Impact of Different Patterns of Organ Failure on Mortality in Acute Necrotizing Pancreatitis

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Objectives: Organ failure (OF) and infected necrosis (IN) are the most important predictors of mortality in necrotizing acute pancreatitis (AP). We studied the relationship between timing (onset and duration) and patterns of OF with mortality and the impact of IN on mortality.

Methods: Consecutive patients with necrotizing AP between January 2017 and February 2020 were analyzed retrospectively for OF and its impact on outcome. Organ failure was divided as single OF, simultaneous multiple OF (SiMOF) and sequential multiple OF (SeMOF). Mortality was compared for timing of onset, total duration and patterns of OF.

Results: Among 300 patients with necrotizing AP, 174 (58%) had OF. Mortality was not associated with onset of OF ($P = 0.683$) but with duration of OF ($P = 0.006$). Mortalities for single OF, SiMOF, and SeMOF were 11.8%, 30.4%, and 69.2% respectively ($P < 0.001$). On Cox proportional hazard analysis, adjusted hazard ratio of risk of mortality for OF with IN versus IN, SiMOF versus single OF and SeMOF versus single OF was 3.183, 2.878, and 8.956, respectively ($P = 0.023$, <0.030, and <0.001, respectively).

Conclusions: Duration of OF was associated with increased mortality and SeMOF had worse outcome than single OF and SiMOF.

Key Words: acute pancreatitis, organ failure, sequential, necrotizing pancreatitis, infected necrosis

(*Pancreas* 2021;00: 00–00)

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Received for publication July 30, 2020; accepted August 6, 2021.

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Guarantor of the article: Rakesh Kochhar.

The authors declare no conflict of interest.

Author Contributions: A.K.S. participated in the acquisition and analysis of data, initial draft of the article, approval to the final version. J.S. participated in the initial draft of the article, critical revision and approval to the final version. J.S. participated in the acquisition of data, initial draft of the article and approval to the final version. C.L.B. participated in the acquisition of data, initial draft of the article, and approval to the final version. J.D. participated in the acquisition of data, initial draft of the article and approval to the final version. P.G. participated in the acquisition of data, initial draft of the article, critical revision, and approval to the final version. P.K.M. participated in the interpretation and analysis of data, initial draft of the article, and approval to the final version. V.G. participated in the conception and design of the study, intellectual content, critical revision, and approval to the final version. T.D.Y. participated in the conception and design of study, intellectual content, critical revision and approval to the final version. S.K.S. participated in the conception and design of study, intellectual content, critical revision, and approval to the final version. R.K. participated in the conception and design of study, intellectual content, revision and approval to the final version.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.pancreasjournal.com).

DOI: 10.1097/MPA.0000000000001880

Organ failure (OF) is the major determinant of outcome in acute pancreatitis (AP).[1,2] Severity of AP is based on the revised Atlanta classification and depends on the presence and duration of OF.[3] Organ failure may develop early (≤2 weeks) because of inflammatory response or later (>2 weeks) in the course of the disease because of infected necrosis (IN) and both contribute to increased mortality.[4] Organ failure and infection of (peri)pancreatic necrosis have been considered as the most important predictors of outcome in severe AP.[5–7] A meta-analysis including 6970 patients confirmed IN and OF as independent predictors of mortality, with the lowest mortality in patients with IN without OF and highest mortality in patients with IN with OF.[8]

With tailored, multidisciplinary management strategies and early identification of IN, mortality has decreased in IN; yet OF continues to be the most important single determinant of outcome in AP.[2] Various characteristics of OF are known to affect the outcome of AP including, number of OF,[9] type of OF (ie, respiratory or cardiovascular),[2] grade of OF, and timing of OF.[10,11] A few of these are well known to affect the outcome, whereas some have been infrequently studied.[2,12] This study was aimed at evaluating the impact of timing (onset and duration) and patterns of OF (simultaneous or sequential) on mortality of such patients.

MATERIALS AND METHODS

Study Protocol

This study was a retrospective analysis of prospectively collected data between January 2017 and February 2020 in a tertiary care center in India. The study was approved by the institute's ethics committee. The study population included adult patients with AP who fulfilled the following criteria: (i) first episode of pancreatitis and (ii) pancreatic or extrapancreatic necrosis on imaging (computed tomography [CT] scan or magnetic resonance imaging [MRI]). Excluded were patients with chronic pancreatitis, recurrent pancreatitis, pancreatic or other malignancy, pregnancy, and patients on immunosuppressive medications.

Definitions of Organ Failure and IN

Organ failure was defined as respiratory, renal or cardiovascular system according to the modified Marshall scoring system.[13] Persistent OF was defined as OF lasting >48 hours. Distinction was made between single and multiple OF (>1 OF). Multiple OF was further identified as simultaneous multiple OF (SiMOF) (when >1 organ systems were involved at the time of onset of OF and the second OF developed within 24 hours of first OF) and sequential multiple OF (SeMOF) (when >1 organ systems were involved during the disease course and the second OF developed after 24 hours of first OF). Sequential multiple OF looked at the 3 organ systems defined in Atlanta criteria and is different from the SOFA (Sequential Organ Failure Assessment) score where 0 to 4 score is given for each of the 6 organ systems (cardiovascular, coagulation, liver, neurological, renal, and respiratory).[14]

Necrotizing pancreatitis was defined as the presence of either pancreatic parenchymal necrosis with or without extrapancreatic necrosis, or extrapancreatic necrosis alone. Infected necrosis was diagnosed in the presence of microbiological confirmation from the percutaneous catheter aspirate of necrosis/collection or air in the collection.

Management of Acute Pancreatitis

Diagnosis of AP was based on the presence of any 2 of the 3 criteria: (1) characteristic abdominal pain with or without radiation to the back, (2) increased serum amylase/lipase level (>3 times the upper limit of normal), and (3) imaging evidence of pancreatitis on ultrasonography, CT scan, or MRI.[3] All patients underwent contrast-enhanced CT abdomen after 5–7 days of pain onset, or earlier if deemed necessary. Patients were managed according to standard guidelines which included aggressive fluid resuscitation, organ system support, pain alleviation, and nutritional support.[15] Antibiotics were used for extrapancreatic infections, suspected or confirmed IN.[15,16]

"Step-up" approach was used for management of pancreatic necrosis/collections starting with conservative approach followed by percutaneous catheter drainage (PCD) and minimally invasive surgery.[17] Indications for PCD included persistent sepsis, suspected or confirmed IN failing to improve with conservative approach, worsening OF with conservative management, or pressure symptoms (gastric outlet obstruction/biliary obstruction).[18,19]

Data Collection

Data were collected prospectively and included demographic profile, etiology of pancreatitis, body mass index; severity scores (Acute Physiology and Chronic Health Evaluation [APACHE] II, Bedside Index of Severity in Acute Pancreatitis [BISAP], and CT severity index [CTSI] scores); onset, duration and pattern of OF; invasive intervention (ie, PCD or surgical debridement); hospital and intensive care unit (ICU) stay; and mortality. Organ failure data were recorded daily during the hospital stay. All the discharged patients were further followed for 3 months, and data on readmission, recurrence of OF, or mortality were noted.

Patients with necrotizing AP were divided into those with and without OF and baseline and outcome parameters were compared. Characteristics of OF in relation to time of onset, duration, and pattern were noted, and their association with mortality was studied. Among patients with multiple OF, association with mortality was compared for SiMOF and SeMOF. Association between infected pancreatic necrosis (with or without OF) with mortality (first hospitalization and at 3 months) was also analyzed.

Statistical Analysis

All the collected data were entered in Microsoft Excel 2010 (Redmond, Wash) and SPSS version 23.0 (IBM, Armonk, N.Y.) was used to analyses. Continuous variables were represented as mean (standard deviation [SD]) or median (interquartile range) and proportions were expressed as percentage. The mean among 2 groups was compared using independent sample *t* test for normally distributed variables and Mann-Whitney *U* test for skewed data. For categorical data, χ^2 test/Fisher exact F test with corrections were used. Association of OF was analyzed for first admission mortality, as well as 3-month mortality. Variables found significant for mortality on univariate analysis ($P < 0.05$) were included for multivariable analysis using Cox regression to analyze the effect independently related to mortality in a time to event model. Other independent variables, including age, sex, etiology of pancreatitis, comorbidities (defined as per the Charlson Comorbidity Index), were also included in the model to calculate the adjusted hazard ratio (HR). The results are presented as unadjusted and adjusted HRs with 95% confidence intervals (CIs). The Kaplan-Meier estimate was used to draw the survival curve for difference patterns of organ failure. A 2-sided *P* less than 0.05 was considered statistically significant.

RESULTS

Between January 2017 and February 2020, among 616 patients with AP seen, 300 had necrotizing AP. Excluded patients had pancreatitis without (peri-)pancreatic necrosis (n = 178), recurrent pancreatitis (n = 72), or incomplete records (n = 66). Among the 300 patients with necrotizing AP, 174 (58%) had OF.

Table 1 gives characteristics of patients with and without OF. Patients with OF had higher baseline severity scores (systemic inflammatory response syndrome, BISAP ≥2, APACHE II, and CTSI), total leukocyte counts, a higher percentage of pancreatic parenchymal necrosis and they more often developed IN. They also had a prolonged hospital and ICU stay, and more often needed an intervention (PCD or surgical necrosectomy). Overall, 49 (16.3%) patients died at the end of 3 months and mortality was significantly higher in patients with OF when compared with patients with no OF ($P < 0.001$). Supplemental Table 1 (http://links.lww.com/MPA/A895) compares patients who survived at the end of 3 months with those who died.

Patterns of Organ Failure

Among 174 patients with OF, 163 (93.6%) patients developed respiratory failure with mortality in 44 (27%) at the end of 3 months. Renal failure developed in 65 (37.3%) patients with mortality in 25 (38.5%), whereas 45 (25.8%) patients developed cardiovascular failure and had the highest mortality (27 patients, 60%) among all organ system failure at 3 months (Supplemental Table 2, http://links.lww.com/MPA/A895). Transient OF was noted in 5 patients with no mortality. Mortality outcome was assessed during first admission and at 3 months and was found to be increased with the number of organ system failed (Fig. 1). Table 2 shows that of the 169 patients with persistent OF, 97 (57.3%) had single OF with 3 months mortality of 12.4%. Seventy-two (42.6%) patients had multiple OF with 3 months mortality in 12 of 46 (26.1%) patients with 2 OF and 20 of 26 (76.9%) patients with 3 OF (Table 2 and Supplemental Table 3, http://links.lww.com/MPA/A895).

Patients with multiple OF (n = 72) were further divided into SiMOF (n = 46, 63.8%) and SeMOF (n = 26, 37.2%). Among 26 SeMOF patients, first organ involved was respiratory in 18, renal in 7, and cardiovascular in 1 patient. Subsequently, another single OF developed in 19 patients, whereas 7 developed 2 OF (Supplemental Fig. 1, http://links.lww.com/MPA/A895). The second OF developed at a median duration of 7.5 days (interquartile range [IQR], 3–12.5 days) after the first OF. Of the 26 patients with SeMOF, 23 had undergone PCD for persistent OF. Upgradation of initial PCD or a second PCD was required in 20 (87%) of these patients for persistent/worsening OF (n = 16) or persistent fever with rise in serum procalcitonin (n = 4). Of these 20 patients, 14 died at 3 months (Supplemental Fig. 2, http://links.lww.com/MPA/A895). Mortality was significantly higher in SeMOF compared with SiMOF at 3 months (30.4% vs 69.2%; adjusted HR, 2.960; 95% CI, 1.310–6.688; $P = 0.009$) (Tables 3 and 4 and Supplemental Table 4, http://links.lww.com/MPA/A895).

On Cox proportional hazard analysis, SiMOF had unadjusted and adjusted HR of 3.287 (95% CI, 1.492–7.243) and 2.878 (95% CI, 1.109–7.472), respectively, for risk of mortality compared with patients with single OF (Fig. 2). Similarly SeMOF had unadjusted and adjusted HR of 9.587 (95% CI, 4.509–20.381) and 8.956 (95% CI, 3.895–20.594), respectively, for risk of mortality compared with patients with single OF (Table 4).

TABLE 1. Baseline Characteristics of Patients With and Without OF in Necrotizing Pancreatitis

Parameters	OF (n = 174)	No OF (n = 126)	*P*
Demographic parameters			
Age, mean (SD), y	40.89 (12.53)	40.64 (13.63)	0.87
Sex, male, n (%)	115 (66.1)	96 (76.2)	0.68
Etiology of AP, n (%)			0.265
Alcohol	83 (47.7)	71 (56.3)	
Gallstone	55 (31.6)	30 (23.8)	
Other	36 (20.7)	25 (19.8)	
Comorbidities, n (%)			
DM	40 (23)	12 (9.5)	0.002
HTN	29 (16.7)	10 (7.9)	0.026
CAD	10 (5.7)	3 (2.4)	0.25
Days between onset of pain and hospitalization, median (IQR)*	8 (5–15.5)	22 (10–44)	<0.001
Severity parameters			
SIRS at admission, n (%)	169 (97.1)	68 (54)	<0.001
BISAP ≥2, n (%)	159 (91.4)	40 (31.7)	<0.001
APACHE II score, mean (SD)†	19.98 (6.25)	5.45 (2.61)	<0.001
CTSI, mean (SD)‡	7.47 (1.88)	6.18 (2.06)	<0.001
CRP before PCD, mean (SD), mg/dL§	414.22 (362.3)	139.11 (226.79)	<0.001
IAH at presentation, n (%)	79/140 (56.4)	4/41 (9.8)	<0.001
Baseline biochemical parameters			
Hemoglobin, mean (SD), g/L‡	102.94 (22.53)	110.89 (14.52)	<0.001
Total leucocyte counts, mean (SD), /mm^3	19,578 (9923)	13,128 (6483)	<0.001
Urea, median (IQR), mg/dL‡	34 (19.5–84.5)	20 (15–28)	<0.001
Creatinine, mean (SD), mg/dL‡	1.89 (2.54)	0.71 (0.23)	<0.001
Procalcitonin, median (IQR), ng/mL§	2 (1–8.5)	0 (0–1)	<0.001
Radiological parameters, n (%)			
Pancreatic necrosis	158/172 (91.9)	92/126 (73)	<0.001
Percentage of pancreatic necrosis			0.002
≤50%	123/172 (71.5)	109/126 (86.5)	
>50%	49/172 (28.5)	17/126 (13.5)	
Infections, n (%)			
Infected pancreatic necrosis	100 (57.5)	25 (19.8)	<0.001
Extra pancreatic infection	41/174 (23.6)	25/125 (20)	0.464
Outcome parameters			
Hospitalization required, n (%)	174 (100)	34 (74.6)	<0.001
No. readmissions within 3 mo of initial admission, mean (SD)	1.20 (0.5)	1.13 (0.42)	0.19
Total hospitalization, median (IQR), d†	23 (14–42)	7 (0–15)	<0.001
ICU admission required, n (%)	103 (59.2)	16 (12.7)	<0.001
ICU stay, median (IQR), d†	3(0–14)	0 (0–0)	<0.001
PCD required, n (%)	131 (75.3)	33 (26.2)	<0.001
Surgery, n (%)	18 (10.3)	2 (1.6)	0.002
Mortality, n (%)			
1st admission	37 (21.3)	2 (1.6)	<0.001
3 mo	44 (25.3)	5 (4)	<0.001

*Missing data: <10%.

†Missing data: <5%.

‡Missing data: <1%.

§Missing data: >20%.

ALI, acute lung injury; AKI, acute kidney injury; CAD, coronary artery disease; CRP, C-reactive protein; CVSF, cardiovascular failure; DM, diabetes mellitus; HTN, hypertension; IAH, intraabdominal hypertension; SIRS, systemic inflammatory response syndrome.

Timing of Onset and Duration of Organ Failure and Effect on Mortality

Respiratory system, renal, and cardiovascular failure had set-in at a median interval of 10 days (IQR, 5–18 days), 7 days (IQR, 4.5–21 days), and 24.5 days (IQR, 11.25–48.75 days) after onset of pain and persisted for 12 days (IQR, 6–19 days), 7 days (IQR, 3–15 days), and 6 days (IQR, 3–9.75 days), respectively. Mortality at 3 months was not associated with onset of persistent OF ($P = 0.378$, Table 5 and Supplemental Table 5, http://links.lww.com/MPA/A895). Mortality was, however, associated with the total duration of OF with highest mortality being seen in

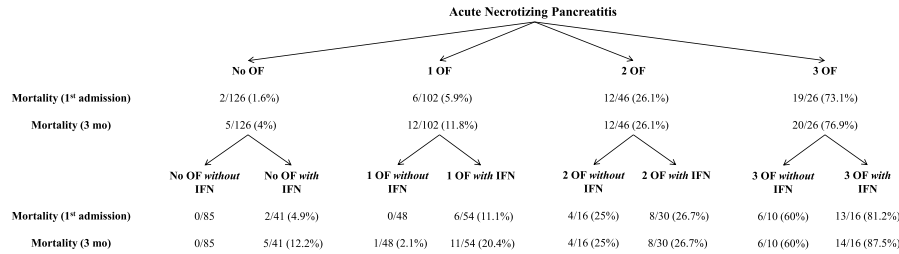

FIGURE 1. Mortality (first admission and at 3 months) in patients with necrotizing acute pancreatitis based on the presence or absence of OF and IN.

patients with OF longer than 3 weeks (Table 5 and Supplemental Table 5, http://links.lww.com/MPA/A895). No mortality differences were noted for SiMOF and SeMOF based on the onset or duration of OF (Supplemental Table 6, http://links.lww.com/MPA/A895).

Infected Necrosis

Of the 300 patients studied, 141 (47%) had IN, of whom 100 (70.9%) also had OF (54 [54%] having single OF and 46 [46%] with multiple OF [30 SiMOF and 16 SeMOF]). There were 159 patients who had sterile necrosis, of whom 74 (46.5%) developed OF. Mortality at 3 months was significantly higher in patients with IN compared with those with sterile necrosis (27% vs 6.9%, $P < 0.001$). Among sterile necrosis patients, 3 months mortality in those with OF was 14.9%, whereas no mortality was reported in patients without OF (Supplemental Table 7, http://links.lww.com/MPA/A895).

When patients with IN with OF were compared with sterile necrosis with OF, mortality was statistically higher in the former group on both univariate (33% vs 14.9%) and multivariate analyses, but when adjusted for age, sex, comorbidities, etiology of pancreatitis, CTSI, and amount of pancreatic necrosis, mortality was not different (adjusted HR, 1.878; 95% CI, 0.897–3.935) (Table 4). Similarly, when mortality was compared for IN with OF versus IN without OF, it was significantly higher in the former group on univariate analysis, as well as multivariate analysis, even after adjustment for age, sex, comorbidities etiology of pancreatitis, CTSI, and amount of pancreatic necrosis (adjusted HR, 3.183; 95% CI, 1.174–8.628).

Readmission

Apart from initial hospital admission, we also noted need of readmission until 3 months after discharge. Of the 300 study patients, 267 had required primary hospitalization in the gastroenterology ward or ICU, whereas 33 patients were discharged from the emergency room after initial evaluation. Thirty-six patients required readmission, 27 (15.5%) patients in OF group and 9 (9.7%) among no OF ($P = 0.183$). Median number of admissions among the 2 groups was not different ($P = 0.19$).

DISCUSSION

In this single-center study of 300 patients with acute necrotizing pancreatitis with 174 (58%) having OF, duration of OF but not onset of OF was associated with increased mortality. The highest mortality was seen in those with OF persisting for longer than 3 weeks. We also noted that among patients with multiple OF, patients with SeMOF had worse outcome than those with SiMOF.

Organ failure develops in 8% to 20% of AP patients in population-based studies,[20–22] and in up to 40% in tertiary care studies.[2–4] Multiple determinants of OF affect the outcome, for example, type and number of OF, severity of OF, pattern of OF, timing of onset, and duration of OF. Consistent results have been shown for determinants such as severe OF or multiple OF, which carry worse prognosis.[4,6,9,23] However, other variables have shown conflicting results (timing of onset and duration of OF) or not being evaluated adequately (pattern of organ involvement).[2,12]

Several studies, evaluating the timing of onset of OF, had shown higher mortality in early onset OF,[6,11,24] whereas a study by Choi et al[25] showed higher mortality for late onset OF. Contrary to these, 2 recently published studies have shown no mortality difference in early onset versus late onset OF.[2,12] In the present study, we also noted no association of mortality with onset of OF. Better outcome in early OF in recent studies could be attributed to implementation of management guidelines advocating early aggressive fluid resuscitation, nutritional support, and use of step-up approach of management.

TABLE 2. Mortality Based on Number of OF in Patients With Persistent OF (n = 169)

Parameters	Mortality at 3 mo, n (%)
Single OF (any 1 organ system)	12/97 (12.4)
Respiratory	12/89 (13.5)
Renal	0/6 (0)
Cardiovascular	0/2 (0)
Multiple OF (any 2 or more organ systems)	32/72 (44.4)
Any 2 organ systems	12/46 (26.1)
Respiratory and cardiovascular	7/14 (50)
Respiratory and renal	5/30 (16.7)
Renal and cardiovascular	0/2 (0)
All 3 organ systems	20/26 (76.9)

TABLE 3. Mortality in Patients With Multiple OF Based on Sequences of Organ System Involved, Simultaneous MOF Versus Sequential MOF

	Mortality at 3 mo, n (%)	
Parameters	SiMOF (n = 46)	SeMOF (n = 26)
Overall mortality*	14/46 (30.4)	18/26 (69.2)
Any 2 organ systems	3/30 (10)	9/16 (56.2)
Respiratory and cardiovascular	1/5 (20)	3/7 (42.9)
Respiratory and renal	2/23 (8.7)	6/9 (33.3)
Renal and cardiovascular	0/2 (0)	0/0 (0)
All 3 organ systems	11/16 (68.8)	9/10 (90)

*$P = 0.001$.

TABLE 4. Unadjusted and Adjusted HR and 95% CI for Risk of Mortality Using the Cox Proportional Hazard Analysis

Covariate	Unadjusted HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
OF vs no OF*	7.167 (2.838–18.099)	<0.001	3.818 (1.401–10.402)	0.009
Single vs no OF	2.860 (0.994–8.232)	0.051	1.926 (0.630–5.894)	0.251
Simultaneous multiple OF vs no OF	9.470 (3.410–26.302)	<0.001	5.238 (1.562–17.570)	0.007
Sequential multiple OF vs no OF	28.081 (10.390–75.390)	<0.001	18.243 (6.004–55.429)	<0.001
Multiple vs single OF*	5.190 (2.613–10.309)	<0.001	5.503 (2.455–12.334)	<0.001
Simultaneous multiple OF vs single OF	3.287 (1.492–7.243)	0.003	2.878 (1.109–7.472)	0.030
Sequential multiple OF vs single OF	9.587 (4.509–20.381)	<0.001	8.956 (3.895–20.594)	<0.001
Sequential vs simultaneous OF*	2.891 (1.433–5.833)	0.003	2.960 (1.310–6.688)	0.009
OF with IN vs IN†	3.137 (1.222–8.054)	0.017	3.183 (1.174–8.628)	0.023
OF with IN vs OF†	2.339 (1.179–4.642)	0.015	1.878 (0.897–3.935)	0.095

*Adjusted for age, sex, comorbidities (based on CCI), etiology of pancreatitis, CTSI, urea, and creatinine, amount of pancreatic necrosis (≤50% or >50%), presence of IN, and need of necrosectomy.

†Adjusted for age, sex, comorbidities (based on CCI), etiology of pancreatitis, CTSI, amount of pancreatic necrosis (≤50% or >50%).

We, however, found an association of mortality with duration of OF with highest mortality if OF persisted longer than 3 weeks. Previous studies had assessed OF mainly as a binomial variable and in most such studies the absolute duration of OF was not recorded which required daily data collection for OF, it being a dynamic process.[9] Studies on patients in critical care have noted increased mortality with longer ICU stay.[26,27] The Dutch pancreatitis group found no association between duration of OF and mortality,[2] but Shi et al[12] in an analysis of 3084 patients reported increased mortality when OF persisted for longer than 2 weeks.

Studies have shown that presence of multiple OF leads to worse prognosis with higher mortality.[2,9] There are no data on the effect of occurrence of sequential or simultaneous OF on outcome of AP. We noted that of the 72 patients with multiple OF, 46 had SiMOF and 26 had SeMOF. The SeMOF group had higher 3 month mortality compared with the SiMOF group (69.2% vs 30.4%, respectively). Ineffective drainage, secondary infection of residual necrosis, or hospital acquired extrapancreatic infections could have contributed to development of SeMOF. Because none of the previous studies has looked at this aspect, it would be interesting to have more data on this under reported phenomenon.

Apart from OF, IN is the other determinant of outcome in AP.[5,28] Although a number of studies have reported a synergistic effect of the 2 on mortality,[4,5,8] recent data suggest that OF predicts outcome better than IN.[2,7,29,30] Our data also suggest that OF was a stronger determinant of mortality compared with IN. It has been suggested that recent improvements in ICU care and use of "step-up" approach have improved the outcome in IN.[2,31] The clinical impact of IN, however, differs worldwide, depending on available local expertise for management of AP and minimally invasive procedure.[2,32] We, as a tertiary care center, follow a conservative "step-up" approach with expertise available in pancreatic interventions.

A few studies have looked at sequelae of AP and readmission over 30 days.[33,34] However, these studies have limited their observations to the outcomes in the first admission. We studied the need

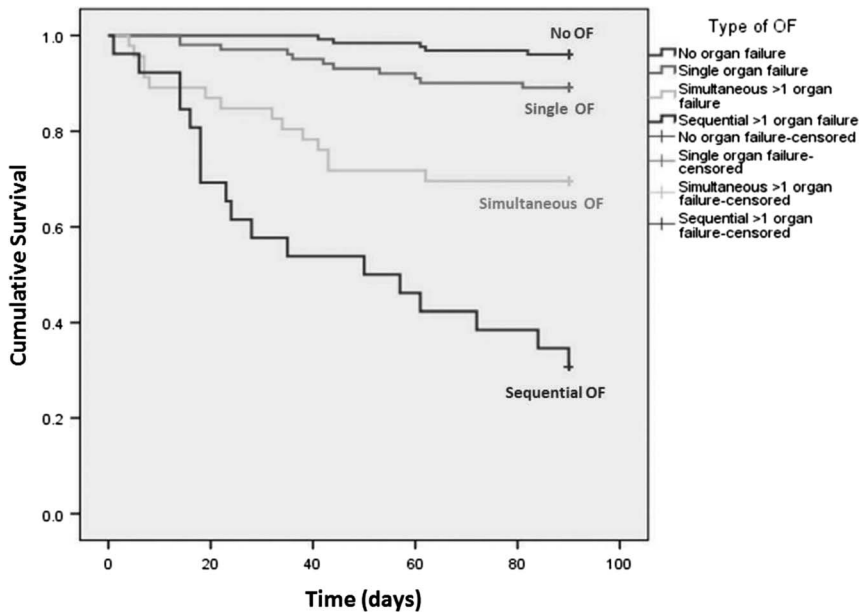

FIGURE 2. Survival curve for different patterns of OF.

TABLE 5. Mortality Based on Duration (Absolute Number of Days) and Onset of OF for Patients With Persistent OF (Irrespective of Number of Organ System Involved)

Days of OF	Mortality at 3 mo, n (%)
Based on duration of OF*	
48 h–1 wk	10/48 (20.8)
1–2 wk	11/52 (21.2)
2–3 wk	8/37 (21.6)
>3 wk	15/32 (46.9)
Based on onset of OF†	
<48 h	2/10 (20)
48 h–1 wk	14/64 (21.9)
1–2 wk	9/40 (22.5)
>2 wk	19/55 (34.5)

*$P = 0.031$.
†$P = 0.378$.

for readmission at 3 months vis-à-vis presence of OF during the first admission. A total of 36 (13.5%) patients required readmission within 3 months of index admission. Readmission rates were not different among patients with and without OF ($P = 0.167$). Among the patient requiring readmission, 10 additional deaths were noted within 3 months of discharge, 7 among OF and 3 among patients without OF. These results suggest that patients with OF, even after initial recovery, are at a risk of reinfection with necrosis or recurrence of OF and require close follow-up. As the number of patients with readmission were small in our study, further prospective studies will be needed to assess the impact of OF on subsequent course of events.

This is one of the largest single-center studies looking at different facets of OF and their impact on outcome. We found that mortality increases with prolonged duration of OF and with number of organ systems involved. We also noted lack of increased mortality in patients with combined OF and IN. In this observational study, we noted that among patients with multiple OF, those with SeMOF have worse outcome than those with SiMOF. Once we identify factors predicting the sequential OF, we can plan interventional strategies to counter that.

There are limitations in the study, though. Being a referral tertiary care center, we often do not encounter patients in the initial phase of illness who would have died otherwise at the center of primary presentation. The retrospective nature of the study was an important limitation, although the data were recorded prospectively. Our categorization of OF into SeMOF and SiMOF was applied to the data retrospectively. Ideally, we should have validated our classification in a preliminary study. We acknowledge this as a limitation of our study. We do not have the data to identify the inciting events for OF in the SeMOF group. The possibility of coincidental IN leading to sequential MOF cannot be ruled out and needs further studies. We had a limited number of patients with transient OF and the effect of transient OF on mortality could not be assessed. Another point of research is the cause of late mortality after the initial discharge. We could not identify the causes of late mortality during readmissions because of the retrospective nature of the study.

In conclusion, our results reiterate that in patients with necrotizing pancreatitis, onset of OF and IN do not affect the mortality; however, mortality increases with prolonged duration of OF. We also found that among patients with multiple OF, those with SeMOF have worse outcome than those with single OF and SiMOF.

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