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Impact of aspirin on pancreatic cancer in the elderly: analysis of socioeconomic status and outcomes of national matched cohorts

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Abstract

Background Pancreatic cancer is a neoplastic condition with a high disease burden. It is projected to be the second most common cause of cancer-related deaths by 2030. However, evidence supporting the long-term use of aspirin in cancer prevention and treatment remains insufficient. We aimed to investigate the association between aspirin use and pancreatic cancer outcomes in the elderly population group.

Methods The 2020 National Inpatient Sample was used to investigate records of elderly patients admitted with pancreatic cancer, identified by ICD-10 CM codes. The data were categorized based on long-term aspirin use. We assessed inpatient mortality as the primary outcome, while secondary outcomes included costs and length of stay, as well as other inpatient complications.

Results We identified 19,249 hospitalizations of patients aged over 60 years. The mean age was 73.8 years, and 49.3% were male. In a survey multivariate logistic and linear regression model, adjusting for patient characteristics and hospital factors, long-term aspirin use was associated with lower inpatient mortality (adjusted odds ratio [aOR] 0.55, 95% confidence interval [CI] 0.33-0.92; P=0.023), a shorter hospital stay (beta coefficient -0.52, 95%CI -0.93 to -0.11; P=0.012), lower odds of acute kidney injury (aOR 0.76, 95%CI 0.59-0.98; P=0.039), and lower odds of shock (aOR 0.23, 95%CI 0.06-0.78; P=0.019]. Post-propensity matching revealed similar patterns.

Conclusions Long-term aspirin use is associated with a lower rate of inpatient mortality and other clinical outcomes in hospitalized elderly patients with pancreatic cancer. The etiologies behind this relationship should be explored with a view to better understanding.

Keywords Aspirin, pancreatic cancer, mortality

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Introduction

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States, with an overall survival rate of only 6% [1]. The use of aspirin in pancreatic patient has emerged as a promising approach in cancer prevention and treatment [2]. Although numerous interventions have been used to reduce the burden in this population group, the in-hospital mortality of patients admitted with pancreatic cancer remains significant [3]. Furthermore, with an increasingly aging population and changing demographics, pancreatic cancer is expected to become the second greatest cause of cancer-related deaths in 2030 [4]. Exploring other interventions that are widely available may provide an alternative option in combatting this lethal condition. The previous literature indicates an association between socioeconomic factors, such as race and income, and clinical outcomes [5-7]. However, comprehensive analyses of the socioeconomic profile and comorbidities of elderly patients who are admitted with pancreatic cancer are still limited.

To the best of our knowledge, no prior studies have investigated the relationship between long-term aspirin use and the in-hospital clinical outcomes of patients with pancreatic cancer, particularly in the elderly population. In this propensity-matched, retrospective cohort study using the 2020 National Inpatient Sample, we aimed to evaluate the clinical outcomes associated with aspirin use, and to conduct a comprehensive review of factors predicting inpatient mortality rates and other clinical outcomes, using multiple data relating to the socioeconomic status and comorbidities available in this nationally representative dataset.

Materials and methods

Data source

This study was based on data from the 2020 Health Care Utilization Project National Inpatient Sample (HCUP-NIS). The HCUP-NIS, sponsored by the Agency for Healthcare Research and Quality, is the largest publicly available all-payer inpatient database in the United States. It contains discharge data from non-federal, non-rehabilitation, acute-care and short-term hospitals. Cost-to-charge ratios, also available in the HCUP-NIS database, were used to capture the cost of care. Costs such as wages, supplies and utility, better reflect the actual resource consumption of healthcare [8]. The HCUP-NIS does not include other federal hospitals, psychiatric, substance abuse, and long-term care facility hospitalizations as they do not reflect each hospitalization episodes cost [9].

The HCUP-NIS employs a multilevel survey design database that captures approximately 20% of hospital admissions and discharges across the country. By doing so, it provides national estimates regarding patient characteristics, diagnoses and hospital-based procedures performed in acute-care hospitals across the United States. All hospital discharges within the sample are recorded and weighted to ensure accurate representation of the national landscape of inpatient care.

Study cohort

In our study, we focused on individuals aged 60 years and older who were hospitalized with pancreatic cancer during the period spanning January to December 2020. Although general guidelines have defined a threshold of over 65 years as elderly, we believe that the age of 60, as used by the World Health Organization, will provide a more comparable subpopulation group for future research [10]. We excluded records designated as elective hospitalizations and records with primary cancer other than pancreatic cancer. The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) coding system was used to identify eligible discharge records for inclusion in our analysis. We then stratified eligible hospitalizations into 2 groups: those with long-term aspirin use and those without. We used the ICD-10 code Z79.82 to identify patients with long-term aspirin use, as in various prior publications that used this code to define aspirin use in various diseases [11-13]. The ICD-10-CM code for identification of pancreatic cancer was C25. We used C00-D49 as the ICD-10-CM code for non-pancreatic cancer. Fig. 1 demonstrates the inclusion and exclusion flow of records that were analyzed in this study.

We used the Charlson Comorbidity Index (CCI), the most widely used comorbidity index, to categorize patient severity [14]. The CCI was developed to predict 1-year mortality among 604 patients based on comorbidity data obtained from a hospital chart review [15]. It contains 19 factors, including diabetes with diabetic complications, congestive heart failure, peripheral vascular disease, chronic pulmonary disease, mild and severe liver disease, hemiplegia, renal disease, leukemia, lymphoma, metastatic tumor, and acquired immunodeficiency syndrome (AIDS). Each of these comorbidities was weighted according to their potential influence on mortality.

Additionally, we used propensity score matching to balance between the 2 cohorts. Each of the variables is matched to generate a propensity-matched cohort [16], in order to ensure that there are minimal differences in baseline characteristics. A combination of various balancing, matching, weight readjustment, and interpretation strategies is used to ensure a balance between both cohorts. The process of using propensity score analysis has been well-described and was appropriate for use in our study [17]. In this paper, we used nearest-neighbor 1-to-5 matching to minimize confounding, and we achieved 1-to-3 matching cohorts. A standardized difference of <10% suggested adequacy of the match between 2 groups among the measured covariates, with less potential for bias [18]. Fig. 2 demonstrates the standardized difference before and after matching.

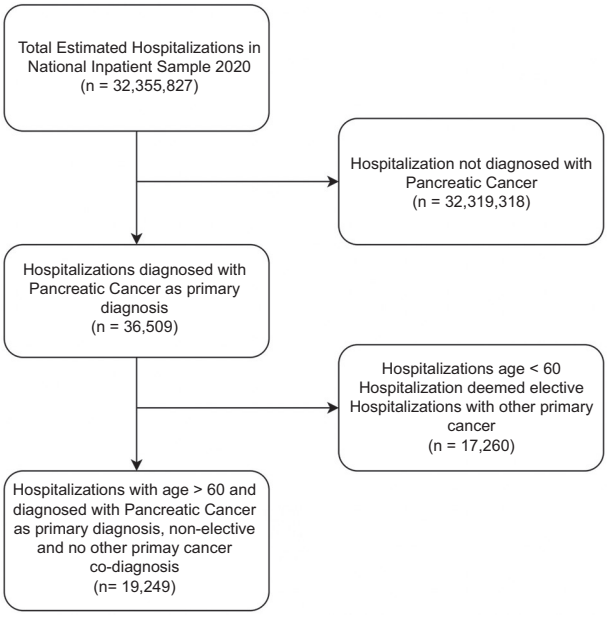

Figure 1 Inclusion flow diagram for elderly patients admitted with pancreatic cancer

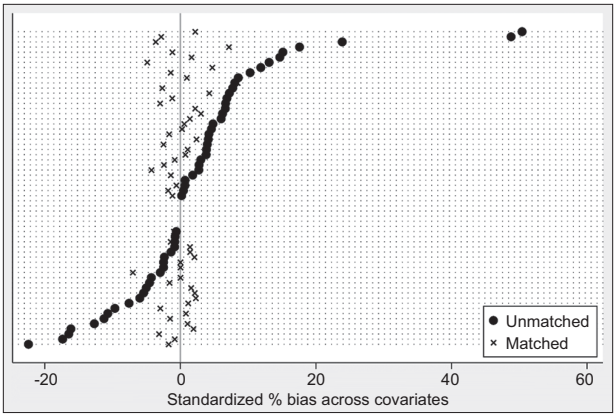

Figure 2 Comparison of cohorts before and after propensity matching

Outcome measures

In our study, the primary outcome was inpatient mortality, compared between the groups with and without long-term aspirin use, among patients hospitalized with pancreatic cancer. Additionally, we evaluated the presence of other clinical outcomes and operative complications, hospitalizations, and related costs. Other variables included demographics and socioeconomic information, such as comorbidities, race, hospital types and regions, and patient's insurance status.

Statistical analysis

Data analyses were performed using StataBE 17.0 software (StataCorp, College Station, TX). To generate nationally representative estimates, we employed weighted sampling techniques in accordance with the HCUP-NIS guidelines. Descriptive statistics were computed for continuous variables, yielding mean and standard deviation (SD), and for categorical variables, expressed as percentages. To compare proportions, Fisher's exact test was used for categorical variables, while the Student's *t*-test was employed for continuous variables. Covariates included in our analyses were selected based on a comprehensive literature review, prior research findings, and well-established confounding factors. Multivariate survey logistic regression models were constructed to calculate adjusted odds ratios (aORs) for primary and secondary outcomes. For continuous outcomes, multivariable linear regression analyses were conducted. Outcomes were adjusted for potential patient and hospital-level confounders, including age, sex, race, CCI, median income, hospital size (no. of beds), hospital location, teaching status, insurance type, diagnoses for which aspirin is a major treatment option (such as stroke and coronary artery disease), presence of metastasis, history of chemotherapy, history of radiotherapy and other comorbidities. A P-value of <0.05 was considered statistically significant.

Ethical considerations

Since the NIS database lacks patient and hospital-specific identifiers, our study did not require Institutional Review Board approval. However, we ensured that our study adhered to the ethical standards for studies of human subjects.

Data availability

The NIS is a publicly available all-payer inpatient database, encompassing hospitalization data from over 7 million hospital stays. This extensive dataset allows for the assessment of national and regional estimates across a wide range of healthcare topics. The NIS database is available at: https://www.hcup-us.ahrq.gov.

Results

Baseline characteristic of the study cohorts

A total of 19,248 elderly hospitalizations of patients with pancreatic cancer were identified. Among these patients, 2914 (15.14%) were identified as long-term users of aspirin. Table 1 shows the baseline characteristics of the study population. Before propensity score matching, we found statistically significant differences between the aspirin-using and non-aspirin groups, in terms of race, hospital region, insurance status, and some comorbidities. After matching the cohorts, the total hospitalizations in the non-aspirin group came to 7294, whereas the aspirin cohort totaled 2724 cases. After post-propensity analysis, only hyperlipidemia and coronary artery disease proportion in each analysis group differ significantly in the post-propensity group.

Inpatient mortality

Crude mortality rates in both groups were reported. Supplementary Table 1 shows the outcomes for records hospitalized with pancreatic cancer, stratified by the use of aspirin, under multivariate analysis. After adjusting for socioeconomic status and potential cofounders, we found that patients with long-term aspirin use had statistically lower odds of inpatient mortality compared to the non-aspirin cohort (3.26% vs. 6.34%, aOR 0.55, 95% confidence interval [CI] 0.33-0.92; P=0.023). Fig. 3 illustrates the ORs for mortality across multiple patient variables. Table 2 shows the outcomes using the propensity-matched cohorts. Under propensity score matching, with matched socioeconomic status and other comorbidities (Table 2), patients taking aspirin still had statistically lower odds of inpatient mortality (3.12% vs. 6.03%, aOR 0.49, 95%CI 0.28-0.85; P=0.011). Supplementary Table 2 shows the inpatient mortality odds for socioeconomic data and comorbidities used in this study, for non-stratified records with pancreatic cancer, when compared to baseline for each factor. An analysis of other socioeconomic data and comorbidities without stratifying by the presence of aspirin (Supplementary Table 2) revealed that only stroke had statistically significant odds of altering inpatient

Table 1 Baseline characteristics for elderly patients with pancreatic cancer, stratified by the long-term use of aspirin

Factors	With aspirin (%)	Without aspirin (%)	P-value
% of hospitalizations with pancreatic cancer	16,334 (84.86%)	2914 (15.14%)	
Race			0.041
Caucasians	70.33%	74.17%	
African Americans	13.16%	14.49%	
Hispanics	8.83%	6.28%	
Asians	4.39%	2.44%	
Natives	0.34%	0.52%	
Others	2.94%	2.09%	
Hospital location			0.837
Rural	4.01%	3.77%	
Urban non-teaching	14.02%	13.21%	
Urban teaching	81.97%	83.02%	
Hospital region			0.003
Northeast	22.62%	16.64%	
Midwest	22.59%	25.90%	
South	33.32%	40.31%	
West	19.47%	17.15%	
Insurance Status			<0.001
Medicare	75.92%	84.04%	
Medicaid	5.37%	2.28%	
Private insurance	17.14%	12.63%	
Self-payment	1.57%	1.05%	
Patient location			0.558
Central metro area	31.64%	29.60%	
Suburban metro area	24.67%	26.51%	
250K – 1M area	20.77%	18.76%	
50K – 250K area	8.08%	7.92%	
Micropolitan area	8.17%	9.29%	
Others	6.67%	7.92%	
Hospital type			0.910
Government	10.38%	10.98%	
Non-profit	78.73%	78.39%	
For-profit	10.90%	10.63%	
Comorbidities			
Hypertension	49.22%	55.75%	0.004
Hyperlipidemia	43.13%	66.72%	<0.001
Diabetes mellitus	18.76%	20.58%	0.319
Coronary artery disease	15.52%	37.05%	<0.001
Obesity	8.51%	10.46%	0.136
Chronic kidney disease	14.14%	18.52%	0.006
End-stage renal disease	1.29%	1.20%	0.866
COPD	10.38%	15.44%	<0.001
Tobacco use	0.46%	0.69%	0.478
COVID-19	0.46%	1.03%	0.082
Stroke	0.80%	0.86%	0.878
Peripheral artery disease	2.94%	6.69%	<0.001
Heart failure	11.17%	13.21%	0.154
Metastatic presence	17.17%	12.67%	<0.001
Alcoholic use	3.70%	2.40%	0.113
Chemotherapy history	5.73%	2.90%	0.009
Radiation history	3.83%	2.71%	0.200

Bold denotes statistically significant at P<0.005

GI, gastrointestinal; M, millions; K, thousands; COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease

mortality outcomes (0.81%, aOR 3.36, 95%CI 1.27-8.89; P=0.014). Supplementary Table 3 shows the inpatient mortality odds for socioeconomic and comorbidity data used in this study, in patients taking long-term aspirin, when compared to baseline in each factor. An analysis of factors predicting inpatient mortality rates (Supplementary Table 3) showed that only stroke

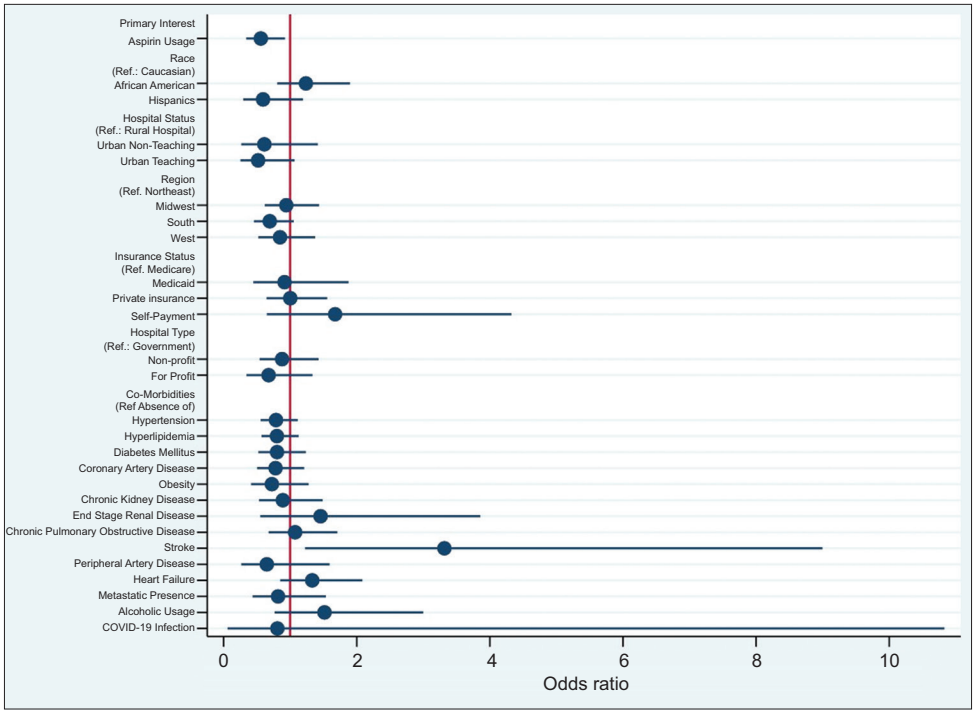

Figure 3 Odd ratios for effect of various demographic and socioeconomic data on inpatient mortality

Table 2 Outcomes for elderly patients with pancreatic cancer, stratified by the use of aspirin, with propensity score matching

Outcome	Without aspirin (%)	With aspirin (%)	aOR (95%CI) multivariate	P-value
Number of hospitalizations	7294	2724		
Inpatient mortality	6.32%	3.28%	0.57 (0.33, 0.96)	0.036
Mean length of stay (days)	6.47	5.69	-0.72 (-1.17, -0.26)	0.002
Mean total hospital cost	18,326.60	17,275.86	-893.87 (-2,361, 573)	0.233
Acute kidney injury	23.78%	21.10%	0.80 (0.61, 1.04)	0.106
Acute respiratory failure	4.66%	2.94%	0.60 (0.34, 1.08)	0.091
Shock	2.74%	0.55%	0.18 (0.05, 0.68)	0.011
Sepsis	3.50%	1.83%	0.52 (0.26, 1.05)	0.070
Mechanical ventilation	1.44%	0.73%	0.38 (0.12, 1.22)	0.107
Palliative use	2.33%	1.83%	0.69 (0.34, 1.39)	0.303
Coagulopathy	5.28%	3.30%	0.61 (0.37, 1.02)	0.063
Mental status change	5.89%	5.14%	0.87 (0.55, 1.37)	0.554
DVT/PE	6.65%	4.59%	0.76 (0.47, 1.24)	0.285

Bold denotes statistically significant at P<0.005
DVT, deep vein thrombosis; PE, pulmonary embolism

increased the odds of inpatient mortality (0.86%, aOR 3.31, 95%CI 1.22-8.99; P=0.019). Using the adjusted cohorts, stroke still had a statistically significant impact on inpatient mortality. Supplementary Table 4 shows the factors predicting inpatient mortality, adjusted for socioeconomic status and comorbidities, after propensity score matching.

Resource utilization and other clinical outcomes

In the aspirin cohort, our findings indicated a significantly shorter mean length of stay (beta coefficient -0.52, 95%CI -0.93 to -0.11; P=0.012), as well as lower odds of shock (aOR 0.23, 95%CI 0.06-0.78; P=0.019), and lower

odds of acute kidney injury (aOR 0.76, 95% CI 0.59-0.98; P=0.039). After cohorts were matched using the propensity score method, the previous statistically significant outcomes remained mostly significant. It should be noted that no diagnosis of gastrointestinal bleeding was found in any of our elderly subpopulation.

Discussion

To our knowledge, this is the first study to explore the effect of long-term use of aspirin on elderly patients admitted with pancreatic cancer. Furthermore, this is also the first study to investigate the factors that predict the odds of inpatient mortality, using comprehensive socioeconomic status factors in the analysis. We report that the long-term use of aspirin is associated with a lower risk of inpatient mortality and other clinical outcomes, even after compensating for socioeconomic status and comorbidities. In addition, some socioeconomic factors and comorbidities contribute to the risk of overall inpatient mortality. However, after propensity matching of both cohorts, those factors may not impact the odds of inpatient mortality.

We found higher proportions of Caucasians and African Americans associated with long-term aspirin use. This is similar to a study by Sanchez *et al* [19], who found a larger proportion of Caucasians who used aspirin, compared to other races. We also found statistically significant differences in the prevalence of aspirin use in relation to hospital region. Although some prior publications have reported this association [20], exploring it further may provide a better context for aspirin use in the future. As expected, the aspirin cohort had a lower prevalence of hypertension, hyperlipidemia, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease and peripheral artery disease. This is due to the possible or prior use of aspirin in these patient groups, as similarly reported in the literature [21]. The role of aspirin in the prevention of atherosclerotic cardiovascular disease is well documented in the literature [22], and supports the results in our study. The capability of aspirin to reduce vascular complications is primarily attributed to its inhibition of cyclooxygenase, which leads to a decrease in thromboxane A2 levels, thereby preventing platelet activation and aggregation. Additionally, aspirin interferes with the release of inflammatory cytokines and growth factors, disrupting key processes that contribute to the development of cardiovascular-related complications [23,24]. Similarly, aspirin use was associated with a lower prevalence of metastases. This association is similar to that reported by Algra *et al* [25], who found that regular aspirin decreases metastasis for various cancers, and to the finding of Rothwell *et al* [26] that aspirin use reduced the risk of distant metastasis. These outcomes may be attributed to several proposed mechanisms, including reduction of growth factors that promote metastatic migration, inhibition of tumor suppressor genes, and reduction of pro-metastatic signals through disruption of the phospholipid metabolism [27].

We found a reduction in the odds of inpatient mortality, in pancreatic cancer hospitalizations with long-term aspirin usage, even after adjusting using propensity score matching. Although prior research found that aspirin use was linked to a lower incidence of pancreatic cancer [28-30], this is the first study to establish an association between inpatient mortality and long-term aspirin use. In a study of a population with hepatocellular carcinoma [31], a similar inverse association of long-term aspirin use and inpatient mortality was also observed. We postulate several reasons that may contribute to this result. First, aspirin is a cyclooxygenase inhibitor, and cyclooxygenase enzymes are directly involved in the proliferation of cancer cells [32,33]. Aspirin also contains other interference mechanisms, such as lowering chemoradiation resistance [34], cancer-associated inflammation [35] and platelet driven anticarcinogenic activities [36]. These may help counteract the high mortality rates pancreatic cancer patients usually encounter [37]. Second, the lower odds of shock in the aspirin cohort may indirectly reduce the inpatient mortality rates. In our study, aspirin cohorts had lower odds of shock, as reported in the studies of Iqbal *et al* study [38] and Ahsberg *et al* [39], in which aspirin use had a lower risk of a fatal outcome. We hypothesize that aspirin could reduce the activation of inflammation cascades and increase their resolution, as seen in a study by Otto *et al* [40], but additional investigation needs to be conducted regarding this relationship. Finally, the lower prevalence of metastasis in aspirin-taking cohorts compared to non-aspirin cohorts may indirectly affect the inpatient mortality rates. Metastasis is one of the major conditions that contribute to mortality in cancer patients [41], and the reduction of metastasis in the aspirin population group, may have contributed to the lower inpatient mortality.

Although gastrointestinal bleeding is one of the major concerns for the use of aspirin, our study find no records of co-diagnosis of this complication. The current literature reports a lower severity of these bleedings with the use of aspirin [42], and additional studies should be conducted to verify these safety concerns.

Regarding the factors predicting inpatient mortality for elderly hospitalizations with pancreatic cancer, we found that only stroke increased the risk of inpatient mortality in our nationally representative sample, in the absence of stratification by the presence of aspirin. The results build upon those of Chan *et al* [43], who found that pancreatic cancer is linked to higher odds of stroke. Our study is similar to that of Bonnerot *et al* [44], who suggested that inflammatory cytokines may play a role in developing stroke and worsening outcomes. Although a temporal relationship cannot be established, given the nature of the study database, stroke prevention care may provide more benefits for those who are admitted with pancreatic cancer.

The study's substantial strength derives from its extensive, nationally representative sample, which effectively mitigates the referral bias commonly observed in single-center cohort studies. The diverse patient population accurately reflects the inpatient disease burden and clinical characteristics

of pancreatic cancer patients across the United States. Furthermore, the sizable dataset enhances the study's statistical power, enabling the detection of even subtle disparities between groups [45]. Through rigorous adjustments for patient demographics, hospital characteristics, and the CCI, coupled with propensity score matching, we sought to mitigate the potential confounding effects of these variables on our analysis.

However, this study was not without limitations. The administrative and cross-sectional nature of the NIS database restricted the acquisition of crucial patient-level data, such as clinical characteristics, radiographic, echocardiographic and laboratory results, which are essential for stratifying patient severity and accurately characterizing their health status. In addition, the lack of detail of aspirin use, such as dose, duration and rationale of use, may reduce the level of granularity in applying these findings in practice. Despite our best efforts to capture patient cancer status and staging by chemotherapy use, radiotherapy use and distant metastasis, additional staging data would assist the clinician in applying these data in a more practical approach. Moreover, the database's exclusive emphasis on in-hospital occurrences may inadvertently overlook significant post-discharge sequelae, including out-of-hospital sudden cardiac death, long-term mortality and the emergence of complications. Additionally, the inherent constraints of observational research impede the definitive establishment of causal linkages between in-hospital complications and pancreatic cancer, as the temporal sequence between these events cannot be conclusively ascertained.

In the context of pancreatic cancer, there is very limited literature exploring the association between non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs) and inpatient mortality. While a study by Lad *et al* found no association between non-aspirin NSAIDs and pancreatic cancer mortality, it also reported no significant association between aspirin use and pancreatic cancer mortality, which contrasts with our findings [46]. This also warrants further studies to explore the effect of other NSAIDs or antiplatelet agents on pancreatic cancer mortality. Our findings underscore the inverse relationship in pancreatic cancer patients, linking the use of aspirin with lower mortality rates and a lower incidence of adverse events. Future research can be expanded to investigate the association between different types of antiplatelet agents or other non-aspirin NSAIDs and inpatient mortality in patients with pancreatic cancer. Further epidemiological investigations are necessary to elucidate the causal mechanisms underlying the observed associations between aspirin and adverse outcomes in elderly patients with pancreatic cancer. Understanding the etiology and causality between aspirin and pancreatic cancer may lead to better outcomes in this subpopulation group. To enhance the care of elderly patients, it may be necessary to optimize care pathways, implement early interventions to mitigate adverse outcomes, and provide comprehensive multidisciplinary support to address their complex medical needs.

Summary Box

What is already known:

- Pancreatic cancer is one of the leading causes of death in the United States
- Aspirin has a promising role in cancer prevention and treatment
- Racial status has an impact on clinical care in this subpopulation group

What the new findings are:

- Aspirin use was associated with lower inpatient mortality in elderly patients with pancreatic cancer
- Stroke was associated with higher inpatient mortality in this subpopulation
- Propensity matching, after adjusting for possible bias, produced similar results

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Supplementary material

Supplementary Table 1 Outcomes for elderly patients with pancreatic cancer, stratified by the use of aspirin, before propensity score matching

Outcome	Without aspirin (%)	With aspirin (%)	aOR (95%CI) multivariate	P-value
Number of hospitalizations	16,334 (84.86%)	2,914 (15.14%)		
Inpatient mortality	6.34%	3.26%	0.56 (0.34, 0.94)	0.028
Mean length of stay (days)	6.40	5.83	-0.52 (-0.93, -0.11)	0.012
Mean total hospital cost	18,606.12	17,540.21	-510 (-1,835, 814)	0.450
Acute kidney injury	22.44%	21.27%	0.76 (0.59, 0.98)	0.039
Acute respiratory failure	4.65%	3.43%	0.66 (0.38, 1.14)	0.145
Shock	2.69%	0.51%	0.23 (0.06, 0.78)	0.019
Sepsis	3.67%	2.40%	0.57 (0.30, 1.09)	0.090
Mechanical ventilation	1.25%	0.86%	0.52 (0.16, 1.61)	0.259
Palliative use	2.08%	1.72%	0.89 (0.47, 1.66)	0.724
Coagulopathy	5.39%	3.43%	0.64 (0.40, 1.02)	0.065
Mental status change	6.21%	5.83%	0.90 (0.58, 1.37)	0.628
DVT/PE	7.44%	4.63%	0.86 (0.55, 1.35)	0.531

Bold denotes statistically significant at P<0.005
DVT, deep vein thrombosis; PE, pulmonary embolism

Supplementary Table 2 Factors predicting inpatient mortality for elderly patients with pancreatic cancer, without stratification for the use of aspirin

Factors	Total (% of subcategory)	Mortality odds	
		Multivariate analysis	Multivariate P-value
Race			
Caucasians	70.92%	Reference point for race	
African Americans	13.36%	1.23 (0.80, 1.89)	0.330
Hispanics	8.45%	0.59 (0.29, 1.20)	0.147
Asians	4.09%	1.08 (0.50, 2.29)	0.839
Natives	0.37%	N/A	0.190
Others	2.82%	0.47 (0.15, 1.44)	
Hospital location			
Rural	3.97%	Reference point for hospital location	
Urban non-teaching	13.90%	0.61 (0.26, 1.42)	0.260
Urban teaching	82.13%	0.51 (0.25, 1.06)	0.074
Hospital region			
Northeast	21.71%	Reference point for hospital region	
Midwest	23.09%	0.92 (0.61, 1.41)	0.726
South	36.08%	0.68 (0.44, 1.03)	0.073
West	19.12%	0.84 (0.52, 1.36)	0.491
Insurance type			
Medicare	77.15%	Reference point for insurance type	
Medicaid	0.49%	0.94 (0.46, 1.94)	0.881
Private insurance	16.46%	1.01 (0.65, 1.57)	0.951
Self-payment	1.49%	1.70 (0.65, 4.40)	0.271
Patient location			
Central metro area	31.33%	Reference Point for Patient Location	
Suburban metro area	24.95%	1.17 (0.77, 1.79)	0.444
250K – 1M area	20.46%	0.99 (0.62, 1.57)	0.975
50K – 250K area	8.06%	1.51 (0.89, 2.58)	0.125
Micropolitan area	8.34%	0.95 (0.48, 1.88)	0.892
Others	6.86%	1.23 (0.67, 2.28)	0.491
Hospital type			
Government	10.47%	Reference Point for Hospital Type	
Non-profit	78.68%	0.88 (0.54, 1.42)	0.610
For-profit	10.86%	0.68 (0.34, 1.33)	0.264
Comorbidities			
Hypertension	50.21%	0.78 (0.55, 1.10)	0.161
Hyperlipidemia	46.70%	0.77 (0.55, 1.08)	0.137
Diabetes mellitus	19.04%	0.80 (0.52, 1.23)	0.317
Coronary artery disease	18.78%	0.72 (0.47, 1.11)	0.147
Obesity	8.81%	0.70 (0.39, 1.24)	0.233
Chronic kidney disease	14.81%	0.88 (0.52, 1.49)	0.645
End-stage renal disease	1.27%	1.48 (0.55, 3.95)	0.425
COPD	11.14%	1.05 (0.66, 1.66)	0.833
Tobacco use	0.49%	N/A	
COVID-19	0.55%	0.82 (0.06, 10.47)	0.881
Stroke	0.81%	3.36 (1.27, 8.89)	**0.014**
Peripheral artery disease	3.51%	0.61 (0.25, 1.51)	0.294
Heart failure	11.48%	1.35 (0.87, 2.11)	0.176
Metastatic presence	49.87%	0.83 (0.44, 1.56)	0.567
Alcoholic use	3.51%	1.53 (0.78, 3.02)	0.212

Bold denotes statistically significant at P<0.005

GI, gastrointestinal; N/A denotes too small or no deaths in subpopulation group; M, millions; K, thousands; COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease

Supplementary Table 3 Factors predicting inpatient mortality for elderly patients with pancreatic cancer, taking long-term aspirin, before propensity score matching

Factors	Total (% of subcategory)	Mortality odds	
		Multivariate analysis	Multivariate P-value
Race			
Caucasians	74.17%	Reference Point for Race	
African Americans	14.49%	1.23 (0.80, 1.89)	0.332
Hispanics	6.28%	0.59 (0.29, 1.19)	0.143
Asians	2.44%	1.04 (0.49, 2.22)	0.899
Natives	0.52%	N/A	
Others	2.09%	0.46 (0.15, 1.41)	0.178
Hospital location			
Rural	3.77%	Reference point for hospital location	
Urban non-teaching	13.21%	0.61 (0.26, 1.41)	0.251
Urban teaching	83.02%	0.51 (0.25, 1.06)	0.074
Hospital region			
Northeast	16.64%	Reference point for hospital region	
Midwest	25.90%	0.94 (0.61, 1.43)	0.781
South	40.31%	0.69 (0.45, 1.05)	0.087
West	17.15%	0.84 (0.52, 1.37)	0.503
Insurance type			
Medicare	84.04%	Reference point for insurance type	
Medicaid	2.28%	0.91 (0.44, 1.87)	0.811
Private insurance	12.63%	1.00 (0.64, 1.55)	0.993
Self-payment	1.05%	1.67 (0.64, 4.32)	0.286
Patient location			
Central metro area	29.60%	Reference point for patient location	
Suburban metro area	26.51%	1.18 (0.77, 1.79)	0.440
250K – 1M area	18.76%	0.98 (0.61, 1.55)	0.939
50K – 250K area	7.92%	1.49 (0.87, 2.56)	0.138
Micropolitan area	9.29%	0.94 (0.47, 1.87)	0.868
Others	7.92%	1.23 (0.66, 2.27)	0.507
Hospital type			
Government	10.98%	Reference point for hospital type	
Non-profit	78.39%	0.87 (0.54, 1.42)	0.601
For-profit	10.63%	0.67 (0.34, 1.33)	0.261
Co-morbidities			
Hypertension	55.75%	0.78 (0.55, 1.11)	0.177
Hyperlipidemia	66.72%	0.80 (0.57, 1.12)	0.202
Diabetes mellitus	20.58%	0.80 (0.52, 1.23)	0.319
Coronary artery disease	37.05%	0.78 (0.50, 1.20)	0.268
Obesity	10.46%	0.72 (0.41, 1.27)	0.266
Chronic kidney disease	18.52%	0.89 (0.53, 1.48)	0.657
End-stage renal disease	1.20%	1.45 (0.55, 3.85)	0.448
COPD	15.44%	1.07 (0.67, 1.70)	0.760
Tobacco use	0.69%	N/A	
COVID-19	1.03%	0.80 (0.06, 10.82)	0.872
Stroke	0.86%	3.31 (1.22, 8.99)	0.019
Peripheral artery disease	6.69%	0.64 (0.26, 1.59)	0.345
Heart failure	13.21%	1.33 (0.85, 2.08)	0.210
Metastatic presence	42.51%	0.81 (0.43, 1.53)	0.532
Alcoholic use	2.40%	1.51 (0.76, 2.99)	0.232

Bold denotes statistically significant at P<0.005

GI, gastrointestinal; N/A denotes too small or no deaths in subpopulation group; M, millions; K, thousands; COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease

Supplementary Table 4 Factors predicting inpatient mortality for elderly patients with pancreatic cancer, taking long-term aspirin, with propensity score matching

Factors	Total (% of subcategory)	Mortality odds	
		Multivariate analysis	Multivariate P-value
Race			
Caucasians	74.50%	Reference point for race	
African Americans	14.50%	1.10 (0.59, 2.07)	0.751
Hispanics	6.06%	0.89 (0.34, 2.33)	0.824
Asians	2.57%	1.87 (0.65, 5.35)	0.242
Natives	0.37%	N/A	
Others	2.02%	0.71 (0.19, 2.58)	0.610
Hospital location			
Rural	3.85%	Reference point for hospital location	
Urban non-teaching	13.39%	0.90 (0.21, 3.86)	0.894
Urban teaching	82.75%	0.97 (0.27, 3.42)	0.962
Hospital region			
Northeast	17.43%	Reference point for hospital region	
Midwest	25.69%	1.14 (0.61, 2.13)	0.661
South	39.08%	0.92 (0.50, 1.68)	0.805
West	17.80%	0.83 (0.41, 1.67)	0.612
Insurance type			
Medicare	83.85%	Reference point for insurance type	0.611
Medicaid	2.20%	0.67 (0.14, 3.07)	0.781
Private insurance	13.03%	1.09 (0.58, 2.05)	0.960
Self-payment	0.92%	0.94 (0.12, 7.27)	
Patient location			
Central metro area	30.64%	Reference point for patient location	
Suburban metro area	26.61%	1.28 (0.72, 2.26)	0.395
250K – 1M area	18.17%	1.16 (0.60, 2.23)	0.640
50K – 250K area	7.89%	1.39 (0.59, 3.24)	0.443
Micropolitan area	9.54%	1.28 (0.51, 3.22)	0.588
Others	7.16%	0.83 (0.29, 2.32)	0.727
Hospital type			
Government	10.83%	Reference Point for Hospital Type	
Non-profit	79.08%	1.09 (0.48, 2.49)	0.825
For-profit	10.09%	0.67 (0.22, 2.03)	0.488
Co-morbidities			
Hypertension	55.60%	0.79 (0.46, 1.36)	0.410
Hyperlipidemia	66.61%	0.78 (0.51, 1.19)	0.258
Diabetes mellitus	20.37%	0.84 (0.45, 1.56)	0.592
Coronary artery disease	35.60%	0.91 (0.55, 1.56)	0.724
Obesity	10.83%	0.54 (0.24, 1.24)	0.149
Chronic kidney disease	17.80%	0.87 (0.39, 1.95)	0.747
End-stage renal disease	1.28%	0.80 (0.15, 4.06)	0.791
COPD	14.86%	1.04 (0.56, 1.92)	0.883
Tobacco use	0.55%	N/A	
COVID-19	0.73%	N/A	
Stroke	0.73%	4.77 (1.46, 15.57)	0.010
Peripheral artery disease	6.06%	0.69 (0.23, 2.10)	0.523
Heart failure	12.84%	1.48 (0.76, 2.88)	0.247
Metastatic presence	42.94%	1.21 (0.49, 2.95)	0.669
Alcoholic use	2.57%	1.57 (0.50, 4.93)	0.437
Chemotherapy history	2.90%	1.39 (0.74, 2.62)	0.303
Radiotherapy history	2.71%	1.29 (0.60, 2.75)	0.507

Bold denotes statistically significant at P<0.005

GI, gastrointestinal; N/A denotes too small or no deaths in subpopulation group; M, millions; K, thousands; COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease