ORIGINAL ARTICLE

Non-Caucasian Race, Chronic Opioid Use and Lack of Insurance or Public Insurance were Predictors of Hospitalizations in Cyclic Vomiting Syndrome

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Introduction: Cyclic vomiting syndrome (CVS) is associated with frequent hospitalizations; risk factors for this are unknown. We sought to determine predictors of increased hospitalizations and length of hospital stay (LOS).

Methods: We performed a retrospective review of patients with CVS at a tertiary referral center. Clinical characteristics and details about yearly hospitalizations and LOS were assessed; follow-up was divided into two one-year periods before and after the initial clinic visit. Negative binomial regression was used to assess predictors of hospital admission and total length of stay for each time period; the regression results are presented as ratio ratios (RRs).

Results: Of 118 patients (70% female, 73% Caucasian), mean follow up was 3.4 ± 2 years. During the first year of follow up, chronic opioid use (Rate Ratio [RR] 2.22) and being uninsured or having public health insurance (RR, 2.39) were associated with higher rates of hospitalization. Non-Caucasians had a longer LOS (RR 2.76). During subsequent follow up (after 1 year of enrollment), non-Caucasian race (RR, 2.77) and opioid use during the first year of enrollment (RR, 2.4) increased rate of hospitalizations. Non-Caucasian race (RR, 6.27) and opioid use during the first year (RR, 3.78) were also predictors for a longer LOS during this same time period. Tricyclic antidepressant use reduced overall hospitalization rates.

Conclusions: Non-Caucasian race, chronic opioid use and lack of health insurance/public insurance are associated with increased hospitalizations in CVS: reasons for these disparities warrant further investigation. Universal health care and opioid-sparing therapies can improve outcomes.

Keywords: cyclic vomiting syndrome, hospitalization, length of stay, non-Caucasian, opioid use

INTRODUCTION

Cyclic vomiting syndrome (CVS) is a chronic disorder of gut brain interaction (DGBI) characterized by recurrent episodes of vomiting and is diagnosed with Rome criteria (1). CVS is treated with prophylactic medications such as amitriptyline, which is considered first-line therapy (2, 3). This reduces the frequency of emergency department (ED) visits and hospitalizations (2). However, patients continue to be hospitalized for acute CVS flares. Reasons for CVS-related hospitalizations in these patients are unknown. Multiple causes such as disparities in access to health care, chronic opioid use and chronic marijuana use have been purported (4-6).

Hospitalizations in CVS have serious social and economic consequences. They can result in reduced productivity (workdays lost, job loss), and sometimes social problems like divorce (8, 9). In a study using the Nationwide Inpatient Sample, total hospital charges incurred in CVS-related hospitalizations were ~$400 million in 2 years (10). It is crucial to understand risk factors for hospitalizations given the significant impact of CVS on patients and the health care system.

The primary aim of our study was to determine risk factors for CVS-related hospitalizations and length of stay (LOS) in patients with CVS. We hypothesized that history of psychiatric comorbidity, chronic opioid use, lack of insurance and African American (AA) ethnicity would increase the risk of hospitalizations.

METHODS

A retrospective chart review was performed on patients with a diagnosis of CVS and followed at a tertiary referral center between 2006-2014. Approval was obtained by the Institutional Review Board (IRB) at the Medical College of Wisconsin. All patients were seen in the tertiary care clinic of the senior author and had a confirmed diagnosis of CVS based on Rome criteria. Data about patients seen at this tertiary referral center are stored in a clinical registry housed in REDCap (**R**esearch **E**lectronic **D**atabase **Cap**ture) and data is easily retrievable. The diagnosis and information were then confirmed independently by co-authors VK and TT by reviewing records in EPIC (electronic health care system). We included only patients in the Greater Milwaukee area as information about their hospitalizations was readily available to us through our electronic health records as opposed to those from other states where there would be a considerable amount of missing information. Exclusion criteria included pregnancy, chronic conditions such as congestive heart failure, cirrhosis, chronic obstructive pulmonary disease, inflammatory bowel disease, end stage renal disease or active malignancies. Demographics, disease characteristics, comorbidities, information regarding hospitalizations and discharges, medication compliance, use of TCAs, opioids, and marijuana were obtained. Marijuana and opioid use were defined as any use within the last year, respectively.

Enrollment was defined as the index visit/first visit of the patient in the CVS clinic at our center. Number of CVS-related hospitalizations and LOS were recorded for each patient in the first year of follow up starting from the date of enrollment and in the subsequent years up to the end of the follow-up period. Outcomes included the number of hospitalizations and LOS during the first year after enrollment and subsequent years. For the time period after the first year, the average number of hospitalizations and LOS per year were calculated as the follow-up varied between patients.

Statistical analysis

Descriptive statistics were calculated for all variables. The primary outcomes, hospitalization rates and LOS in the first year following enrollment, were each modeled using negative binomial regression. Age at diagnosis, gender, race, insurance type, basal metabolic index (BMI), duration of symptoms prior to enrollment, prior drug use (TCA, opioid, selective serotonin reuptake inhibitor [SSRI], benzodiazepine and antipsychotic use one year prior to enrollment), job loss, disability and delay in education were all considered as potential predictors of each outcome. Univariate results were obtained for each predictor and a p-value < 0.2 was used to select covariates for multiple regression modeling. Backwards selection (criteria $p < 0.05$) was then used for final model selection. Results from the final negative binomial regression model were reported as rate ratios (RRs).

A subset analysis was completed for patients with different patterns of TCA use. Three different TCA groups were considered: no TCA one year prior to and none after enrollment (No/No), no TCA prior to but prescribed after enrollment (No/Yes), and TCA use prior to and continued after enrollment (Yes/Yes). There were no patients who had TCA use prior to but not after enrollment (Yes/No). Within each group, the number of hospitalizations per year and LOS (days) per year, were compared prior to and following enrollment using Wilcoxon signed-rank tests. Within each TCA group, three different comparisons of each outcome were made: first year prior to vs. first year post enrollment, first year prior to vs. subsequent years post enrollment, and first year vs. subsequent years post enrollment. All variables were similarly compared across racial groups (Caucasian vs. non-Caucasian patients).

All analyses were completed using SAS software version 9.4 (Cary, NC). Subset analysis of TCA groups and graphics were produced using R software version 3.1.0. The frequency of missing values was reported for all study variables and all analyses employed an "available case" approach to missing data. All p-values were 2-sided and p-value<0.05 was considered statistically significant. No adjustments were made for multiple testing.

RESULTS

Demographics and clinical characteristics of CVS patients

There were 118 patients (70% female) of whom 86 (73%) were Caucasians and 32 (27%) were non-Caucasians (28 were non-Caucasian/AAs and 4 were Hispanic) **(Table 1)**. The mean age of diagnosis was 36 ± 12.3 years and mean duration of symptoms was 8.5 ± 8.2 years. Most were overweight with a mean BMI of 27.7 ± 7.3. Mean duration of follow up was of 3.4 ± 2.1 years in 94.9% (N=112) of patients. Follow up was < 1 year in 6 patients. Only a minority of patients were married (30%). Most patients had private insurance (62.8%) and were compliant (84.7%) with the prescribed medications for CVS. Thirty percent of patients had job loss, disability, or delay in education. Marijuana use (defined as any marijuana use within the past year) was reported by 46 (39%) of patients. All demographics data including symptoms, medication use and comorbidities are shown in **Table 1**.

Table 1. Demographics and baseline characteristics of patients with CVS.

Age in years (mean ± SD)	36.0 ± 12.3
Gender, Female n (%)	83 (70.3%)
Race n (%) Caucasian Non-Caucasian	 86 (72.9%) 32 (27.1%)
Marital status Single n (%)	 71 (60.2%)
BMI median (mean ± SD)	27.7 ± 7.3
Insurance status Private insurance n (%) Public or lack of health insurance	 71 (62.8%) 47 (37.2%)
Marijuana use n (%)	46 (39.3%)
Number of hospitalizations in the year prior to enrollment (mean ± SD)	9.9 ± 18.9
Chronic opioid use during the year prior to enrollment n (%)	32 (28.6%)
TCA use prior to enrollment n (%)	18 (16.1%)
TCA use after enrollment n (%)	90 (80.4%)
Patients with at least 1 year of follow up n (%)	112 (94.9%)
Personal history of migraine n (%)	61 (51.7%)
Comorbid conditions n (%)	
Irritable bowel syndrome	31 (26.3%)
Anxiety	58 (49.2%)
Depression	52 (44.1%)
Bipolar disorder	6 (5.1%)
Fibromyalgia	5 (4.2%)
Interstitial cystitis	2 (1.7%)
Chronic fatigue syndrome	11 (9.3%)
Duration of symptoms prior to enrollment in years (mean ±SD)	8.5 ± 8.2
Presence of prodrome n (%)	84 (82.4%)

Presence of triggers n (%)	75 (77.3%)
Compliance with medications, n (%)	100 (84.7%)
Job loss n (%)	26 (34.7%)
History of disability application or approval n (%)	26 (32.9%)
Delay in education n (%)	20 (27%)

Hospitalizations and length of hospital stay during the first year after enrollment

Of 118 patients seen in clinic, 43 (36.4%) were hospitalized during the first year of follow up, of which 20% of the hospitalizations occurred during the winter months. A gastroenterology consultation was obtained only in 9% of patients who were hospitalized for CVS flares during this time. Most patients who were admitted with a CVS flare were discharged with appropriate follow-up appointments (84.1%).

Univariate analysis of risk factors for hospitalizations during the first year of follow up after enrollment revealed that non-Caucasians had an almost three-fold increased rate of hospitalizations compared to Caucasians (RR 2.97, CI 1.4-6.2, p=0.004) (Table 2). Also, patients with public health insurance or no health insurance had a 3.4 times increased rate of hospitalizations (RR 3.4, CI 1.7-6.8, p=0.0006) compared to those with private insurance. Those with a history of prior opioid use (RR 3.06, CI 1.45-6.43, p = 0.003) and TCA use (RR 3.33, CI 1.37-8.10, P=0.007) were hospitalized at a higher rate. On multivariate analysis, public or no health insurance (RR 2.39, CI 1.22-4.68, p=0.01), prior TCA use (RR 2.67, CI 1.20-5.94, p=0.01) and prior chronic opioid use (RR 2.22, CI 1.10-4.45, p=0.02) were shown to significantly increase the rate of hospitalizations during this time period (**Table 2**).

On univariate analysis for LOS during the first year after enrollment, public or no health insurance (RR 2.97, CI 1.1-7.6, p=0.02), non-Caucasian race (RR 2.75, CI 1.0-7.5, p=0.04) and chronic opioid use prior to enrollment (RR 3.43, CI 1.26-9.34, p=0.01) were associated with a longer LOS. Longer LOS prior to enrollment was significantly associated with longer LOS after enrollment (RR 1.04, CI 1.01-1.08, p=0.004). On multivariate analysis, non-Caucasian race had a 2.7-fold increased rate (RR 2.76, CI 1.01- 7.54, p=0.04) for a longer LOS compared to Caucasians **(Table 2)**.

Hospitalizations and LOS stay during follow-up period (after 1 year of enrollment)

Univariate analysis of variables that are associated with risk of hospitalizations and LOS in the subsequent follow up period (after the first year of enrollment) are shown in **Table 3**. Patients with a greater number of hospitalizations during the first year of follow up, those admitted in winter and those who had gastroenterology consultations while hospitalized appeared to have an increased rate of hospitalizations during the follow up period. Non-Caucasians continued to have a significantly higher rate of hospitalizations during the follow up period (RR 3.8, CI 1.3-11.5, p=0.014). In the same analysis, the use of TCAs prior to enrollment significantly increased the rate of hospitalizations during the follow-up period (RR 5.59, CI 1.73-18.05, p=0.0039) **(Table 3)**. However, those patients who were initiated on TCAs during the first year after enrollment had a significant reduction in the number of hospitalizations.

Table 2. Predictors of hospitalizations and length of stay during the first year after enrollment.

Univariate Analysis		
Variables	**Hospitalizations RR, (95% CI), P-value**	**Length of Stay RR, (95% CI), P-value**
Age at diagnosis	0.98 (0.95-1.02), 0.42	0.98 (0.94-1.02), 0.46
BMI	1.03 (0.99-1.08), 0.09	1.05 (0.99-1.11), 0.09
Duration of symptoms prior to enrollment	0.96 (0.91-1.01), 0.19	0.93 (0.87-0.99), **0.02**
Hospitalizations during the year prior to enrollment	1.19 (1.07-1.33), **0.001**	NA, NA
LOS during the year prior to enrollment	NA, NA	1.04 (1.01-1.08), **0.004**
Male gender	0.8 (0.35-1.79), 0.58	0.70 (0.25-1.96), 0.50
Non-Caucasian race	2.97 (1.40-6.26), **0.004**	2.75 (1.001-7.55), **0.04**
Public insurance/Uninsured	3.42 (1.70-6.89), **<0.001**	2.97 (1.16-7.60), **0.02**
Use of TCAs prior to enrollment	3.33 (1.37-8.10), **0.007**	3.26 (0.95-11.18), 0.05
Use of opioids prior to enrollment	3.06 (1.45-6.43), **0.003**	3.43 (1.26-9.34), **0.01**
Use of SSRIs prior to enrollment	1.23 (0.50-3.01), 0.64	2.16 (0.69-6.69), 0.18
Use of benzodiazepines prior to enrollment	1.64 (0.75-3.58), 0.21	1.73 (0.62-4.80), 0.29
Use of antipsychotics prior to enrollment	1.23 (0.27-5.56), 0.78	1.36 (0.19-9.57), 0.75
Job loss	1.13 (0.46-2.78), 0.78	0.93 (0.29-3.01), 0.91
Disability	0.98 (0.40-2.40), 0.97	0.84 (0.26-2.72), 0.78
Delay of education	1.62 (0.58-4.46), 0.35	1.68 (0.42-6.60), 0.45
Multivariate Analysis		
Variables	**Hospitalizations RR, (95% CI), P-value**	**Length of Stay RR, (95% CI), P-value**
Public insurance/uninsured	2.39 (1.22-4.68), **0.01**	NS
Use of TCAs prior to enrollment	2.67 (1.20-5.94), **0.01**	NS
Use of opioids prior to enrollment	2.22 (1.10-4.45), **0.02**	NS
LOS during the year prior to enrollment	NA	1.03 (1.006-1.07), **0.01**

Non-Caucasian race	NS	2.76 (1.01-7.54), **0.04**

On multivariate analysis, non-Caucasian race (RR 2.77, CI 1.18-6.51, p=0.019), greater number of hospitalizations in the first year of follow-up (RR 1.54, CI 1.23-1.91, p=0.0001), TCA use prior to the index clinic visit (RR 3.19, CI 1.2-8.4, p=0.019) and opioid use during the first year of follow-up (RR 2.4, CI 1.07-5.41, p=0.033) significantly increased the rate of hospitalizations during the follow-up period. Patients who required gastroenterology consultation while hospitalized during the first year also had a slightly higher rate of hospitalizations (RR 1.02, CI 1.01-1.04, p<0.001) (**Table 3**).

Factors such as use of TCAs prior to enrollment, higher BMI, higher LOS during the first year and greater proportion of hospitalizations during the winter months were each associated with a higher LOS during the follow-up period on univariate analysis. Multivariate analysis continued to show a significantly higher rate for higher LOS during the follow-up period in patients with higher LOS during the first year (RR 1.14, CI 1.05-1.23, p=0.0007), use of TCAs prior to enrollment (RR 4.09, CI 1.13-14.8, p=0.03), non-Caucasian race (RR 6.27, CI 2.21-17.78, p=0.0005), and opioid use during the first year (RR 3.78, CI 1.47-9.70, p= 0.005) (**Table 3**).

Table 3. Predictors of hospitalizations and length of stay during the subsequent follow up period after enrollment.

Univariate Analysis		
Variables	**Hospitalizations RR, (95% CI), P-value**	**Length of Stay RR, (95% CI), P-value**
Age at diagnosis	1.00 (0.95-1.05), 0.92	0.99 (0.93-1.05), 0.85
BMI	1.06 (1.00-1.13), **0.04**	1.07 (1.002-1.15), **0.04**
Duration of symptoms prior to enrollment (years)	0.96 (0.89-1.03), 0.29	0.94 (0.85-1.03), 0.19
Hospitalizations during the first year after enrollment	1.60 (1.24-2.07), **<0.001**	NA, NA
LOS during the first year after enrollment	NA, NA	1.19 (1.06-1.34), **0.003**
Hospitalizations during winter months during the first year after enrollment	1.02 (1.01-1.04), **<0.001**	1.02 (1.01-1.04), 0.001
Hospitalizations during the first year after enrollment that required GI consultation	1.02 (1.001-1.05), **0.04**	1.02 (0.99-1.06), 0.09
Discharges during the first year without scheduled follow up	1.01 (0.99-1.03), 0.05	1.02 (0.99-1.04), 0.07
Male gender	1.57 (0.50-4.92), 0.43	0.98 (0.24-3.94), 0.98
Non- Caucasian race	3.89 (1.31-11.58), **0.01**	3.55 (0.90-13.9), 0.06
Publicly insured/Uninsured	1.84 (0.64-5.27), 0.25	2.00 (0.56-7.05), 0.27
Use of TCAs prior to enrollment	5.59 (1.73-18.05), **0.003**	6.13 (1.38-27.28), **0.01**
Use of TCAs after enrollment	1.62 (0.42-6.18), 0.47	1.95 (0.40-9.52), 0.40
Marijuana use	1.86 (0.62-5.53), 0.26	1.07 (0.28-4.09), 0.91
Opioid use after enrollment	2.52 (0.89-7.08), 0.07	2.26 (0.64-7.93), 0.20

SSRI use after enrollment	0.25 (0.04-1.30), 0.10	0.39 (0.06-2.61), 0.33
Benzodiazepine use after enrollment	2.65 (0.95-7.34), 0.06	2.83 (0.83-9.60), 0.09
Job loss	1.52 (0.39-5.88), 0.54	1.43 (0.27-7.46), 0.66
Disability	1.09 (0.27-4.30), 0.89	1.28 (0.24-6.70), 0.76
Delay in education	1.35 (0.32-5.63), 0.67	1.81 (0.32-10.10), 0.49
Multivariate Analysis		
Variables	**Hospitalizations RR, (95% CI), P-value**	**Length of Stay RR, (95% CI), P-value**
Hospitalizations during the first year after enrollment	1.54 (1.23-1.91), **<0.001**	NA, NA
Hospitalizations during the first year after enrollment that required GI consultation	1.02 (1.01-1.04), **<0.001**	1.04 (1.02-1.05), **<0.001**
Use of TCAs prior to enrollment	3.19 (1.20-8.44), **0.01**	4.09 (1.13-14.80), **0.03**
Non-Caucasian Race	2.77 (1.18-6.51), **0.01**	6.27 (2.21-17.78), **<0.001**
Use of opioids during the first year after enrollment	2.41 (1.07-5.41), **0.03**	3.78 (1.47-9.70), **0.005**
LOS during the first year after enrollment	NA	1.14 (1.05-1.23), **<0.001**
Hospitalizations during winter months during the first year after enrollment (%)	NS	1.01 (1.0004-1.02), **0.04**

Abbreviations: RR, Rate ratio; BMI, basal metabolic index; LOS, length of stay; GI, gastrointestinal; TCA, tricyclic antidepressants; SSRI, selective serotonin reuptake inhibitors, NS, not significant, NA, not applicable.

Use of TCAs as prophylactic therapy in CVS reduced number of hospitalizations and LOS

Initiation of TCAs at the time of the first clinic visit significantly reduced the number of hospitalizations during the first year ($p<0.001$) and the follow up period ($p<0.001$), compared to when TCAs were initiated the year prior to enrollment as shown in **Figure 1**. Similarly, initiation of TCA therapy during or after the index clinic visit significantly reduced the LOS during the first year ($p<0.001$) and follow-up period ($p<0.001$) compared to the group who were already on TCAs prior to enrollment as shown in **Figure 2**. In the 18 patients who were already on TCAs prior to enrollment, a trend in decline in hospitalizations was evident during the follow-up period but this was not statistically significant **(Figure 1).** A significant decrease in LOS was observed during the first year ($p=0.031$) and the subsequent follow up period ($p=0.006$) **(Figure 2).**

Relationship between race and hospitalizations

Post hoc analysis of Caucasian versus non-Caucasian patients was performed to identify possible factors that increased the number of hospitalizations and LOS in this subgroup. Non-Caucasians were mostly publicly insured or uninsured (59.4% vs 32.6%, $p=0.01$), had greater cannabis use history (59.4% vs 31.8%, $p=0.01$), admitted more often in winter months (37.6% vs 14.8%, $p=0.0007$), discharged more often without follow-up appointments (23.5% vs 11.7%, $p=0.006$), and were hospitalized more during the year prior to enrollment (4.6 vs 1.7, $p<0.001$) compared to Caucasians. Use of TCAs was not significantly different between Caucasians and non-Caucasians.

Nevertheless, non-Caucasian race appeared to have an independent effect on hospitalizations and LOS during the first year as well as the follow up period after the initial clinic visit.

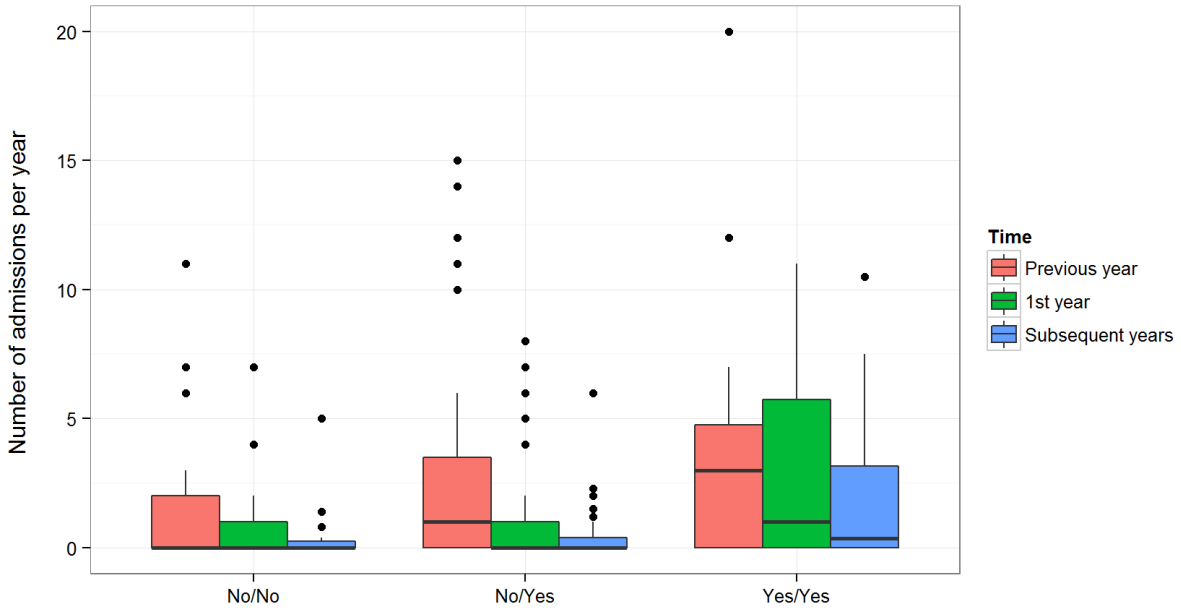

Figure 1. Effect of tricyclic antidepressant (TCA) on hospitalizations per year. *

*Statistical significance on comparison of three groups was as follows: previous year vs. 1st year (TCA No/No: p=0.233, TCA No/Yes: p<0.001, TCA Yes/Yes: 0.285), previous year vs. subsequent years (TCA No/No: 0.155, TCA No/Yes: p<0.0001, TCA Yes/Yes: p=0.017) and 1st year vs. subsequent years (TCA No/No: 0.106, TCA No/Yes: p=0.030, TCA Yes/Yes: 0.169).

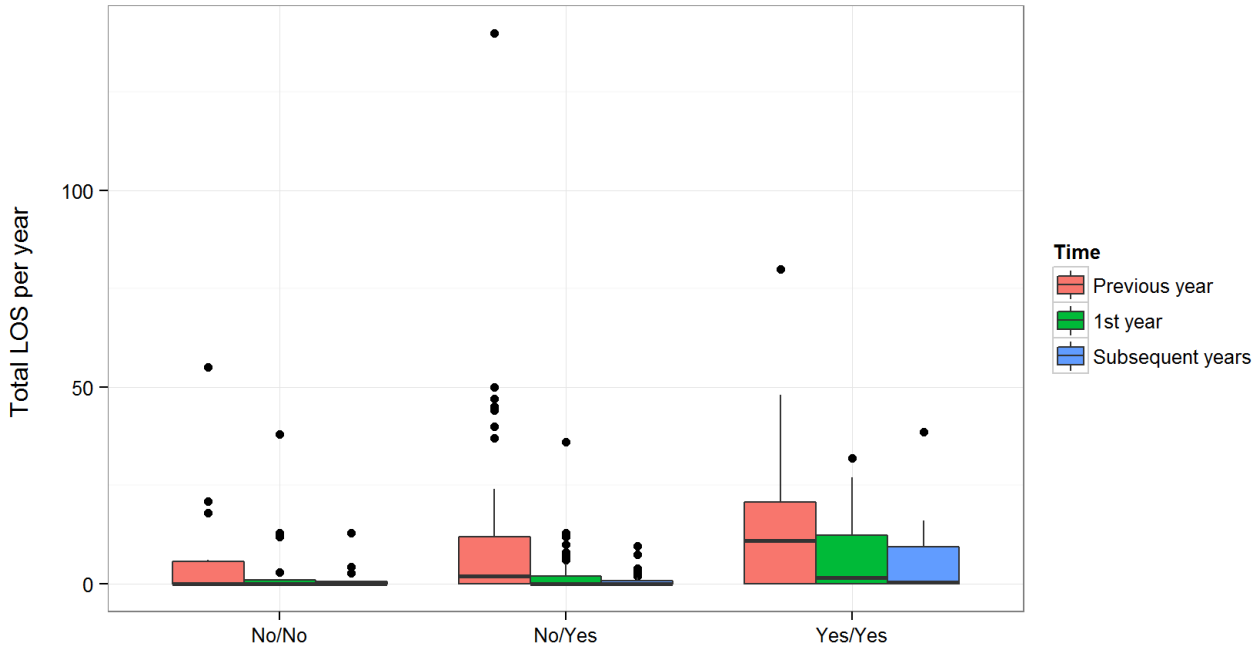

Figure 2. Effect of tricyclic antidepressant (TCA) on length of stay (LOS) per year. *

* Statistical significance on comparison of three groups was as follows: previous year vs. 1st year (TCA No/No: p=0.119, TCA No/Yes: p<0.001, TCA Yes/Yes: 0.031), previous year vs. subsequent years (TCA No/No: 0.155, TCA No/Yes: p<0.0001, TCA Yes/Yes: p=0.006) and 1st year vs. subsequent years (TCA No/No: 0.271, TCA No/Yes: p=0.023, TCA Yes/Yes: 0.477)

DISCUSSION

Patients with CVS patients are frequently hospitalized for management of acute flares (10, 11). Our study focused on identifying factors leading to increased rates of CVS-related hospitalizations and increased LOS. Salient findings of our study were that non-Caucasian patients had a significantly higher number of hospitalizations and LOS compared to their Caucasian counterparts. In our study, the non-Caucasian group consisted of only 4 Hispanic patients and 28 AA patients. Hence, the differences in outcomes noted in the non-Caucasian group were mostly driven by AA patients. While the higher rates of hospitalization in non-Caucasian patients could be, at least in part, due to the lack of insurance/public insurance and higher cannabis use compared to Caucasians, this needs further study. Other more complex issues such as the effects of poverty and racism may be the cause of these health care disparities. Our study findings are corroborated by previous studies underscoring racial disparities leading to serious healthcare consequences including the more recent COVID-19 crisis which has disproportionately affected African American communities and other minorities (12-16). Non-Caucasian ethnicity was also associated with longer LOS in our study. Previous studies also highlight such racial disparities in LOS and merit rigorous study (17, 18).

Other notable findings are that patients who had public insurance or no health insurance had a three-fold increased rate of hospitalization in the short-term and this persisted after adjusting for ethnicity. Lack of insurance can lead to reduced access to outpatient care and the much-needed education about CVS and management strategies to manage CVS episodes. This may explain the increased hospitalizations in patients without adequate insurance in our study and emphasizes the need for universal health care.

Patients on opioids prior to enrollment also had increased rates of hospitalization in the first year and subsequent follow-up period. Rates of opioid use in this study are consistent with previous studies in CVS (22). Chronic opioid use has been associated with non-response to standard therapy in CVS (2). Opioid use has also been associated with narcotic bowel dysfunction, but all patients in this study met Rome criteria for CVS. Narcotic bowel syndrome is characterized by chronic or frequently recurring abdominal pain that worsens with continued or escalating dosages of narcotics (23). While nausea and vomiting can also be a feature of narcotic bowel dysfunction, the predominant symptom is abdominal pain. We did not examine doses of narcotics used or relationship with abdominal pain in this study as this was not the aim of our study. Given that abdominal pain is also seen in CVS, opioid-sparing therapies in CVS are needed to improve outcomes.

Another important consideration is the use of marijuana in CVS. The overall prevalence of cannabis use in this study is consistent with prior studies by our group (22, 24). One notable finding in this study was that non-Caucasians were more likely to use marijuana compared to Caucasians. Reasons for this could be poor access to health care and patients trying to address issues such as pain and mental health problems such as anxiety and or depression. Reasons for these are unclear and need to be explored in the future.

Marijuana use in this cohort also raises the question of possible cannabinoid hyperemesis syndrome (CHS) in some of these patients. However, none of the subjects in this study met criteria for CHS. CHS is a condition that is characterized by recurrent episodes of vomiting, like CVS, but is associated with chronic heavy cannabis use. Abstinence from cannabis should result in resolution of symptoms (1). Though there have been several case series and reports in the literature regarding CHS, there is considerable variation in diagnostic criteria. The reader is referred to a recent systematic review of CHS as part of the management guidelines in CVS by the American Neurogastroenterology and Motility Society for a thorough review of CHS (25). Whether CHS is a subset of CVS or a separate entity remains to be determined.

Other factors that impacted hospitalizations was the initiation of TCAs upon enrollment. TCA initiation upon enrollment significantly reduced hospitalizations and LOS during the first year and subsequent years after enrollment. TCAs are first-line treatment in the management of CVS (3). Contrary to other DGBIs like irritable bowel syndrome, the recommended dosage for TCAs in CVS is 75 to 100 mg daily. Lower doses are usually ineffective but the emergence of side effects in up to 25% of patients limit its utility.

Hospitalization rates also decreased over time in patients who were not on TCAs. The specialty CVS clinic in our center provides ongoing comprehensive care with a dedicated and knowledgeable team of ancillary providers (physician assistants and nurses) and this could explain this decrease regardless of TCA use. Future studies are needed to determine the effects of specialized care at high volume centers on hospitalizations in CVS compared to low volume centers.

The presence of psychiatric co-morbidity did not influence hospitalizations in our study, and this was not prospectively confirmed using Diagnostic and Statistical Manual (DSM) IV criteria as this was a retrospective study and is a limitation. There are other limitations to our study. We only included patients from the greater Milwaukee area and thus, the results are not generalizable to other centers. However, this was because we had easy access to records allowing us to collect accurate information pertaining to hospitalizations and LOS.

Our study was performed in a tertiary care center and thus this study is subject to referral bias with the possibility of a cohort with more severe disease. This was also a retrospective study with the inherent limitations related to recall and accuracy of documentation. However, our results highlighting disparities in health care outcomes based on race, insurance status and chronic opioid use have been shown in other disease states and are not surprising. These warrant future studies that can inform public health policy and research initiatives to address these important barriers to health equity in CVS.

In conclusion, our study demonstrates that non-Caucasian race, chronic opioid use and lack of insurance/public insurance increase rates of hospitalizations in CVS. The use of TCAs reduced hospitalizations overall and should be initiated in patients with moderate-to-severe CVS. Future studies to address barriers to health care, particularly among African Americans are warranted.

Notes

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