A Population-Based Evaluation of Severity and Mortality Among Transferred Patients With Acute Pancreatitis

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Objectives: This study aimed to compare severity of acute pancreatitis (AP) and mortality rates between transferred and nontransferred patients and to determine the factors that influence the decision to transfer.

Methods: A retrospective analysis coding a statewide administrative database in Maryland was conducted. *Severity* was defined by presence of organ failure (OF), need for intensive care unit (ICU), mechanical ventilation (MV), or hemodialysis.

Results: There were 71,035 discharges for AP, with 1657 (2.3%) patient transfers. Transferred patients had more multisystem OF (5.6% vs 1.2%), need for ICU (22.8% vs 4.3%), MV (13.1% vs 1.4%), hemodialysis (4.2% vs 2.7%), and higher mortality (6.1% vs 1.1%) compared with nontransferred patients ($P < 0.0001$). After adjusting for disease severity, mortality was similar between the transferred patients and the nontransferred patients (OR, 1.37; 95% confidence interval, 0.96–1.97). Younger (OR, 0.99), African American (OR, 0.55), and uninsured (OR, 0.46) patients were less likely to be transferred, whereas patients with multisystem OF (OR, 3.5), need for ICU (OR, 2.3), or MV (OR, 2.1) were more likely to be transferred ($P < 0.0001$).

Conclusions: Transferred patients with AP have more severe disease and higher overall mortality. Mortality is similar after adjusting for disease severity. Disease severity, insurance status, race, and age all influence the decision to transfer patients with AP.

Key Words: acute pancreatitis, transfer, mortality, severity

Abbreviations: AP – acute pancreatitis, CI – confidence interval, ERCP – endoscopic retrograde cholangiopancreatography, HD – hemodialysis, *ICD-9-CM – International Classification of Diseases, Ninth Revision, Clinical Modification*, ICU – intensive care unit, LOS – length of stay, MSOF – multisystem organ failure, MV – mechanical ventilation, OF – organ failure, SS OF – single-system organ failure

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There are approximately 275,000 yearly admissions for acute pancreatitis (AP) in the United States with a mortality rate of 1.0% and a yearly cost of \$2.6 billion.[1–3] Despite a decrease in mortality for the past 2 decades, the number of admissions due to AP continues to increase in the United States and Western Europe.[4–7] Although conservative management results in clinical improvement in most patients, approximately 15% to 20% of patients develop severe AP.[8,9] Many studies have shown that the increased mortality among patients with severe AP is primarily caused by persistent or multisystem organ failure (MSOF), whereas one recent analysis reported that organ failure (OF) and infected pancreatic necrosis result in equivalent mortality rates.[10–12]

Given the higher mortality of severe AP, prior studies and consensus guidelines have recommended transferring these patients to referral centers.[13–15] However, there is little evidence showing improved outcomes by transferring these patients. Among consecutive patients with AP, de Beaux et al[14] found increased severity on the basis of MSOF (51% vs 26%) and higher mortality rates (18.8% vs 1.9%) in transferred patients compared with patients who were directly admitted. Among patients with severe AP, the results of prior studies are conflicting.[13,16–18] Two studies demonstrated increased disease severity (on the basis of the Acute Physiology and Chronic Health Evaluation II scores, OF, and infected necrosis) and higher mortality rates among transferred patients,[13,18] whereas 2 other studies found comparable severity and mortality.[16,17]

The aims of this study were to use a population-based administrative database to (1) compare the severity of AP between transferred and nontransferred patients, (2) compare the mortality between transferred and nontransferred patients after adjusting for disease severity, and (3) identify the factors that influence the decision to transfer patients.

MATERIALS AND METHODS

Population

The Maryland Health Services Cost Review Commission database contains data on all patient discharges from nonfederal acute care hospitals in the state of Maryland. Each patient discharge contains information on demographic characteristics, primary and secondary diagnoses, primary and secondary procedures, source of admission, insurance type, length of stay (LOS), hospital charges, as well as disposition.[19] Using the Maryland Health Services Cost Review Commission database, we evaluated all adult patient (18 years and older) discharges with a primary diagnosis of AP (*International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* [*ICD-9-CM*] of 577.0) between January 1, 1994, and December 31, 2010. *Nontransferred patients* were defined as those who remained in the same hospital to which they initially presented until discharge or death, whereas *transferred patients* were defined as those who were transported to another facility. Hospitals with less than 10 discharges during the study period (n = 6), that closed (n = 4), or that focus on rehabilitation services (n = 4) were excluded.

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Definition of Severity

Severity was defined by the presence of OF, need for intensive care unit (ICU), mechanical ventilation (MV), or hemodialysis (HD). *Organ failure* was defined using the *ICD-9-CM* codes as described in a prior study.[20] Renal failure (*ICD-9-CM* codes 584.0–584.9, and 586), pulmonary failure (*ICD-9-CM* codes 518.81, 518.82, 518.85, 786.09, and 799.1), and cardiovascular failure (*ICD-9-CM* codes 458.0, 785.5, 785.51, 785.59, 458.8, 458.9, and 796.3) were all evaluated. The presence of OF in 2 or more systems was defined as *MSOF*. Interventions included ICU stay, MV (*ICD-9-CM* procedure codes 96.70–96.72), and HD (*ICD-9-CM* procedure code 39.95). *Mortality* was defined as death occurring during hospitalization.

Predictors of Transfer

Demographic variables included patient age, sex, race, and type of insurance. Comorbidity was tabulated using the Elixhauser scale.[21] *Length of stay* was defined as the total number of inpatient days in the hospital from which the patient was ultimately discharged. For transferred patients, LOS and total hospital charges did not include the inpatient stay and charges resulting from the patient's initial hospitalization (before transfer). *Teaching hospitals* were defined as those hospitals that have graduate medical education programs. *High-volume hospitals* were defined as those that have 118 or more AP admissions per year on the basis of a prior study evaluating the National Inpatient Sample.[22] Hospital bed size across the state of Maryland was divided into thirds (<141, 141–280, and >280 beds). *Referral hospitals* were defined as those facilities to which patients were transferred for subsequent care.

Statistical Analysis

Continuous variables were compared using the Student *t* test and categorical variables were compared using the χ^2 test between the transferred patients and the nontransferred patients. The trends for mortality over time were evaluated using the Cochran-Armitage test. Demographic, hospital, and severity variables were evaluated using multivariable logistic regression to identify the predictors

TABLE 1. Demographic, Clinical, and Hospital-Based Characteristics of the Transferred Patients and the Nontransferred Patients With AP

	Nontransferred (n = 69,378)	Transferred (n = 1657)	*P*
Age, mean (SD), y	51.4 (16.8)	52 (16.5)	0.20
Male, n (%)	36,017 (51.9)	894 (54)	0.10
Race, n (%)			
White	36,934 (53.2)	1086 (65.5)	
African American	29,127 (42)	443 (26.7)	
Other	3317 (4.8)	128 (7.7)	<0.0001
Payor, n (%)			
Medicare	19,897 (28.7)	510 (30.8)	
Medicaid	12,474 (18)	228 (13.8)	
Commercial	27,280 (39.3)	828 (50)	
Uninsured	9727 (14)	91 (5.5)	<0.0001
Teaching hospital, n (%)	21,120 (30.4)	1210 (73)	<0.0001
High-volume hospital, n (%)	30,970 (44.6)	1161 (70.1)	<0.0001
Hospital bed size, n (%)			
<141	11,634 (16.8)	149 (9.0)	
141–280	23,944 (34.5)	302 (18.2)	
>280	33,800 (48.7)	1206 (72.8)	<0.0001
Referral hospital, n (%)	4477 (6.5)	958 (57.8)	<0.0001
LOS, mean (SD), d	5.1 (6.2)	14 (21)	<0.0001
Total charges, mean, (SD), $	8255 (15,908)	38,867 (80,937)	<0.0001
ICU, mean (SD), d	5.8 (10.1)	18.9 (24)	<0.0001
No. comorbidities, n (%)			
0	7447 (10.7)	236 (14.2)	
1	13,662 (19.7)	342 (20.6)	
2	16,232 (23.4)	415 (25.1)	
3	14,041 (20.2)	302 (18.2)	
≥4	17,996 (26)	362 (21.9)	<0.0001
OF, n (%)			
None	64,117 (92.4)	1347 (81.3)	
SS OF	4408 (6.4)	217 (13.1)	
MSOF	853 (1.2)	93 (5.6)	<0.0001
HD, n (%)	1859 (2.7)	70 (4.2)	<0.0001
MV, n (%)	986 (1.4)	217 (13.1)	<0.0001
ICU, n (%)	2956 (4.3)	378 (22.8)	<0.0001
Mortality, n (%)	784 (1.1)	101 (6.1)	<0.0001

TABLE 2. Predictors of Mortality Among All 71,035 Patients With AP

	Odds Ratio*	95% CI
Transferred patient	1.38	0.96–1.97
Age[†]	1.50	1.41–1.61
Male sex	1.18	1.00–1.38
African American race	0.94	0.78–1.12
Payor (vs commercial)		
Commercial	Reference	
Medicare	1.50	1.19–1.90
Medicaid	1.32	0.99–1.74
Uninsured	1.23	0.86–1.75
No. comorbidities		
0	Reference	
1	0.97	0.61–1.57
2	1.09	0.70–1.71
3	1.27	0.81–1.98
≥4	1.37	0.88–2.11
OF		
SS OF	5.03	4.11–6.15
MSOF	11.52	8.88–14.94
HD	2.63	2.0–3.41
MV	12.2	9.53–15.57
ICU	2.75	2.21–3.49
Nonteaching hospital	1.36	1.09–1.71
Low-volume hospital (<118 cases/y)	1.24	1.03–1.49
Hospital bed size		
>280	Reference	
141–280	0.84	0.69–1.03
<141	0.59	0.44–0.80
Nonreferral hospital	0.74	0.53–1.05
LOS, >7 d	0.57	0.47–0.71

*Multivariable analysis of predictors of mortality adjusted for all other factors in table.

[†]In this analysis, age is studied as a unit of every 10 years.

of mortality and for transfer. All analyses were performed using SAS version 9.2 (Cary, NC).

RESULTS

Description of the Population

There were a total of 71,035 patient discharges with AP from 48 hospitals during the 17-year study period. Table 1 demonstrates the comparison of demographics, hospital characteristics, and clinical parameters between the transferred patients and the nontransferred patients. There were 1657 (2.3%) transferred patients, whereas 69,378 (97.7%) patients remained in the same hospital until discharge or death. There was no difference in age and sex between the 2 groups. A significantly higher proportion of white patients were transferred (65.5% vs 53.3%, $P < 0.0001$) compared with African American patients (26.7% vs 42%, $P < 0.0001$). Fewer uninsured patients were transferred (5.5% vs 14%, $P < 0.0001$). The transferred patients were more commonly found in teaching hospitals (73% vs 30.4%, $P < 0.0001$), high-volume centers (70.1% vs 44.6%, $P < 0.0001$), and referral hospitals (57.8% vs 6.5%, $P < 0.0001$). The mean LOS (14 vs 5.1 days, $P < 0.0001$) and total hospital charges ($38,867 vs $8255, $P < 0.0001$) were significantly higher among the transferred patients.

Severity

The transferred patients had a higher incidence of single-system OF (SS OF; 13.1% vs 6.4%, $P < 0.0001$), MSOF (5.6% vs 1.2%, $P < 0.0001$), need for HD (4.2% vs 2.7%, $P < 0.0001$), need for MV (13.1% vs 4.1%, $P < 0.0001$), and need for ICU (22.8% vs 4.3%, $P < 0.0001$) when compared with the nontransferred patients.

Mortality

Mortality was higher among the transferred patients (6.1% vs 1.1%, $P < 0.0001$) with AP. Table 2 demonstrates the multivariate analysis of factors, which predict mortality in the full cohort of 71,035 patients with AP. The analysis revealed that transfer status was not a predictor of mortality (OR, 1.38; 95% confidence interval [CI], 0.96–1.97), when adjusted for all other factors. Multisystem OF (OR, 11.5; 95% CI, 8.9–14.9) and need for MV (OR, 12.2; 95% CI, 9.5–15.6) were the most significant predictors of mortality in the adjusted analysis. Older age (OR, 1.50; 95% CI, 1.4–1.6), male sex (OR, 1.2; 95% CI, 1.0–1.4), Medicare insurance (OR, 1.5; 95% CI, 1.2–1.9), need for HD (OR, 2.6; 95% CI, 2.0–3.4), and admission to nonteaching hospitals (OR, 1.4; 95% CI, 1.1–1.7) or low-volume hospitals (OR, 1.2; 95% CI, 1.0–1.5) were the less significant predictors of mortality in the multivariable analysis.

Table 3 illustrates the mortality rates between the transferred and the nontransferred patients stratified by disease severity subgroups. There were similar mortality rates between the transferred and the nontransferred patients in nearly all subgroups. Among the patients with the most severe AP, characterized by MSOF, need for ICU, and MV, mortality rates were equivalent (48.6% in the transferred patients vs 49.8% in the nontransferred patients, $P = 0.85$). Interestingly, the mortality rate was higher (55.6% vs 24.2%, $P = 0.04$) in the transferred patients with MSOF who required ICU but did not require MV as compared with the nontransferred patients with similar disease severity.

Overall, the mortality rates of AP have declined for both the transferred patients and the nontransferred patients over time ($P < 0.0001$ for trend). For each increase in year, there was a 5% decrease in the risk for mortality among the transferred patients (OR, 0.95; 95% CI, 0.94–0.97) and a 9% decrease in the risk for mortality among the nontransferred patients (OR, 0.91; 95% CI, 0.88–0.96).

TABLE 3. Mortality Rates in the Transferred Patients Versus the Nontransferred Patients Based on Severity Subgroup

Severity Subgroups	Nontransferred, n (%)	Transferred, n (%)	*P*
OF−, ICU+, MV+	24/108 (22.2)	7/44 (15.9)	0.38
OF−, ICU+, MV−	31/1871 (1.7)	4/124 (3.2)	0.2
OF−, ICU−, MV−	215/62,063 (0.3)	7/1171 (0.6)	0.15
SS OF, ICU+, MV+	59/214 (27.6)	24/79 (30.4)	0.64
SS OF, ICU+, MV−	43/405 (10.6)	7/52 (13.5)	0.54
SS OF, ICU−, MV−	89/3632 (2.5)	3/77 (3.9)	0.42
MSOF, ICU+, MV+	132/263 (49.8)	34/70 (48.6)	0.85
MSOF, ICU+, MV−	23/95 (24.2)	5/9 (55.6)	0.04

χ^2 Analysis.

+, present; −, not present.

Factors Influencing Decision to Transfer

Table 4 demonstrates the results of the multivariate analysis of the factors that influence the decision to transfer patients. Younger (OR, 0.99; 95% CI, 0.990–0.998) and African American patients (OR, 0.55; 95% CI, 0.49–0.62) were less likely to be transferred. Uninsured patients (OR, 0.46; 95% CI, 0.38–0.57) or those with Medicaid (OR, 0.77; 95% CI, 0.65–0.90) were also less likely to be transferred, whereas there was no difference for Medicare patients (OR, 1.00; 95% CI, 0.87–1.16) compared with patients with commercial insurance. Patients with SS OF (OR, 2.42; 95% CI, 2.17–2.84), MSOF (OR, 3.51; 95% CI, 2.69–4.59), need for MV (OR, 2.14; 95% CI, 1.67–2.74), or need for ICU (OR, 2.29; 95% CI, 1.94–2.70) were more likely to be transferred. Hemodialysis and comorbidity did not influence the transfer of patients. With regard to hospital characteristics, nonteaching hospitals (OR, 2.51; 95% CI, 2.07–3.05), low-volume centers (OR, 1.24; 95% CI, 1.10–1.40), and hospitals with fewer beds (<280 beds) were more likely to transfer patients with AP. An LOS of more than 7 days at the hospital of origin did not influence the decision to transfer patients.

DISCUSSION

There are several important findings from this study. The first is that the transferred patients with AP have more severe disease compared with the nontransferred patients. The second is that there is no difference in mortality rates between the transferred patients and the nontransferred patients after adjusting for the severity of disease. The third is that the decision to transfer patients is influenced by both clinical factors, such as disease severity, and nonclinical factors, such as race and insurance status.

TABLE 4. Predictors of Transfer Among Patients With AP

	Odds Ratio*	95% CI
Age	0.99	0.99–1.00
Male sex	1.07	0.96–1.18
African American race	0.55	0.49–0.62
Payor (vs commercial)		
Commercial	Reference	
Medicare	1.00	0.87–1.16
Medicaid	0.77	0.65–0.90
Uninsured	0.46	0.38–0.57
No. comorbidities		
0	Reference	
1	0.97	0.79–1.18
2	1.04	0.85–1.27
3	1.15	0.94–1.40
>4	1.11	0.91–1.35
OF		
SS OF	2.42	2.17–2.84
MSOF	3.51	2.69–4.59
HD	1.06	0.80–1.41
MV	2.14	1.67–2.75
ICU	2.29	1.94–2.70
Nonteaching hospital	2.51	2.07–3.05
Low-volume hospital (<118 cases/y)	1.24	1.10–1.40
Hospital bed size		
>280	Reference	
141–280	1.31	1.14–1.50
<141	1.79	1.52–2.1
Nonreferral hospital	1.17	0.79–1.73
LOS, >7 d	1.14	1.00–1.30

*Multivariable analysis of predictors of transfer status adjusted for all other factors in the table.

The patients with AP who are transferred tend to have more severe disease with significantly higher rates of OF, need for ICU, need for MV, and need for HD compared with the nontransferred patients. As a result, the mortality rate (6.1% vs 1.1%) for transferred patients was much higher compared with the nontransferred patients. One potential implication of our finding is that transferred patients should be excluded from retrospective clinical studies of AP because these patients will lead to overestimations of severity, which can bias study findings. This is particularly important in single-center studies.

A limited number of prior studies have evaluated outcomes among the transferred patients with AP with mixed results. Authors de Beaux et al[14] evaluated 279 consecutive patients with AP from 1989 to 1993 and found higher rates of mortality and MSOF among transferred patients compared with nontransferred patients. However, mortality was never adjusted for disease severity. Prior studies comparing mortality between transferred and nontransferred patients with severe AP have had conflicting results. One study[13] reported higher mortality in transferred patients, whereas 2 studies found no difference in mortality between transferred and nontransferred patients.[16,17] These differences are likely caused by geographic variations in clinical practice and institutional resources as well as small patient populations.

The present study found no difference in mortality between the transferred patients and the nontransferred patients after adjusting for disease severity. In addition, a multivariate analysis of factors influencing mortality demonstrated that transfer status (OR, 1.38; 95% CI, 0.96–1.97) was not a predictor of mortality. Although there was a trend toward significance, the present study used a large sample size, which should have sufficient power to detect such a difference. There are several potential explanations for this finding. First, there are few specific therapies for severe AP and treatment is largely focused on supportive care. This was demonstrated in a recent study from Taiwan, which found no differences in mortality for patients with severe AP at high-versus low-volume centers after adjusting for cholecystectomy, total parenteral nutrition, MV, and vasopressor support.[23] These supportive care measures are offered at most hospitals in the United States. Second, the management of AP has likely improved at community hospitals. This is reflected by the declining mortality rates of AP throughout the United States and Europe[4,6,7] as well as in the present study. Niederau and Hippenstiel[24] reported that appropriate conservative management of AP in community hospitals results in low rates of complications, mortality, and patient transfer to tertiary centers. One recent study compared the management of AP between a tertiary care hospital and a community hospital in Australia using the British Society of Gastroenterology guidelines.[25,26] Although there was poor overall compliance in initial severity stratification, both facilities successfully managed AP in accordance with the British Society of Gastroenterology guidelines with no differences in mortality. The authors suggested the presence of endoscopic retrograde cholangiopancreatography (ERCP) and improved ICU facilities in regional hospitals as significant factors in improving the management of AP. Third, there was a 28% increase in the total number of ICU beds in the United States from 1985 to 2000 and this has also likely contributed to the declining mortality of AP.[4,27]

The present study demonstrates no mortality benefit to transferring patients with AP, and interestingly, some subgroups actually have a higher mortality when transferred. There was a higher mortality among the transferred patients (55% vs 25%, $P = 0.04$) with MSOF who required ICU but no MV compared with the nontransferred patients. Although the total number of patients in the transferred subgroup was small (n = 9) and the increased mortality may reflect selective transfer of patients with more comorbidities coupled with persistent MSOF, this finding may also potentially reflect the risks associated with interhospital transport. A number of prior studies have demonstrated that critically ill patients have an increased risk for morbidity and mortality during transport from one facility to another.[28–31] Although we do not want to suggest that patients with AP should not be transferred, particularly in situations where the supportive care of an ICU or specialized procedure is required, our results warrant a critical reevaluation of current practice guidelines for transferring all patients with severe AP.

The present study is the first to evaluate potential factors that influence the decision to transfer patients. Younger, African American, uninsured, and Medicaid patients were all less likely to be transferred, whereas those with more severe disease were more likely to be transferred. Smaller, low-volume, and nonteaching facilities were more likely to transfer patients with AP. Not surprisingly, the presence of MSOF (OR, 3.51) had the greatest influence on the decision to transfer patients. The role of nonclinical factors in influencing the decision to transfer patients has been described, although it has been described never before in AP. Prior studies have shown that uninsured patients are transferred less often compared with insured patients.[32,33] Race has also been shown to influence transfers as a recent analysis demonstrated that fewer African American patients with acute myocardial infarction were transferred for revascularization compared with white patients.[34] Further studies will be needed to examine these disparities.

There are several limitations to this study. The first is that the use of an administrative database relies on the accuracy of the *ICD-9-CM* coding. A recent study found that the sensitivity, specificity, as well as positive and negative predictive values of the *ICD-9-CM* code 577.0 for AP were 96%, 85%, 80%, and 98%, respectively.[35] These values are similar to prior studies examining the accuracy of discharge diagnosis coding for AP. The high sensitivity and negative predictive value suggest that patients with true AP are rarely missed. The second limitation is that we were unable to link the records of individual transferred patients to their hospital of origin. Therefore, we could not assess whether the timing of transfer for individual patients affects mortality. A prior study found lower mortality rates when patients were transferred within 1 week of presentation.[14] However, this study did not adjust for the severity of the disease and it is unclear whether the lower mortality among patients transferred within a week was related to less severe disease or the potential benefit of care at another facility. The third limitation is the inability to assess whether the need for specialized procedures, such as ERCP or surgical pancreatic debridement, influenced the decision to transfer the patients. However, the overall impact on mortality for transferred patients undergoing these procedures is unclear because ERCP has never been shown to improve mortality in acute biliary pancreatitis and surgical pancreatic debridement is associated with increased mortality if performed too early.[36–38] The fourth limitation is our inability to differentiate those patients with necrotizing pancreatitis from those patients with interstitial pancreatitis. However, OF has been accorded greater importance than pancreatic necrosis for defining severe AP in the recent revision of the Atlanta classification and the incidence of infected pancreatic necrosis continues to fall for unclear reasons.[39,40] The fifth limitation is that the criteria for ICU admission is likely to be different between community and referral hospitals. This may call into question our examination of the mortality rates between the nontransferred patients and the transferred patients on the basis of different severity subgroups. However, if the severity of illness resulting in ICU admission at a community hospital was truly less than that of referral centers, we would expect that this would translate into lower mortality rates, but what we found was that the mortality rates were equivalent across nearly all of the severity subgroups. Despite these limitations, this study is the first population-based evaluation of disease severity and outcomes in patients transferred with AP. Furthermore, the study evaluated a large number of patients for a long period and included all nonfederal hospitals across the state of Maryland, including a large number of referral and community hospitals in both urban and nonurban settings.

In conclusion, patients with AP who are transferred have more severe disease and a higher overall mortality. However, after adjusting for important determinants of disease severity, mortality rates seem to be similar between transferred patients and nontransferred patients. Clinical factors, such as severity of disease, and nonclinical factors, such as payor status, race, and age, influence the decision to transfer patients with AP. Further studies are needed to determine which patients with severe AP are most likely to benefit from being transferred to determine the optimal timing of transfer and to further explore and mitigate the influence of insurance status and race on the decision to transfer patients.

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