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Retrospective Cohort Study

Epidemiologic risk factors for patients admitted with chronic pancreatitis and pancreatic ductal adenocarcinoma in the United States

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Abstract

BACKGROUND

Epidemiological studies of chronic pancreatitis (CP) and its association with pancreatic ductal adenocarcinoma (PDAC) are limited. Understanding demographic and ethno-racial factors may help identify patients at the highest risk for CP and PDAC.

AIM

To evaluate the ethno-racial risk factors for CP and its association with PDAC. The secondary aim was to evaluate hospitalization outcomes in patients admitted with CP and PDAC.

METHODS

This retrospective cohort study used the 2016 and 2017 National Inpatient Sample databases. Patients included in the study had ICD-10 codes for CP and PDAC. The ethnic, socioeconomic, and racial backgrounds of patients with CP and PDAC were analyzed.

RESULTS

Hospital admissions for CP was 29 *per* 100000, and 2890 (0.78%) had PDAC. Blacks [adjusted odds ratio (aOR) 1.13], men (aOR 1.35), age 40 to 59 (aOR 2.60), and being overweight (aOR 1.34) were significantly associated with CP (all with $P < 0.01$). In patients with CP, Whites (aOR 1.23), higher income, older age (aOR 1.05), and being overweight (aOR 2.40) were all significantly associated with

PDAC (all with $P < 0.01$). Men (aOR 1.81) and Asians (aOR 15.19) had significantly increased mortality ($P < 0.05$). Hispanics had significantly increased hospital length of stay (aOR 5.24) ($P < 0.05$).

CONCLUSION

Based on this large, nationwide analysis, black men between 40-59 years old and overweight are at significantly increased risk for admission with CP. White men older than 40 years old and overweight with higher income were found to have significant associations with CP and PDAC. This discrepancy may reflect underlying differences in healthcare access and utilization among different socioeconomic and ethno-racial groups.

Key Words: Chronic pancreatitis; Pancreatic cancer; Ethno-racial; Risk factors; Hospitalization outcomes; Adult

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Core Tip: What is known chronic pancreatitis (CP) and pancreatic ductal adenocarcinoma (PDAC) rates are rising. Pancreatitis admissions costed 133 million dollars, and accounted for the 3rd leading cause of hospital admissions. There is lack of data identifying those at highest risk for admissions with CP and PDAC. What we found Black men between 40-59 years old and overweight are at significantly increased risk for admission with CP. White men with higher income were found to have significantly increased risk for admissions with CP and PDAC. Asians/Pacific Islanders had the highest risk for mortality from CP and PDAC.

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INTRODUCTION

The overall incidence of chronic pancreatitis (CP) is increasing worldwide, and accounts for significant healthcare utilization and costs. In the United States, CP hospital admissions costed 133 million dollars, and pancreatitis accounted for the 3rd leading cause of hospital admissions among gastrointestinal diseases in 2015[1]. The most common reason for CP-related admission is abdominal pain, but other complications can develop including pancreatic ductal adenocarcinoma (PDAC). PDAC is currently the fourth leading cause of cancer-related deaths in the United States and is projected to become the second leading cause by 2030[2]. CP is the major risk factor for developing PDAC[3-5].

There have been few epidemiological studies available for CP[6-14], and fewer studies for CP and PDAC[3,15-18]. Ethnic and socioeconomic factors including insurance status, median income, type and hospital factors are lacking.

Herein, we utilize hospital discharges from a large nationwide database to examine the demographic, ethno-racial, socioeconomic, and hospital factors associated with hospitalizations for CP and its association with PDAC. We also sought to determine the association between ethnicity/race on hospitalization outcomes in patients admitted with CP and PDAC.

MATERIALS AND METHODS

Data source

This retrospective cohort study utilized the 2016 and 2017 National Inpatient Sample (NIS) databases. The NIS is a database of inpatient stays derived from billing data based upon discharge abstracts. As such, it contains de-identified clinical and nonclinical elements at both the patient and hospital level. The NIS 2016 database contains data from 7.1 million hospital stays in 4575 hospitals in 47 states, while the 2017 database contains data from 7.1 million hospital stays in 4584 hospitals in 48 states. Using the combination of the NIS 2016 and 2017 databases allowed for inclusion of a greater total number of cases/patients.

Study population

Patients included in the study carried a primary diagnosis of CP based on ICD-10 codes (K86.0, K86.1, K90.3). The demographics and ethnic/racial profiles of those with CP were compared to the general population and examined for any associations. Subsequently, all patients with CP were then evaluated for PDAC based on ICD-10 diagnostic codes C25.0-C25.9. The demographic and ethnic/racial profiles of those with only CP were compared to the ethnic/racial profiles of those who also had PDAC and were examined for any associations. Finally, we analyzed the associations between ethnicity/race and hospitalization outcomes in patients admitted for PDAC.

Inclusion and exclusion criteria are shown in [Figure 1](#). Institutional Review Board approval was not required for this study as it was performed using de-identified and nationally available data.

Census data

The estimated national population during 2016-2017 was obtained from the United States Census Bureau (www.census.gov).

Study variables

Patient demographics included age, gender, race, median household income, primary expected payer, hospital bed size, hospital teaching status, hospital region, and urban location. Burden of comorbidities was assessed using the Charlson comorbidity index.

Study outcomes

The primary outcomes were the ethno-racial factors associated with CP hospital admissions as compared to the general population and the ethno-racial factors associated between CP and PDAC. Secondary outcomes were the associations between ethnicity/race and hospitalization outcomes (mortality, hospital length of stay (LOS), expenses), in patients admitted with CP and PDAC.

Statistical analysis

Statistical analyses were performed using STATA, version 16.0 (StataCorp., College Station, Texas, United States). Weighting of patient-level observations was implemented. Univariate analysis was initially performed to calculate unadjusted odds ratio and determine confounders significantly associated with the outcomes. Multivariate regression analysis was used to adjust for potential confounders. Multivariate regression model was then built by including all confounders that were found to be significant by univariate analysis, to calculate an adjusted odds ratio (aOR). Logistic regression was used for binary outcomes and linear regression was used for continuous outcomes. Proportions were compared using Fisher's exact test, and continuous variables were compared using Student's *t*-test. All *P*-values were two-sided, with 0.05 as the threshold for statistical significance. Calculated rates of hospital admissions *per* 100000 population was performed using the United States Census Bureau national population estimates.

RESULTS

CP cohort

In our sample (NIS 2016-2017) of 14.2 million admissions, 371275 (2.6%) adult patients were found to have a diagnosis of CP. The mean age was 57.72 years, and most patients were white (64.82%) men (55.76%). Medicare was the primary payer insurance (40.2%). The majority of admissions were in teaching hospitals (69.54%). Additional patient and hospital characteristics are presented in [Table 1](#). Overall hospitalization rate for 2016 and 2017 was 29 *per* 100000 (95%CI: 57.9-58.2).

On multivariate regressions analysis, men (aOR 1.35), Blacks (aOR 1.13), age between 40 and 59 years old (aOR 2.60), and body mass index (BMI) between 25 and 29.9 (aOR 1.34) were at higher risk of developing CP as compared to the general population ($P < 0.01$). On the contrary, women (aOR 0.65), Hispanics (aOR 0.63) or Asian/Pacific Islanders (aOR 0.50) and those above 80 years old (aOR 0.46) had a significantly decreased likelihood of having CP as compared to the general population (all with $P < 0.01$) ([Table 2](#)).

PDAC and CP cohort

Of the 371275 adult patients admitted with a primary diagnosis of CP, 2890 (0.78%) also had PDAC. Patients with PDAC and CP were significantly older ($P < 0.05$), White ($P < 0.01$), had Medicare as the primary insurance ($P < 0.01$), were from a higher income population ($P < 0.01$), were admitted to teaching hospitals ($P < 0.01$), and had a higher burden of comorbidities ($P < 0.01$) ([Table 3](#)). Overall hospitalization rate for 2016 and 2017 was 0.45 *per* 100000 (95%CI: 0.44-0.47).

On multivariate regressions analysis, older age (greater than 40 years old) (aOR 1.05), and BMI between 25 and 29.9 (aOR 2.40) had a higher risk of developing PDAC in patients with CP (all with $P < 0.01$). On the contrary, women (aOR 0.77), Blacks (aOR 0.77) and Hispanics (aOR 0.66) were associated

Table 1 Demographics, ethno-racial, socioeconomic, and hospital factors for patients hospitalized with chronic pancreatitis

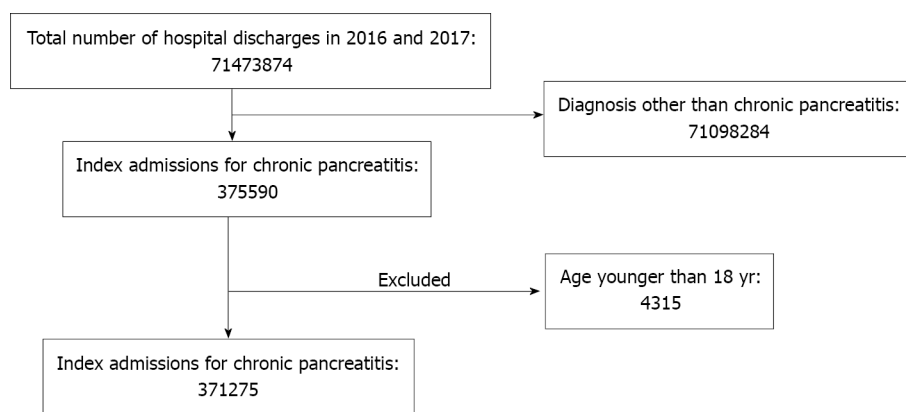
Variable	n = 371275
Race	
White	64.82%
Black	22.35%
Hispanic	8.4%
Asian or Pacific Islander	1.31%
Native American	0.87%
Other	2.25%
Gender	
Women	44.24%
Men	55.76%
Age	
Mean age, years	52.72
Age 18-39 yr	21.63%
Age 40-59 yr	49.84%
Age 60-79 yr	24.26%
Age > 80 yr	4.28%
Insurance provider	
Medicare	40.2%
Medicaid	30.28%
Private	22.53%
Uninsured	6.99%
Charlson comorbidity index	
0	24.09%
1	25.97%
2	17.37%
3 or more	32.58%
Median income in patient zip code	
\$1-\$38999	36.17%
\$39000-\$47999	26.11%
\$48000-\$62999	21.78%
\$63000	15.94%
Hospital region	
Northwest	17.54%
Midwest	24.63%
South	40.23%
West	17.6%
Hospital location	
Rural	8.29%
Urban	91.71%
Hospital size	
Small	19%

Medium	28.34%
Large	52.65%
Type of hospital	
Teaching	69.54%
Non-teaching	30.46%

Table 2 Multivariate regressions analysis for demographic, socioeconomic, and hospital factors associated with hospitalizations secondary to chronic pancreatitis

Classification		P value
Age	aOR 0.98	< 0.01
Age 18-39 yr	Reference	
Age 40-59 yr	aOR 2.60	< 0.01
Age 60-79 yr	aOR 0.96	0.37
Age > 80 yr	aOR 0.46	< 0.01
BMI: 18-24.9	Reference	
BMI: 25-29.9	aOR 1.34	< 0.01
BMI: 30-39.9	aOR 0.62	< 0.01
Women	aOR 0.65	< 0.01
Whites	Reference	
Blacks	1.13	< 0.01
Hispanics	0.63	< 0.01
Asians/Pacific Islanders	0.50	< 0.01
Native Americans	1.05	0.31
Other	0.67	< 0.01

aOR: Adjusted odds ratio; BMI: Body mass index.



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Figure 1 Flowchart for patient inclusion.

with a significantly decreased likelihood of PDAC in patients with CP (all with $P < 0.01$) (Table 4).

Hospitalization outcomes in PDAC and CP

Men (aOR 1.81) and Asians/Pacific Islanders (aOR 15.19) had the highest mortality among patients with PDAC and CP (all with $P < 0.05$). Hispanics had the highest hospital LOS (aOR 5.24), charges (adjusted

Table 3 Demographics, ethno-racial, socioeconomic, and hospital factors for patients hospitalized with chronic pancreatitis and pancreatic ductal adenocarcinoma

Variable	CP without PDAC (n = 368385)	CP with PDAC (n = 2890)	P value
Race			< 0.01
Whites	64.75%	74.22%	
Blacks	22.4%	16.76%	
Hispanics	8.43%	4.97%	
Asians or Pacific Islanders	1.31%	1.29%	
Native Americans	0.87%	0.37%	
Other	2.25%	2.39%	
Gender			0.07
Women	44.27%	40.31%	
Men	55.73%	59.69%	
Age			< 0.05
Mean age, years	52.61	66.32	
Age 18-39 yr	21.78%	19%	
Age 40-59 yr	50.02%	26.99%	
Age 60-79 yr	23.97%	60.03%	
Age > 80 yr	4.23%	11.07%	
Insurance provider			< 0.01
Medicare	40.04%	60.64%	
Medicaid	30.44%	10.73%	
Private	22.5%	26.48%	
Uninsured	7.03%	2.15%	
Charlson comorbidity index			< 0.01
0	24.28%	0	
1	26.17%	0	
2	17.35%	19.38%	
3 or more	32.2%	80.62%	
Median income in patient zip code			< 0.01
\$1-\$38999	36.24%	28.22%	
\$39000-\$47999	26.1%	26.81%	
\$48000-\$62999	21.78%	21.34%	
\$63000	15.88%	23.63%	
Hospital region			0.68
Northwest	17.53%	19.38%	
Midwest	24.64%	23.53%	
South	40.25%	38.24%	
West	17.59%	18.86%	
Hospital location			< 0.01
Rural	8.34%	1.56%	
Urban	91.66%	98.44%	
Hospital size			< 0.01

Small	19.08%	8.65%	
Medium	28.43%	16.78%	
Large	52.48%	74.57%	
Type of hospital			
Teaching	69.41%	86.16%	< 0.01
Non-teaching	30.59%	13.84%	

CP: Chronic pancreatitis; PDAC: Pancreatic ductal adenocarcinoma.

Table 4 Multivariate regressions analysis for demographic, socioeconomic, and hospital factors associated with hospitalizations in patients with chronic pancreatitis and pancreatic ductal adenocarcinoma

Classification		P value
Age	aOR 1.05	< 0.01
Age 18-39 yr	Reference	
Age 40-59 yr	aOR 6.79	< 0.01
Age 60-79 yr	aOR 24.17	< 0.01
Age > 80 yr	aOR 21.02	< 0.01
BMI: 18-24.9	Reference	
BMI: 25-29.9	aOR 2.40	< 0.01
Female	aOR 0.77	< 0.01
White	Reference	
Black	aOR 0.77	< 0.05
Hispanic	aOR 0.66	< 0.05
Asian or Pacific Islander	aOR 0.69	0.36
Native American	aOR 0.68	0.60
Other	aOR 0.97	0.94

aOR: Adjusted odds ratio; BMI: Body mass index.

coefficient \$87285), and costs (adjusted coefficient \$15212) amongst patients with PDAC and CP (all with $P < 0.05$). Gender was not found to be a significant contributing factor for hospital expenses.

DISCUSSION

In this nationwide cohort study, we found black men who were overweight had a significantly increased likelihood of being admitted with CP. These findings are consistent with previous studies, most likely due to alcoholic CP, though our current study is not able to definitively elucidate the cause of CP[14]. Our hospitalization rates for CP is much higher compared to the study by Yang *et al*[13], which also used the NIS database from 1988-2004 and found an incident rate of 7.0-8.1 *per* 100000 population[13]. Similarly, population-based studies from Olmsted County, MN, United States found an incident rate of 4.05 *per* 100000 population from 1997-2006 and Allegheny County, PA, United States found incident rate of 7.75 *per* 100000 population[11,12]. Our findings of an increased incidence rate may reflect recent trends in increased hospitalizations with pancreatitis being the 3rd most common reason for hospitalization in 2015 among gastrointestinal diseases[1]. This is likely due in part to increased use of cross-sectional imaging for the evaluation of abdominal pain in adults[19]. Another possible explanation is that our findings may be more of a reflection of prevalence rate rather than incidence rate. In 2014, Lévy *et al*[20] summarized 11 studies and found a prevalence rate ranging up to 41.76 *per* 100000 population[20]. Additionally, patients with CP are reported to have good overall survival despite complications with reported 10-year survival rate of 70%[17]. Taken together, our increased hospitalization rate is likely due to increased diagnosis of CP and longevity of patients with CP.

Other novel demographic findings from our study include the findings that patients with CP-related admissions had predominantly Medicare insurance and were from lower median income families. Additionally, we found patients were more likely to be admitted to teaching hospitals in large urban centers, predominantly in the Southern part of the United States. A potential reason for this finding may correlate with the South having the highest prevalence of obesity at 30% and higher. Furthermore, non-Hispanic Blacks were found to have the highest prevalence of obesity[21]. Our hope is that future studies can use our findings to further evaluate the exact association of CP-related admissions in this high-risk population in an effort to improve patient outcomes and decrease healthcare expenditures. While our study is not able to elucidate the reason for admission, it is presumed that abdominal pain is most likely the cause given extensive findings from previous studies[14,22]. Given that it is well established that abdominal pain is chronic, persistent, and can lead to significant impairment in quality of life including high rates of unemployment as well as recurrent hospitalizations and healthcare expenditure, future research in this area is needed[23,24]. The findings from our study can be used in future studies to target those patients at higher risk for CP-related hospitalizations to improve patient outcomes and limit healthcare expenditures.

A potential complication of CP is the development of PDAC. In our study, we found that 0.78% (approximately 0.39%/year) of patients with CP also carried a diagnosis of PDAC and that these patients were predominantly White men who were overweight and of older age. Our findings are similar to the 2014 Danish nationwide study by Bang *et al*[3], which found a 4.26% rate over a 15-year period (approximately 0.28%/year) of PDAC in CP patients occurring predominantly in older men[3]. While there is moderate amount of literature for the ethno-racial factors for CP and PDAC separately, there is limited data regarding ethno-racial factors specifically in patients with CP and PDAC. Bracci *et al*[25] in 2009 found in a multicenter study that majority of patients with PDAC were White men who were older, however, they did not provide demographic data specifically for PDAC in CP patients[25]. In a meta-analysis published in 2010 containing 22 studies, Raimondi *et al*[15] found a 13 fold increased risk for PDAC in CP patients but did not evaluate the ethno-racial factors[15]. A more recent meta-analysis published in 2017 by Kirkegård *et al*[4] also found an increased risk for PDAC in CP patients but again did not evaluate the ethno-racial factors[4]. To our knowledge, our study is the first to evaluate ethno-racial factors in patients with CP and PDAC. A major caveat to our findings is that we cannot definitively evaluate PDAC development as a progression of CP. Thus, there could be cases where PDAC occurred first and CP developed afterwards. However, current literature suggests the overwhelming likelihood of this occurring is extremely low and may actually be misclassifications given the similarities between the two diseases[4]. An interesting finding from our study was that we found that Blacks had a higher risk for having CP, but this did not translate into having a higher association with CP and PDAC. A potential explanation could be due to discrepancies in healthcare utilization given that our data showed patients with CP and PDAC were significantly more likely to have higher median incomes, lower rates of being uninsured, and high rates of being admitted to large urban teaching hospitals when compared to CP patients alone. Racial disparities have been shown for PDAC in blacks. Khawja *et al*[26] conducted an evidence-based review of PDAC in blacks and found significantly worse outcomes compared to whites. A 2019 review also showed blacks had worse outcomes, but also lower referral rates to see oncology or a surgeon and lower rates of surgical resection and adjuvant chemoradiation[26,27]. Potential reasons for this discrepancy include suboptimal patient communication, greater mistrust of the medical field, and unmeasured differences in morbidity/functional status. Future studies should further evaluate the accuracy of this finding and to evaluate the exact cause of this discrepancy if one exists. Another interesting finding from our study is that we found Asians/Pacific Islanders had an aOR 15.19. This is in contrast to recent data from the American Cancer Society, which showed Blacks had the highest risk of mortality at 15.0/100000 compared to 8.1/100000 with Asians/Pacific Islanders[2]. A possible explanation is that our study evaluated patients with PDAC and CP rather than all PDAC patients, though it is beyond the scope of this study as to why Asians/Pacific Islanders had the highest mortality. Finally, we found that Hispanics had the highest LOS and hospital expenses. Future studies should further evaluate these findings in an effort to identify reasons for increased mortality among Asians/Pacific Islanders and increased LOS and hospital expenses among Hispanics, respectively, to improve patient outcomes and decreased healthcare expenditures.

Limitations of this study include it being limited solely to inpatient encounters. Therefore, our study may not represent a complete epidemiological study given its lack of outpatient encounters. As mentioned previously, there are limitations associated with using the NIS database. We are not able to identify individual patients and review each patients' charts, thus we are not able to identify the reason for CP-related admissions though current literature suggest most likely related to abdominal pain. Additionally, we are not able to determine if patients with CP progressed to PDAC or if PDAC occurred before CP, but again current literature suggests majority of patients develop PDAC after CP. Incidence of PDAC in CP is related to etiology of CP. Risk is significantly higher in hereditary pancreatitis than with alcohol related pancreatitis. As the etiology is not captured in the database it might introduce bias. Duration of CP could not be found, as longer history associated with increased risk. Findings may be applicable only to the population studied and cannot be generalized.

CONCLUSION

In conclusion, based on this large, nationwide analysis, there is an increased trend in hospitalization rates for CP, predominantly among black men between 40-59 years old who were overweight. In patients with CP, white men older than 40 years old who were overweight with higher income had a higher risk of PDAC. The observed disparity may be a consequence of the difference in healthcare access among different ethnic groups.

ARTICLE HIGHLIGHTS

Research background

Chronic pancreatitis (CP) and pancreatic ductal adenocarcinoma (PDAC) rates are rising. Pancreatitis admissions costed 133 million dollars, and accounted for the 3rd leading cause of hospital admissions. There is lack of data identifying those at highest risk for admissions with CP and PDAC.

Research motivation

The main motivation of this study was to establish racial risk factors and their associations with PDAC.

Research objectives

This study had the objective to examine the demographic, ethno-racial, socioeconomic, and hospital factors associated with hospitalizations for CP and its association with PDAC.

Research methods

This retrospective study used the 2016 and 2017 National Inpatient Sample databases. ICD-10 codes compatible with CP and PDAC were used in the study. The ethnic, socioeconomic, and racial backgrounds of patients with CP and PDAC were analyzed.

Research results

Hospital admissions for CP was 29 *per* 100000, and 2890 (0.78%) had PDAC. Blacks [adjusted odds ratio (aOR) 1.13], men (aOR 1.35), age 40 to 59 (aOR 2.60), and being overweight (aOR 1.34) were significantly associated with CP (all with $P < 0.01$). In patients with CP, Whites (aOR 1.23), higher income, older age (aOR 1.05), and being overweight (aOR 2.40) were all significantly associated with PDAC (all with $P < 0.01$). Men (aOR 1.81) and Asians (aOR 15.19) had significantly increased mortality ($P < 0.05$). Hispanics had significantly increased hospital length of stay (aOR 5.24) ($P < 0.05$).

Research conclusions

There is an increased trend in hospitalization rates for CP, predominantly among black men between 40-59 years old who were overweight. Wealthy white men above the age of 40 had a higher PDAC diagnosis.

Research perspectives

Black men between 40-59 years old and overweight are at significantly increased risk for admission with CP. White men with higher income were found to have significantly increased risk for admissions with CP and PDAC. Asians/Pacific Islanders had the highest risk for mortality from CP and PDAC.

FOOTNOTES

Author contributions: Lew D, Kamal F, Phan K, Randhawa K, Cornwell S, and Weissman S assisted with data acquisition, analyses, and manuscript preparation; Lew D drafted and critically revised the manuscript; Lew D, Weissman S, Bangolo AI, and Pandol SJ provided input regarding methodology; Pandol SJ critically revised the manuscript and provided direct supervision and guidance; Weissman S is the article guarantor; All authors agree to the final version of this manuscript.

Institutional review board statement: This retrospective cohort study utilized the 2016 and 2017 National Inpatient Sample (NIS) databases. The NIS is a database of inpatient stays derived from billing data based upon discharge abstracts. As such, it contains de-identified clinical and nonclinical elements at both the patient and hospital level. Making the need for an Institutional review board approval dispensable.

Informed consent statement: The National Inpatient Database was a public-use dataset, of which the informed consent was waived.

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Data sharing statement: This retrospective cohort study utilized the 2016 and 2017 National Inpatient Sample (NIS) databases. The NIS is a database of inpatient stays derived from billing data based upon discharge abstracts. As such, it contains de-identified clinical and nonclinical elements at both the patient and hospital level. The dataset is publicly available.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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