

The Association Between Caustic Ingestion and Psychiatric Comorbidity Based on 396 Adults Within 20 Years

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Purpose: High prevalence of psychiatric comorbidities (PCs) has been widely documented in caustic substance ingestion cases. However, their effect on the clinical features and prognostic outcomes remains unclear due to the paucity of discussion. We report on detailed clinical courses with long-term multifaceted outcomes and review the association between caustic ingestion and each specific PC.

Patients and Methods: The retrospective chart review included 396 adults (median follow-up, 16.6 months) with and 377 without (control group) PCs treated between 1999 and 2018 at Chang Gung Memorial Hospital. All PCs were diagnosed/confirmed by psychiatrists through face-to-face interviews.

Results: The PCs predicted serious esophagogastrroduodenoscopy grading, higher rates of admission/surgery/intensive care unit stay, increments of systemic/gastrointestinal complications, and poorer 5-year overall survival rates. The poor survival among patients with PCs was highly consistent with their baseline characteristics. Significantly advanced age, more non-PCs, alcoholism, illicit drug abuse, and baseline unhealthy status resulted in statistically higher risks of severe complications and limited recovery.

Conclusion: PCs changed clinical patterns and had critical roles in the survival outcomes of caustic injury victims. Clinical awareness achieves benefit by limiting injuries in mild cases or allowing emergent interventions in severe cases. Future studies based on worldwide populations are essential for realizing geographic differences.

Keywords: caustic, corrosive, psychiatric, endoscopy, complications, long-term survival

Introduction

Caustic substance ingestion is uncommon but frequently life-threatening. The broad-spectrum complications place a heavy burden on healthcare organizations.¹⁻⁹ The extent of damage depends on the chemical properties, amount, concentration, and physical form of the ingested substances.^{1-3,5,6,10-14} Patient age, sex, comorbidities, complications, treatment choices, and socioeconomic status have important roles in survival outcomes and postinjury quality of life.^{1,2,4,6,7,12,13,15-21}

Preventive measures have been widely advocated.^{1,6,10,22-25} However, the effectiveness of precautions appears unsatisfactory in adults, among whom suicidal intents and deliberate self-harm accounts for the majority of cases.^{1,4,5,10,17,25} The associated factors include socioeconomic problems, marital/interpersonal conflicts, low educational status, and negligence in handling

caustic substances.^{14,16,23–29} The high prevalence of psychiatric comorbidities (PCs) has been widely reported among caustic injury victims.^{4,10,11,16–19,25,27,28,30,31} Nevertheless, the effect of PCs on the clinical features and prognostic outcomes remains unclear because of limited information and scarce reports on long-term prognoses. To investigate the crucial aspects of caustic GI tract injury, we reviewed 396 cases within 20 years at a north Taiwan medical center.

Taiwan has an extremely high density of population and medical centers. Combined with Taiwan's National Health Insurance, the referral of caustic ingestion cases to medical centers is common, with neither traffic problems nor institutional impediments. Hence, the 20-year experience at our center included diverse scenarios. To our knowledge, this is the first research on caustic injury to simultaneously report detailed information throughout the clinical courses and review the association between long-term multifaceted outcomes and specific psychiatric diagnoses.

Patients and Methods

Study Population

This retrospective chart review of caustic ingestion included 839 adults treated between January 1999 and December 2018 at Chang Gung Memorial Hospital (CGMH) (Figure 1). We excluded 35 cases because of unclear medical records and 31 because of unclear psychiatric status. The remaining 773 cases included 396 with and 377 without (control group for comparison) PCs. All patients were adults (age ≥ 18). The follow-up period of survivors ended on September 1, 2019. This study was reviewed and approved by the CGMH Institutional Review Board (IRB number: 202000583B3).

Baseline laboratory data were collected. The ingested caustic substances were confirmed by the label on containers. Strong acids and alkalis were defined by pH < 2 and > 12 , respectively. Urgent esophagogastroduodenoscopy (EGD) was performed within 24 hours after ingestion if tolerable. Those with toxic signs or other indications received plain chest radiography (CXR) or computed tomography (CT). Once a destabilized condition or respiratory difficulty was encountered, the patient was transferred to the intensive care unit (ICU) for critical care. After discharge, the patients were followed up in the outpatient clinic for at least 6 months. The intent and amount of ingestion, PCs/non-PCs, clinical treatment

courses, and systemic/gastrointestinal (GI) complications were reviewed for each case. We excluded data from vague texts or equivocal narratives.

Endoscopic Survey

EGD was available around the clock at CGMH. EGD was performed by experienced endoscopists using standard Olympus upper GI endoscopes (GIF XQ-230 [9.2 mm], GIF Q-240X [9.4 mm], GIF Q-260J [9.9 mm], and GIF Q-260 [9.2 mm]; Tokyo, Japan). Patients presenting with respiratory difficulty or unclear consciousness were examined under ventilation support and general anesthesia. Caustic mucosal damage was graded using Zargar's modified endoscopic classification (0, 1, 2a, 2b, 3a, and 3b).³² Approximately half of the urgent EGDs were performed by Cheng H-T, who also reviewed the endoscopic photos of all other patients and confirmed the Zargar's grades for consistency and accuracy. The study in several patients was incomplete because of the patients' intolerance, high perforation risks, and mucosal invisibility in urgency.

Psychiatric Comorbidities

All PCs were diagnosed or confirmed by psychiatrists through face-to-face interviews, based on the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision [DSM-IV-TR] published in 2000³³ for cases diagnosed before 2013, and Fifth Edition [DSM-5] updated in 2013³⁴ for those diagnosed after 2013). Because case enrollment spanned these two versions of diagnostic criteria, we set six categories of PCs based on their high prevalence: depressive disorders (DDs), acute stress disorder or adjustment disorder (ASD/AjD), schizophrenia spectrum disorders (SSDs), bipolar disorders (BDs), generalized anxiety disorder (GAD), and alcohol use disorder. These categories were used to reduce the influence of version differences.^{33,34} Cases with uncertain psychiatric diagnoses were excluded from analyses. After discharge, patients with PCs were also followed at the psychiatric clinic.

Complications

Systemic complications included aspiration injury, respiratory failure, hepatic injury (serum alanine aminotransferase or aspartate aminotransferase levels elevated to three times the normal upper limit), renal injury (serum creatinine level > 1.4 mg/dL without other noted renal diseases), and disseminated intravascular coagulation (DIC). GI complications included bleeding (melena, hematemesis,

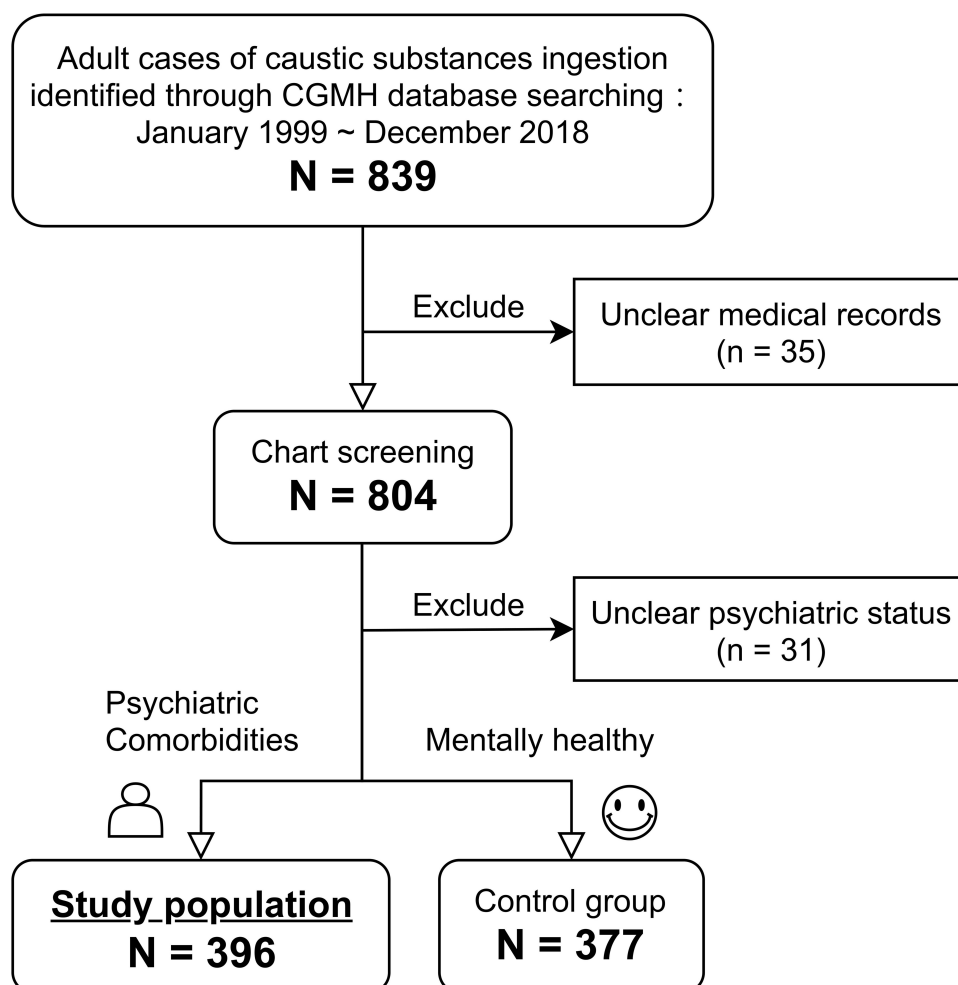


Figure 1 Enrollment diagram for the study population (n=396) and control group (n=377).

or coffee ground vomitus), perforation, fistula, and stricture formation. Perforation and/or fistula was diagnosed using CXR, CT, or endoscopy. Stricture was indicated by symptoms of dysphagia, regurgitation, or odynophagia with confirmation via endoscopy or upper GI radiography.

Statistical Analyses

Continuous variables were expressed as median with interquartile range (IQR = Q3–Q1) as well as whole range (minimum–maximum). Categorical variables were presented as numbers with percentages; percentage calculation excluded missing values. All statistical tests were two-sided and were performed using IBM Statistical Product and Service Solutions (SPSS), version 22 (IBM, Armonk, New York, USA). We performed independent *t*-tests or Mann–Whitney *U*-tests for continuous variables and Pearson χ^2 tests or Fisher's exact tests for categorical variables. The univariate survival analyses were performed

using the Kaplan–Meier method with Log rank tests. The Cox's proportional hazards model was performed alternatively in the multivariate setting to obtain the hazard ratio (HR) with a 95% confidence interval (CI). A *p* value <0.05 was considered statistically significant.

Results

Patient Characteristics

Among the 396 adults with PCs (158 males, 39.9%; 238 females, 60.1%), the median age during caustic ingestion was 46 years (IQR 29, range 18–94). Suicidal ingestion (SI) was the predominant (93.7%) intent. There were 58 patients (14.7%) with a history of suicide attempt by miscellaneous means; 29 had repeated caustic SI. After a survey in the emergency department, 99 patients (25.2%) did not meet the admission criteria. For the 294 admitted patients, the median length of hospital stay (LoHS) was 14 days (IQR 17), with 20 (6.8%) in-hospital deaths.

Systemic and GI complications were observed in 131 (33.3%) and 147 (37.1%), respectively. Median follow-up was 16.6 months (range, 1 day to 254 months). The overall survival rates at 3 and 6 months, and 1, 3, 5, and 10 years were 90.7%, 88.6%, 86.1%, 80.1%, 74.2%, and 53.2%, respectively.

Impacts of PCs

The PCs changed the clinical courses of caustic injury in several ways (Tables 1 and 2). PCs tended to present in the elderly ($p=0.002$) and in females ($p<0.001$). SI and previous suicide attempts were more common, and the ingested caustic amount was statistically significantly different in those with PCs compared to those without PCs. According to the chart review, patients with PCs had significantly higher incidences of underlying hypertension ($p=0.001$), diabetes mellitus ($p=0.046$), hepatitis B or C ($p=0.042$), and thyroid disease ($p=0.003$).

The presence of PCs predicted more requirements for endotracheal intubation for urgent EGD ($p=0.014$) and more frequent incomplete EGD studies ($p=0.019$). Additionally, more systemic complications ($p=0.006$),

upper GI complications ($p=0.006$), and surgical interventions ($p=0.003$) were recorded among them. Regarding delayed sequela, PCs increased the stricture risk and thus a greater requirement for endoscopic dilatation and surgeries for esophageal strictures or gastric outlet obstructions. The 5-year ($p=0.045$) and 10-year ($p=0.005$) overall survival rates were significantly different between those with and without PCs.

Characteristics of Specific PCs

Among the 396 patients with PCs, DDs ($n=219$, 55.3%) was the most common, followed by ASD/AjD ($n=88$, 22.2%), SSDs ($n=51$, 12.9%), BDs ($n=29$, 7.3%), and GAD ($n=19$, 4.8%). Of note, SI, previous suicide attempts, and significantly larger ingestion volumes were associated with DDs, ASD/AjD, SSDs, and BDs. Patients with DDs faced the highest multifaceted risks (Appendix 1).

PCs and Serious Zargar's Grades

Patients with PCs were found with more serious caustic GI tract injuries under EGD (Table 1). Although the proportions of Zargar's grade $\geq 2b$ were not significantly

Table 1 Characteristics of Caustic Ingestion Patients

Variables	Psychiatric Comorbidity		p value
	Present (n=396)	Absent (n=377)	
Baseline status			
Old (>65 years old)	98 (24.7)	59 (15.6)	0.002**
Female	238 (60.1)	153 (40.6)	<0.001***
Suicidal ingestions	370 (93.7)	205 (54.8)	<0.001***
Previous suicide attempts	58 (14.7)	6 (1.6)	<0.001***
Alcohol use disorder	84 (21.2)	56 (14.9)	0.022*
Illicit drug abuse	17 (4.3)	3 (0.8)	0.002**
Caustic ingestion			
Caustic substances			0.368
Acidity	232 (58.6)	219 (58.1)	
Alkalinity	135 (34.1)	122 (32.4)	
Neutral	4 (1.0)	10 (2.7)	
Unknown	25 (6.3)	26 (6.9)	
Strong caustics (pH <2 or >12)	226 (60.3)	209 (59.9)	0.917
Ingestion amount, mL	100 (200)	50 (70)	<0.001***
Urgent EGD survey			
Grade $\geq 2b$	385 (98.0)	373 (99.5)	0.108
Grade $\geq 3a$	190 (58.5)	179 (52.0)	0.095
ETT + MV during EGD	155 (47.7)	127 (36.9)	0.005**
Incomplete study	47 (14.5)	29 (8.4)	0.014*
	40 (12.3)	24 (7.0)	0.019*

Notes: Data are presented as number (%) or median (IQR). The calculation of percentage excluded patients with missing values from chart review. The standards for asterisks are as follows: $p<0.05^*$, $p<0.01^{**}$, and $p<0.001^{***}$.

Abbreviations: EGD, esophagogastroduodenoscopy; ETT + MV, endotracheal tube with mechanical ventilation; IQR, interquartile range.

Table 2 Impacts of Psychiatric Comorbidities on Caustic Ingestion Patients

Variables	Psychiatric Comorbidity		p value
	Present (n=396)	Absent (n=377)	
Clinical courses			
Admission	294 (74.8)	211 (56.7)	<0.001***
Hospital stay, days	10 (17)	5 (9)	<0.001***
In-hospital mortality	20 (6.8)	13 (6.2)	0.774
ICU admittance	84 (21.7)	37 (10.4)	<0.001***
ICU stay, days	8 (8.5)	6 (9)	0.345
Surgical intervention	85 (21.5)	50 (13.3)	0.003**
Emergent surgery	27 (6.9)	11 (2.9)	0.012*
Endoscopic dilatation	54 (13.7)	34 (9.0)	0.043*
Systemic complications			
Aspiration injury	131 (33.3)	90 (24.3)	0.006**
Respiratory failure	82 (20.9)	51 (13.8)	0.010**
Respiratory failure	65 (16.5)	31 (8.4)	0.001**
Hepatic injury	30 (7.6)	20 (5.4)	0.214
Renal injury	40 (10.2)	23 (6.2)	0.047*
DIC	12 (3.1)	8 (2.2)	0.441
GI complications			
Stricture	147 (37.1)	105 (27.9)	0.006**
Bleeding	92 (23.2)	64 (17.0)	0.030*
Perforation	64 (16.3)	53 (14.3)	0.453
Perforation	21 (5.3)	10 (2.7)	0.065
Overall survival			
3 months	264 (90.7)	213 (92.6)	0.442
6 months	249 (88.6)	194 (91.9)	0.222
1 year	217 (86.1)	171 (90.0)	0.216
3 years	153 (80.1)	138 (86.8)	0.096
5 years	118 (74.2)	114 (83.8)	0.045*
10 years	50 (53.2)	65 (73.0)	0.005**

Notes: Data are presented as number (%) or median (IQR). The calculation of percentage excluded patients with missing values from chart review. The standards for asterisks are as follows: $p < 0.05^*$, $p < 0.01^{**}$, and $p < 0.001^{***}$.

Abbreviations: GI, gastrointestinal; ICU, intensive care unit; IQR, interquartile range.

($p=0.095$) different between those with (58.5%) and without (52.0%) PCs, the former group was found with statistically more Zargar's grade $\geq 3a$ (47.7% to 36.9%, $p=0.005$) corresponding to necrotic lesions.

Figure 2 further illustrates the EGD grades in each specific PC category. Compared to patients without PCs (median, Zargar's 2b), patients with DDs ($p=0.010$) or GAD ($p=0.006$) had more serious caustic injuries (median, both Zargar's 3a).

Overall Survival Outcomes

For patients with PCs, each complication, such as respiratory failure, renal injury, DIC, bleeding, perforation, and fistula, had a predicted 5-year survival rate of $<50\%$ (univariate analyses shown in Appendix 2). The multivariate Cox's proportional hazards model is shown in Table 3. The

independently significant covariates (model 1) included intubation during EGD (HR 6.38; 95% CI 2.99–13.60), age ≥ 65 (HR 2.80; 95% CI 1.33–5.91), and GI complications (HR 2.30; 95% CI 1.05–5.02). Survival curves with the Kaplan–Meier method are illustrated in Figure 3.

As aforementioned, the caustic ingestion amount was significantly higher in patients with PCs. However, model 2 in Table 3 found significance in the amount ($p=0.003$) but not in the incidence of PCs ($p=0.376$), suggesting that a large ingested caustic amount is a risk factor but adds no additional risk for those with PCs.

Discussion

To our knowledge, this is the first research to review the association among caustic ingestion patterns, each specific PC, and long-term survival outcomes. The presence of PCs

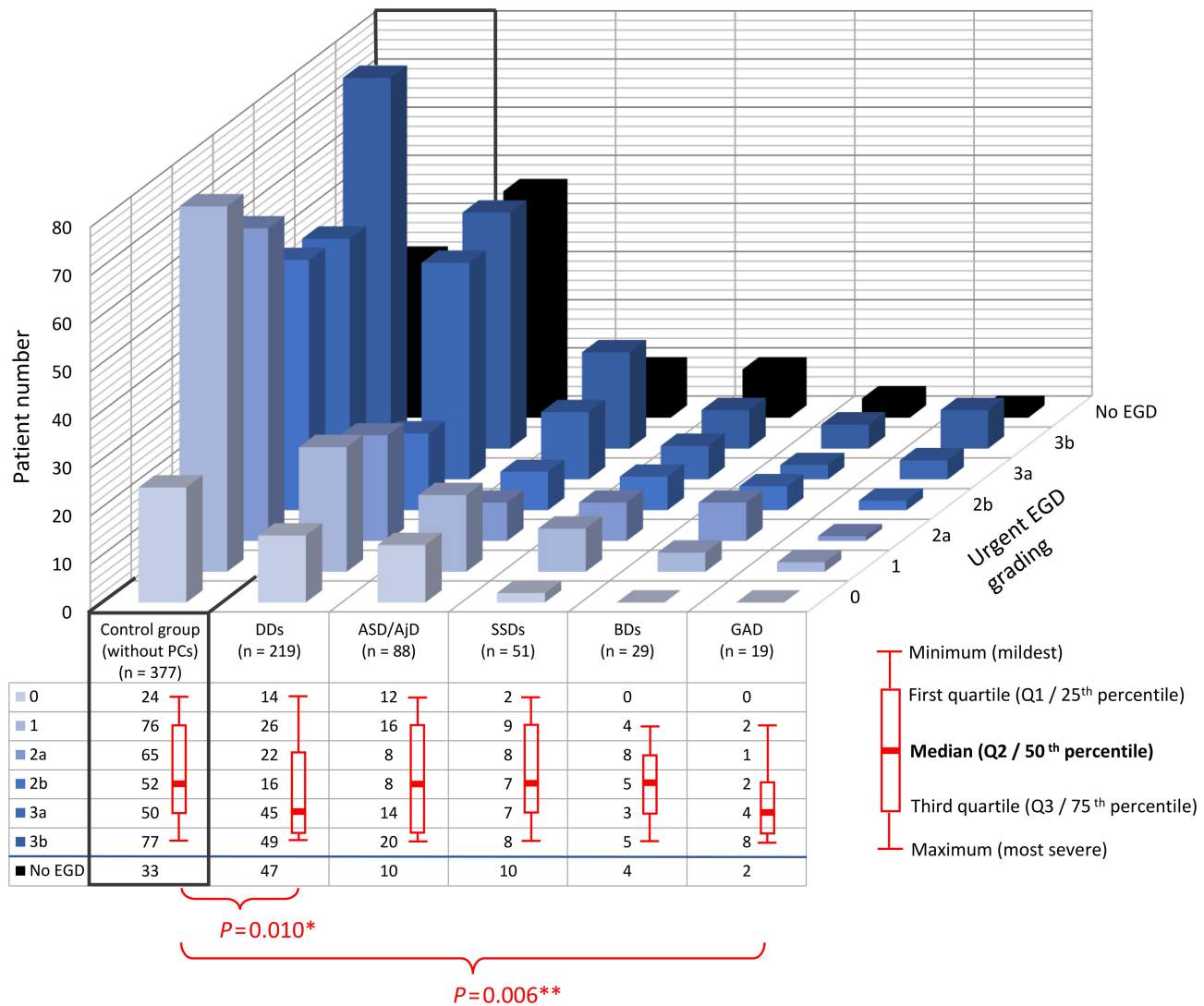


Figure 2 Urgent EGD grading for patients with each specific PC.
Notes: The standards for asterisks are as follows: $p<0.05^*$ and $p<0.01^{**}$.
Abbreviations: ASD/AjD, acute stress disorder or adjustment disorder; BDs, bipolar disorders; DDs, depressive disorders; EGD, esophagogastroduodenoscopy; GAD, generalized anxiety disorder; PC(s), psychiatric comorbidities; SSDs, schizophrenia spectrum disorders.

predicted serious EGD grading, higher rates of admission/surgery/ICU stay, increments of systemic/GI complications, and poor 5-year overall survival rates. Among the PCs, DDs were found to be the most common and caused the highest risk for caustic injury patients.

The incidence of caustic ingestion varies from country to country.^{1,2,5-7,10,13,14,17,19} Although possibly underreported,^{10,12,19} the annual incidence rate of caustic ingestion in Taiwan was estimated as 4.3 per 100,000 adults by the Taiwan National Health Insurance Research Database (NHIRD).⁴ With our 396 cases with PCs and 377 controls, our study enrolled 4% of adult cases in Taiwan. Either PCs (49.3% vs 23.0%) or SI (72.0% vs 38.3%) accounted for a much higher proportion in these 4% of

cases than in the entire NHIRD. Similar results were also found in admission rate, LoHS, and systemic/GI complications. Collectively, our study recruited the group with relatively more serious caustic injuries.

Through analyses, PCs changed the caustic injury patterns in several ways. First, SI was predominant (93.7%) in purpose, with the rate much higher than that in control group (5.8%). This suggested that the link between psychiatric disorders and suicide attempts is strong regardless of caustic ingestion or other means of suicide.^{26,35-37}

Second, advanced age was noticed among cases with PCs, in contrast to our previously reported patient group between 1999 and 2009.¹⁸ The senior population with mental illness had an increasing incidence of caustic

Table 3 Multivariate Cox Proportional Hazards Models of Overall Survival in Patients with PCs

Covariates	Case Number	HR for Death (95% CI)	p value ^a
Model 1: patients with PCs (n=325)			
ETT + MV during EGD			<0.001***
No requirement	278	reference	
Required	47	6.38 (2.99–13.60)	
Age			0.007**
<65	247	reference	
≥65	78	2.80 (1.33–5.91)	
GI complications			0.036*
Absent	222	reference	
Complicated	103	2.30 (1.05–5.02)	
Model 2: comparison with control group (n=615)			
Ingested amount (unit: 100 mL)	615	1.14 (1.05–1.24)	0.003**
Psychiatric comorbidities			0.376
Absent	316	reference	
Present	299	1.28 (0.74–2.23)	

Notes: ^aThe p values were determined using Cox proportional hazards model. The standards for asterisks are as follows: p<0.05*, p<0.01**, and p<0.001***.

Abbreviations: CI, confidence interval; EGD, esophagogastroduodenoscopy; ETT + MV, endotracheal tube with mechanical ventilation; GI, gastrointestinal; HR, hazard ratio.

ingestion in the past decade. This reflects potential public health challenges for aging societies and developed countries.

Third, patients with PCs ingested significantly larger volumes of caustic agents. In our experience, the ingested volume depended on motivation and mental status. Patients with PCs more commonly underwent an “emotional surge,” which led to a “swig of caustic agents.” Such bolus swallowing of irritating substances dramatically increased their choking risks, which potentially explains why they had significantly more aspiration injuries (20.9%, n=82) and respiratory failures (16.5%, n=65). Tseng et al¹⁵ reported a 4.2% (n=15) rate of aspiration pneumonia after intentional strong acid ingestion. They described four mechanisms: rapid ingestion of a large volume, laryngeal dysfunction among the elderly, hesitation in swallowing, and nasogastric-irrigation-induced vomiting. In our study, several patients recalled that hesitation or difficulty in swallowing limited the ingested amount. However, many more patients with PCs ingested large volumes under “emotional surge,” resulting in substantially high complication risk in the respiratory system.

Cheng et al³ have emphasized the importance of early classification of caustic injuries and had implicated Zargar’s 3b as a valuable predictor. Our study found

more advanced EGD grades in the presence of PCs. Approximately half of cases with PCs were diagnosed with necrotic GI tract injuries, equivalent to Zargar’s 3a/3b. Compared with mentally healthy patients, more victims with PCs either could not tolerate a complete EGD study or required ventilation support for EGD because of respiratory difficulty or unclear consciousness. They also required more additional urgent CT scans for suspected perforation or as preoperative preparation. In particular, severe caustic injury was frequently diagnosed in those with DDs and GAD (Figure 2); such patients possibly deserve higher clinical priority and more advanced examinations.

Patients with PCs had poorer long-term overall survival than mentally healthy patients (Table 2). Owing to the statistically similar chemical properties of caustic agents between the two groups, there was little connection between chemical properties and differences in survival. Furthermore, although the larger ingestion amount served as a risk factor, it had no direct impact (p=0.376) on the result of the survival outcomes varying between patients with and without PCs. Univariate and multivariate analyses showed that the poor overall survival among patients with PCs was highly consistent with the GI and systemic complications. This suggests that the presence of PCs

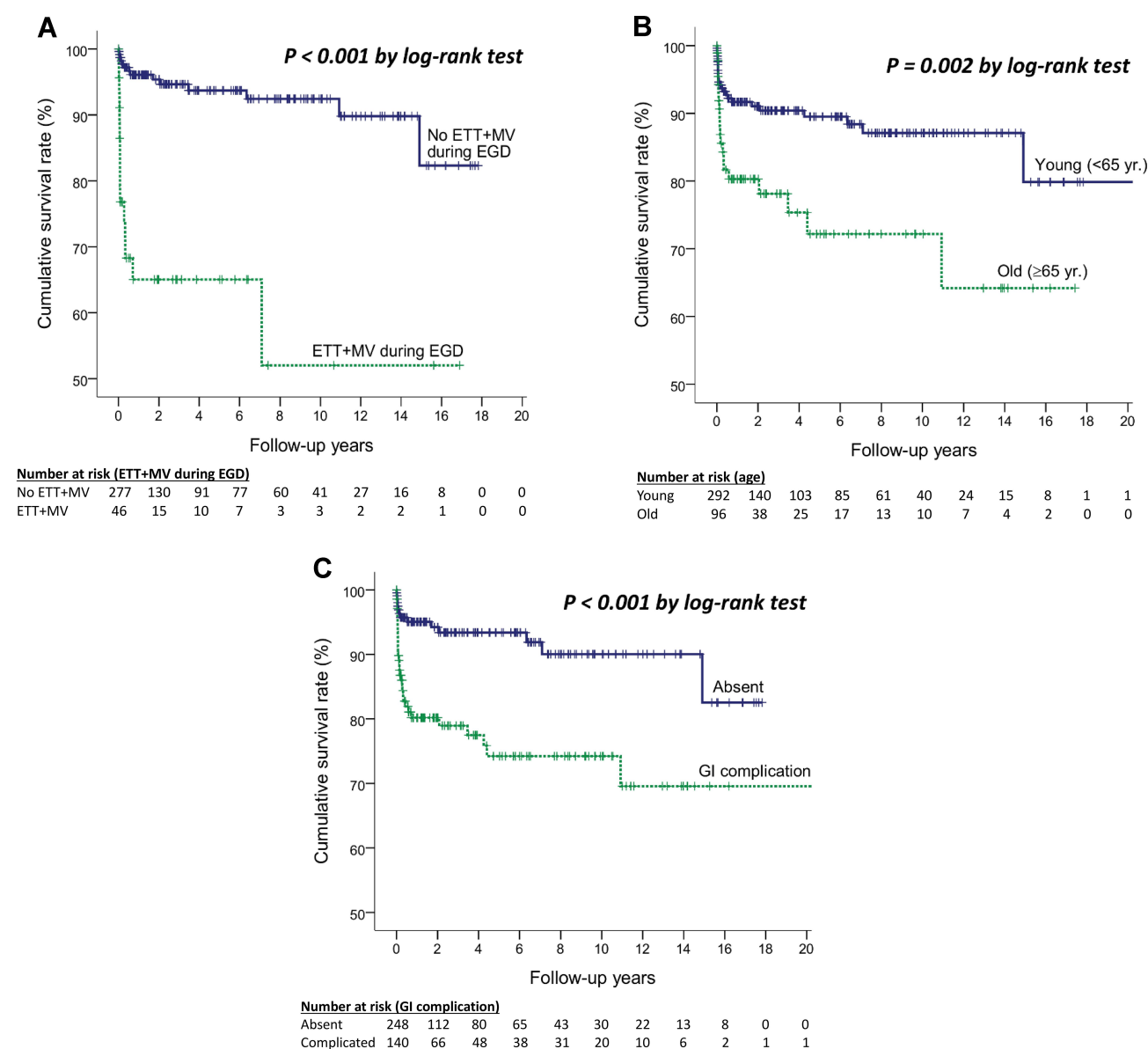


Figure 3 Overall survival analyses with the Kaplan–Meier method. **(A)** ETT + MV during EGD ($p < 0.001$); **(B)** Age ($p = 0.002$); **(C)** GI complication ($p < 0.001$).

Abbreviations: EGD, esophagogastrroduodenoscopy; ETT + MV, endotracheal tube with mechanical ventilation; GI, gastrointestinal.

indicates threats to caustic injury victims by “indirect means,” such as significantly advanced age, more non-PCs, alcoholism, illicit drug abuse, and baseline unhealthy status, resulting in statistically higher risks of complications and limited recovery. Severe complications and delayed sequelae subsequently affected survival outcomes. Both limited recovery and longer LoHS observed in caustic ingestion cases with PCs coincided with previously reported psychological effects (particularly in DDs) on acute cardiac events.³⁶ More healthcare resources were distributed to those with PCs regardless of whether they were within or after the acute stage of caustic injuries.

Ogunrombi et al¹⁶ have reported 27 patients with psychopathologic history, who had a limited degree of caustic injuries and better surgical outcomes. In contrast, our experiences demonstrated that PCs were predictors of severe GI tract injuries and involved greater consumption of healthcare resources, more early complications/delayed sequelae, less preservation of the native esophagus/stomach, and poorer long-term survival outcomes. Nevertheless, the population and etiology of caustic GI tract injury differ from country to country. Despite the inconsistent findings between two populations, we could integrate such valuable information and concluded that

more attention should be paid to those with PCs. Clinical awareness brings early recognition and early management for mild cases to limit injuries, or for severe ones to receive emergent interventions.

Our study was limited by its retrospective nature and potential information bias. However, the actual caustic substances and ingested amounts might have been affected by memory lapses or clerical errors during chart recording. Additionally, the reported 20-year cases spanned two versions of psychiatric diagnostic criteria, which might have influenced our analyses. Nevertheless, the large number of cases and strict exclusion of uncertain diagnoses could compensate for the inevitable inconsistency. We studied 396 cases with detailed clinical courses and long-term multifaceted outcomes. This research, to some extent, overcame the dilemma between large sample size and detailed clinical information in the field of caustic GI tract injury. However, relatively serious scenarios accounted for a higher proportion at our center. Moreover, the etiology of caustic ingestion was roughly related to local customs, thereby presenting geographic differences. Hence, future studies based on worldwide populations are essential to comprehensively understand the association between caustic ingestion and PCs.

Conclusion

For patients with caustic substance ingestion, the presence of PCs predicted serious EGD grading, higher rates of admission/surgery/ICU stay, increments of systemic/GI complications, and poorer 5-year overall survival rates. Advanced age, more non-PCs, substance abuses, and baseline unhealthy status resulted in higher risks of complications and limited recovery from caustic injury. Severe complications and delayed sequelae affected patient survival. Clinical awareness helps limit injuries in mild cases or allows for emergent interventions in severe cases.

Ethics

Our research protocol had been approved by Chang Gung Medical Foundation Institutional Review Board (IRB number: 202000583B0; executing institution: Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan). The IRB reviewed and determined that it is expedited review according to personal information, data, documents, or specimens collected from legal biological databases without hyperlink or identifiable information that can be used for research but cannot be involved in the interests of individuals or groups. On the basis of the aforementioned

statements, the IRB approves the waiver of the participants' consent in the present study.

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Disclosure

The authors report no conflicts of interest in this work.

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