has established the basis of gender pain experience differences between men and women: biological, estrogen and progesterone increasing the propensity for pain and testosterone offering protection, and neural with differences in the sensorimotor areas and spinal inhibition pathways; psychological with cognitive and behavioral factors such as catastrophizing and depression having stronger relationships with pain in women; and treatment response, with differences noted in analgesic efficacy and side effects.[15,16] The descriptive statistics in our study demonstrated that the number of women in the group reporting pain was higher than men; however, the regression model suggested no statistically significant difference between men and women reporting pain. As this was a retrospective study, there may

be variables of interest that were not collected or charted/reported correctly that may have influenced the direction of this relationship. Further rigorous investigation into the gender differences in pain in stroke survivors is critically needed.

Obstructive sleep apnea (OSA), a condition of sleep-disordered breathing in which there is partial or full collapse of airway structures leading to hypopnea, apnea, and fragmented sleep, among other sequelae,[17] was disclosed by 10% of the total cohort with three times as many stroke survivors who reported pain disclosing OSA than those without pain. Formal diagnosis of OSA comes from costly, burdensome polysomnography testing, which may explain the low incidence of OSA diagnosis in this sample. Many with OSA also have chronic pain, with evidence demonstrating shared inflammatory processes in chronic pain conditions and OSA: tumor necrosis factor (TNF-α) and interleukin-6 (IL-6).[18,19] Additionally, hypoxia is shown to increase the expression of central nervous system opioid receptors, making those with OSA more sensitive to opioids.[18] This opioid sensitivity, coupled with the respiratory depressant effects of opioids, is the basis for the current guidelines related to opioid minimization for those with OSA.[18,20] Gabapentinoids also alter respiratory function and should be used with extreme caution. Neurologic impairment, often a consequence of stroke, coupled with OSA, increases the risk of further morbidity from respiratory depression, somnolence, and altered mental status resulting from these drugs warranting the inclusion of sleep apnea screening measures (such as inquiring about snoring or apneic episodes during sleep or elicitation of a pre-stroke sleep apnea diagnosis) during post-stroke assessments.

Curiously, a small percentage of subjects reported analgesic use. This may be a reflection of limited pain management guidelines in stroke recovery. Additionally, providers may be overtaxed by the complex medical needs and comorbidities inherent in stroke, and subsequently limited in the time and resources necessary to incorporate pain assessment and treatment in their care. Most subjects reported gabapentin use, even though there is scarce and low-level evidence supporting its efficacy in post-stroke pain.[21,22] Some disclosed opioids, with many taking both opioids and gabapentin, not a surprising finding as opioids and gabapentinoids are both commonly prescribed for pain, increasing the probability that they will be co-prescribed. Although generally deemed safe, gabapentin and pregabalin have an increased risk of respiratory depression and dependency, a risk shared with opioids.[21,22] These serious side effects are particularly difficult to tolerate and increasingly dangerous for those with neurologic impairment. Additionally, there is the real risk of opioid and gabapentin misuse and abuse, as gabapentinoids are shown to decrease opioid tolerance, thereby increasing the risk of overdose.[22] However, some stroke survivors may indeed have treatment-refractory pain necessitating opioid therapy, and in such instances, providers should be vigilant in their efforts to mitigate the associated risks. Efforts should be made to trial alternative treatments recommended by established pain management guidelines, like non-pharmacological modalities (ie, physical therapy for musculoskeletal pain) and multi-modal pain treatment paradigms.[23]

Many stroke survivors experience more than one type of pain,[7] as did 36% of the subjects in this study. This further complicates stroke-related pain assessment and treatment, as not all assessment tools validly measure all types of pain, and not all treatments are equally efficacious across all pain types.[4] For many stroke survivors, pain assessment is lacking altogether. Stroke survivors present with complex medical needs, and the lack of guidelines supporting uniform pain assessment among providers further confounds clinical practices. Thus, comparing outcomes across providers, facilities, and health systems is difficult, if not impossible. As pain is a multidimensional construct with components of intensity and interference with other quality-of-life constructs such as mood, sleep, relationships, and function, as well as variability in symptom reporting (such as burning, numbness, pinprick, tingling), instruments such as the Brief Pain Inventory that capture pain intensity, variations in how the sensation of pain is expressed, and the biopsychosocial constructs of pain would aid in pain assessment[24] and targeting appropriate treatment, such as neuropathic and musculoskeletal pain treatment recommendations from the International Association for the Study of Pain (IASP).[24] Furthermore, as is probably true for stroke survivors, the pain experience is most likely different for those with neurologic impairment than those without, impeding the use of commonly employed subjective measures such as the numeric pain rating scale.[25,26]

Strengths and Limitations

A major strength of this study is the rigorous model selection process. Although not all covariates in the final logistic regression model showed statistical significance, their inclusion was based on model-based approaches aimed at

optimizing predictive ability rather than traditional variable selection methods that depend solely on p-values. This approach helps retain variables that could have clinical importance or contribute to the model's overall robustness. By capturing the overall variability in the data, the model accounted for potential confounders and improved its predictive performance.

There are several limitations inherent in this investigation. As this is a retrospective review, the scope of our outcomes is limited by the available data. In particular, the intensity and exact location of pain cannot be determined. Additionally, undisclosed pre-existing pain conditions cannot be ruled out. In terms of treatment, some pain medications, such as the SNRIs, may be prescribed for other conditions like depression and/or anxiety rather than pain. Only one facility's assessment records were used and may account for the relatively low NIHSS (median score of 4 and 3 for the no-pain and pain-reported groups, respectively). Additionally, 48% of the sample is within 3 months of the incident stroke. Evidence does demonstrate newly reported pain conditions along the post-stroke continuum for up to a year and more.[3,7] Furthermore, selection bias is another potential limitation of our study, as this data comes from self-report questionnaires submitted prior to a telehealth visit with the care-providing neurologist, the sample may not include those subjects with severe cognitive or physical impairments who could not respond. Also, though some caregivers provided questionnaire responses, this data may fail to capture those with severe impairment lacking such support. Another limitation is the low AUC of the final logistic model. While we do not recommend this model for predicting which individuals will present post-stroke pain in the outpatient setting, it identifies OSA and history of recreational drug use as variables associated with increased odds of experiencing pain. Although non-linear or machine learning models may improve the AUC, the relatively small sample size may result in overfitting with these methods.

Our results indicating an association between recreational drug use and an increased likelihood of pain reporting are supported in substance abuse literature.[27] Evidence demonstrates that those who use recreational drugs have worse pain-reported outcomes. However, the direction of the association is not well established.[27] In our study, for example, it is not possible to distinguish the temporal precedence of pain and recreational drug use: we cannot estimate the use of recreational drugs such as cannabis for unmet pain needs. The associations identified among the predictor set do not imply causation and do not control for unmeasured confounders, but highlight areas that may influence the experience of post-stroke pain. Understanding these associations can help identify variables that warrant further investigation to render methodologically rigorous causal estimates.

Conclusion

More than half of the cohort in various stages of chronic stroke reported pain, and more than a third of these subjects reported more than one type of pain. Up to 20% of those with pain disclosed taking pain medications, and 22% of those with analgesics reported opioid prescriptions. Despite the inherent limitations related to this retrospective study, it is evident that there is a great need for the incorporation of standardized pain assessment tools in the usual care of stroke survivors. Furthermore, the incidence and prevalence of post-stroke pain will remain unknown until evidence-based guidelines incorporate routine pain assessment in post-stroke clinical care. Additionally, further research investigating the efficacy of nonpharmacologic pain management techniques, such as cognitive behavioral therapy, is critically needed. Providers caring for stroke survivors must remain vigilant to the risks of co-prescribed medications, particularly the somnolence and respiratory depression associated with opioids and gabapentinoids.

Data Sharing Statement

Anonymized data can be requested from the corresponding author upon reasonable request, and subject to ethical approval.

Ethics Approval and Informed Consent

The University of Texas Health Science Center Houston IRB (HSC-SN-22-0261) approved this study. All patient information was de-identified, and patient consent was not required. Patient data will not be shared with third parties. This study adheres to the principles outlined in the Declaration of Helsinki.

Consent for Publication

Not applicable. This research analyzed anonymized, retrospective data; no individual patient identifiers are included in the manuscript. The study was conducted in accordance with institutional ethical guidelines and received exempt status from the University of Texas Health Science Center Houston IRB.

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