

ORIGINAL ARTICLE

Caustic ingestion. Spanish multicenter study on prognostic severity factors and diagnostic test performance

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Objective. To characterize the clinical profile of patients treated for oral caustic injury, describe the use of diagnostic tests in emergency departments (EDs), and analyze factors associated with severity and prognosis.

Methods. Multicenter, retrospective, observational study including patients treated in EDs for caustic substance ingestion over a 7-year period (2015–2021). Epidemiological, clinical, and diagnostic variables were analyzed, and the prognostic performance of esophagogastroduodenoscopy (EGD) and computed tomography (CT) was evaluated.

Results. A total of 225 patients were included, with a mean age of 44 (SD, 24) years; 52.4% were women. Intentional ingestion accounted for 49.3% of cases. The most prevalent caustic agents were sodium hypochlorite (48.9%) and hydrochloric acid (16.4%). EGD was performed in 84.4% of patients, CT in 24.9%, and both in 20.4%. In the final predictive model, prognostic factors associated with severe injury (Zargar $\geq$ IIb and/or Ryu $>$ 2) were: intentional ingestion with OR, 4.19 (95% CI 1.71–10.26; $P = .002$), ammonia with OR, 11.39 (95% CI 2.07–62.65; $P = .005$), and the initial presence of digestive and/or respiratory symptoms. CT showed acceptable performance for detecting initial severe lesions, with a negative predictive value of 75% and a negative likelihood ratio of 0.28; however, it does not definitively replace EGD in less severe cases.

Conclusions. Suicidal intent and the use of highly corrosive caustic agents, together with initial clinical findings, are associated with worse prognosis. CT is useful but does not replace EGD in mild or moderate cases.

Keywords: Caustic agents. Esophagogastroduodenoscopy. Poisoning. Emergency department. Computed tomography.

Estudio multicéntrico español sobre los factores pronósticos de gravedad y el rendimiento de las pruebas diagnósticas en la ingesta de cáusticos

Objetivo. Caracterizar el perfil clínico de los pacientes atendidos por causticación oral, describir el uso de las pruebas diagnósticas en urgencias y analizar los factores asociados a la gravedad y al pronóstico.

Métodos. Estudio multicéntrico, retrospectivo y observacional que incluyó a pacientes atendidos en urgencias por la ingesta de sustancias cáusticas entre 2015 y 2021 (7 años). Se analizaron variables epidemiológicas, clínicas y diagnósticas, y se evaluó la capacidad pronóstica de la esofagogastroduodenoscopia (EGD) y la tomografía computarizada (TC).

Resultados. Se incluyeron 225 pacientes, con una edad media de 44 (DE 24) años, el 52,4% mujeres. El 49,3% fueron ingestas voluntarias. Los cáusticos más prevalentes fueron el hipoclorito sódico (48,9%) y el ácido clorhídrico (16,4%). Se realizó EGD al 84,4% y TC al 24,9% (ambas en el 20,4%). En el modelo predictivo final, los factores pronósticos asociados a lesiones graves (Zargar $\geq$ IIb o Ryu $>$ 2) fueron: ingesta voluntaria con OR de 4,19 (IC 95%: 1,71-10,26; $p = 0,002$), amoníaco con OR de 11,39 (IC 95%: 2,07-62,65; $p = 0,005$) y la presencia inicial de síntomas digestivos o respiratorios. La TC mostró rendimiento aceptable para detectar lesiones graves iniciales, con un valor predictivo negativo del 75% y una (razón de verosimilitud positiva) de 0,28, aunque no permite sustituir definitivamente a la EGD en los casos menos graves.

Conclusiones. La intencionalidad suicida y el uso de cáusticos altamente corrosivos junto con hallazgos clínicos iniciales se relacionan con peor pronóstico. La TC es útil, pero no reemplaza a la EGD en casos leves o moderados.

Palabras clave: Cáusticos. Esophagogastroduodenoscopia. Intoxicación. Servicio de urgencias. Tomografía computarizada.

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Introduction

Caustic substances are chemical products, either acidic or alkaline, that can damage any tissue, causing tissue destruction and burns. The most frequently affected parts of the body are those most exposed, such as the face, eyes, and extremities. Contact is usually accidental, generally due to splashing during handling of containers holding these substances or because they are accessible without adequate protection, a situation with a particular impact on preschool children. However, severe and even fatal injuries may occur following oral ingestion.¹

Accidental or suicidal ingestion of caustic substances may cause severe gastrointestinal and respiratory injuries,² with early clinical consequences that make appropriate initial management crucial for reducing mortality and sequelae.³⁻⁵ Despite appropriate clinical care, mortality after ingestion may be high, as reflected by statistics from some Asian countries, where completed suicide rates are particularly high.⁶

The severity of injuries caused by caustic substances depends on multiple factors, including the type of agent, pH, viscosity, concentration or degree of dilution, amount ingested, duration of contact, and the patient's premorbid condition or the pre-existing condition of the gastrointestinal tract. Although pH has traditionally been used to estimate the potential for injury—a parameter often readily available from product labeling—this parameter alone is insufficient and may lead to errors in clinical management.⁷

Titratable acid/alkaline reserve (TAR) quantifies the amount of neutralizing agent required to bring the pH to physiological values. Neutralization of caustic substances occurs at the expense of tissues, generates heat, and causes burns. Caustic substances with a high TAR produce greater tissue damage regardless of their pH; therefore, this parameter may have prognostic value in oral ingestion.⁷

In the household setting, the most common acids are hydrochloric acid or muriatic acid (HCl) and sulfuric acid (H₂SO₄), whereas the most common alkalis are sodium hypochlorite or bleach (NaClO), sodium hydroxide or caustic soda (NaOH), and nitrogen trihydride or ammonia (NH₃).⁶ Sodium hypochlorite is the caustic substance most frequently responsible for visits to emergency departments (EDs) in Spain, as reported in a recent study.⁸ In 2023, poisoning by cleaning products represented the second most common reason for consultation with the Servicio de Información Toxicológica (SIT) (16.8%), surpassed only by medication-related poisoning (50.6%).⁹ International series, such as those from the United States, show similar findings, with a particular impact on preschool children.¹⁰

Regarding management, the past decade has seen extensive scientific reassessment, with studies proposing the initial use of imaging techniques such as computed tomography (CT), which have progressively gained prominence over esophagogastroduodenoscopy (EGD),^{11,12} historically the technique of choice for any

caustic ingestion. As a result of this trend, classification systems have been proposed that relate imaging findings to lesion prognosis or to the indication for specific treatments (Ryu classification),¹³ paralleling the role of EGD findings (Zargar classification).¹⁴

Given the high morbidity and mortality associated with caustic ingestion, a multicenter study involving hospitals from several Spanish autonomous communities was undertaken to describe the epidemiological profile of patients with caustic ingestion, determine its prevalence and clinical characteristics, evaluate the diagnostic resources used, and estimate prognosis. The ultimate aim was to improve clinical outcomes in future patients following caustic ingestion and reduce variability in clinical management during ED care by identifying prognostic factors associated with severity and ultimately proposing a management algorithm.

Methods

We conducted a retrospective, observational, descriptive, multicenter study involving 8 EDs from 7 Spanish autonomous communities. Data were collected over 7 years, from January 1, 2015, through December 31, 2021. Patients were identified by the investigator at each center according to discharge-report coding.

Patients of any age who presented to the ED with symptoms compatible with oral caustic injury or in whom diagnostic testing (EGD or CT) was considered necessary after oral caustic ingestion were included. Patients exposed to caustic substances through routes other than the oral route (ocular, cutaneous, or respiratory), as well as asymptomatic patients for whom no complementary testing was indicated in the ED, were excluded. Cases with incomplete information for key variables required for the primary analysis were also excluded. Because of the retrospective and descriptive nature of the study, no imputation methods were applied.

For each episode, epidemiological variables (age, sex, past medical history), episode-related variables (motivation or cause of ingestion, type of caustic substance, co-ingestion of other toxic substances, site of first medical care, and interval between ingestion and medical assessment), clinical symptoms, complementary investigations (laboratory tests, EGD, and CT), therapeutic measures, disposition after ED care, and sequelae were recorded.

Lesion severity was defined according to previously validated classification systems. Lesions identified by EGD were graded using the Zargar classification, with lesions $\geq$ IIb considered severe. Lesions detected by CT were graded using the Ryu radiological classification, with lesions > 2 defined as severe. The literature indicates that these cutoff points are associated with a higher risk of complications, a greater need for therapeutic intervention, and a worse short- and long-term prognosis.^{13,14}

Data for each case were collected retrospectively by the investigator at each center and entered into a data-

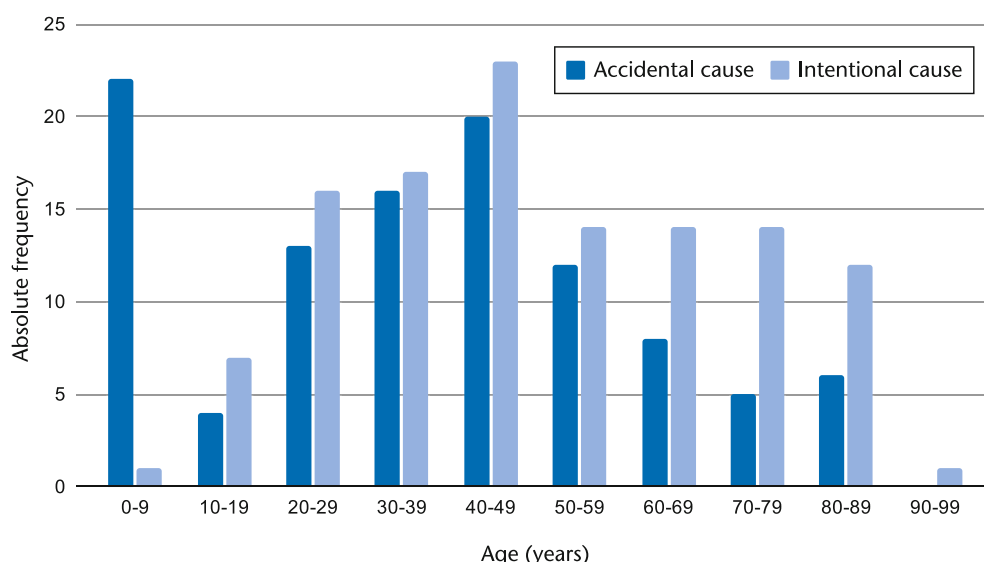


Figure 1. Distribution of the causes of ingestion (accidental and intentional) grouped into 10-year age intervals. Accidental ingestions predominate in pediatric patients (0-9 years), whereas intentional ingestions increase progressively during adulthood and peak in the 40-49-year age group.

base specifically created for this study, with episodes anonymized.

All statistical analyses were performed using SPSS for Windows version 25.0 (SPSS Inc., Chicago, IL, United States). Continuous variables were expressed as mean and SD or median and IQR (25th and 75th percentiles). Categorical variables were expressed as frequencies. The Student t test or Mann-Whitney U test was used to compare continuous variables according to distribution normality, which was assessed using the Kolmogorov-Smirnov test. The chi-square test or Fisher exact test was used to compare categorical variables. *P* values < .05 were considered statistically significant.

A logistic regression model was applied to identify factors associated with greater severity. In addition, the prognostic performance of EGD according to the Zargar classification and CT according to the Ryu classification was evaluated using adjusted models and receiver operating characteristic (ROC) curves. Their diagnostic performance and the degree of agreement between both techniques were also estimated.

The study was conducted in full compliance with the principles outlined in the Declaration of Helsinki for research involving human participants and was approved by the Comité de Ética de Investigación con medicamentos de las Islas Baleares (IB 5159/23) and the Comité de Ética de Investigación con medicamentos de Girona (2023.076). The requirement to obtain informed consent was waived because this was an epidemiological study using anonymized data.

Results

A total of 225 patients were included, 118 of whom were women (52.4%), with a mean age of 44 years (SD, 24). In 111 cases (49.3%), ingestion was inten-

tional, whereas 114 (50.7%) were accidental, the latter being concentrated in childhood and up to middle age (Figure 1). In 28 cases (12.4%), the caustic substance had been diluted in water. The interval from ingestion to first medical assessment could be established in 146 cases (64.9%), with a mean of 2.2 hours (SD, 3). The most prevalent caustic substances were sodium hypochlorite (bleach), 110 cases (48.9%); hydrochloric acid (muriatic acid), 37 (16.4%); nitrogen trihydride (ammonia), 25 (11.1%); and sodium hydroxide (caustic soda), 12 (5.3%).

A single diagnostic test was performed in 154 patients (68.4%): EGD in 144 cases (93.5%) and CT in 10 (6.5%). Both tests were performed in 46 patients (20.4%), and neither was performed in 25 (11.2%). Overall, 190 EGDs (84.4%) and 56 CT scans (24.9%) were performed. The mean interval between ED arrival and EGD was 9.4 hours (SD, 12), whereas the corresponding interval for CT was 5.8 hours (SD, 7.6). Among patients who underwent both tests, the elapsed time from first medical assessment to completion of both diagnostic tests could be determined in 35 cases (76%). CT was performed first in most cases (*n* = 21; 60%). When both tests were performed, the reports were concordant in 31 cases (67.4%) and discordant in 11 (23.9%); in the remaining cases (8.69%), the radiological report was incomplete, preventing comparison of the findings.

Initial-care variables associated with a higher risk of severe lesions on EGD (Zargar ≥ IIb) or CT (Ryu > 2) included suicidal or other intentional ingestion, involvement of certain products (hydrochloric acid and ammonia), older patient age, pre-existing conditions (psychiatric disease or chronic renal failure), and the presence of respiratory symptoms (stridor, increased respiratory rate) and GI symptoms (oral burning, epigastric pain, or severe retrosternal pain). All of these

Table 1. Relevant variables at initial assessment after caustic ingestion, grouped according to predefined severity criteria

Variable	Lower severity N = 99 n (%)	Higher severity N = 126 n (%)
Age, years [mean (SD)]	39.7 (24.6)	47.4 (22.7)
Male sex	47 (47.5)	60 (47.6)
Psychiatric history	30 (30.3)	66 (52.4)
Cause		
Accidental	64 (64.6)	42 (33.3)
Intentional	33 (33.3)	78 (61.9)
Type of caustic substance		
Bleach	63 (63.6)	47 (37.2)
Hydrochloric acid	2 (2.0)	35 (27.8)
Ammonia	4 (4.0)	21 (16.7)
Caustic soda	5 (5.1)	7 (5.6)
Detergent/descaling agent	21 (21.2)	11 (8.7)
Product diluted in water	20 (20.2)	8 (6.3)
Initial vital signs [mean (SD)]		
HR, bpm	87 (20)	92 (21)
SBP, mmHg	131 (23)	129 (21)
DBP, mmHg	77 (13)	77 (16)
Temperature, °C	36.1 (0.5)	36.1 (0.8)
RR, breaths/min	17 (3)	22 (5)
O ₂ saturation, %	97 (2)	96 (6)
Initial symptoms		
Tongue lesion	8 (8.1)	37 (30.6)
Epigastric pain	26 (26.3)	58 (47.9)
Sialorrhea	7 (7.1)	19 (15.4)
Dyspnea	1 (1.0)	26 (21.0)
Stridor	0 (0)	7 (5.7)
Time to medical assessment, hours [mean (SD)]*	1.76 (2.02)	2.62 (3.54)
Initial blood tests [mean (SD)]		
pH	7.37 (0.04)	7.31 (0.12)
Bicarbonate, mmol/L	25.4 (3.0)	21.7 (5.3)
Lactate, mg/dL	5.6 (8.3)	8.2 (10.2)

*Interval from ingestion to first medical assessment.

SD: standard deviation; HR: heart rate; bpm: beats per minute; SBP: systolic blood pressure; DBP: diastolic blood pressure; RR: respiratory rate; O₂: oxygen. saturation.

may constitute early, reliable, and readily identifiable warning signs of a worse clinical course. Conversely, factors associated with lower severity included accidental ingestion, sodium hypochlorite (bleach) as the substance involved, and prior dilution of the product in water (Table 1).

Some blood gas parameters (pH and bicarbonate) were added to Table 1 because of their early availability during initial assessment and their statistical correlation with severe lesions detected by EGD and/or CT.

In multivariable analysis, a worse clinical course was independently associated with suicidal intent, ingestion of hydrochloric acid or ammonia, the presence of tongue lesions and epigastric pain, and initial laboratory abnormalities, including low bicarbonate levels and leukocytosis. After evaluation of the different models, the final predictive model identified suicidal intent, ammonia ingestion, tongue lesions, and epigastric pain as independent predictors of worse prognosis (Table 2).

The area under the ROC curve (AUROC) for the final predictive model was 0.876 (95% CI, 0.82-0.93;

Table 2. Factors associated with poor prognosis in GI caustic injury according to multivariable models

Variable	OR	95% CI	P value
Demographic and caustic-agent model			
Suicidal intent	2.55	1.21-5.39	.014
Ammonia	4.52	1.28-15.91	.019
Hydrochloric acid	8.15	1.55-42.71	.013
Clinical model (initial symptoms)			
Tongue lesion	5.17	2.15-12.43	< .001
Epigastric pain	2.74	1.44-5.22	.002
Constant	0.46	–	< .001
Laboratory model (biochemical)			
Bicarbonate	0.83	0.73-0.94	.004
Leukocyte count	1.12	1.03-1.21	.010
Final predictive model (predicted probability)			
Suicidal intent	4.19	1.71-10.26	.002
Ammonia	11.39	2.07-62.65	.005
Tongue lesion	3.42	1.03-11.40	.046
Epigastric pain	2.58	1.01-6.63	.049

OR: odds ratio; 95% CI: 95% confidence interval; constants represent the model intercept.

Bold values denote statistical significance ($P < .05$).

$P < .001$), indicating very good discriminative ability for identifying the most severe cases. Variables that contributed significantly to the model were suicidal intent, ammonia ingestion, tongue lesions, and epigastric pain (Figure 2).

CT demonstrated good ability to identify severe lesions, with a sensitivity rate of 82.6% and a specificity rate of 63.1% when EGD was used as the reference standard. CT was particularly useful for guiding initial decisions in patients presenting with more severe early symptoms, but it could not replace EGD in cases of mild or moderate ingestion (Table 3).

Discussion

In this series, probably one of the largest published in Europe on severe GI caustic injuries, the sex distribution was balanced. There was a slight predominance of women (52.4%), and the mean age was 44 years. Accidental ingestion accounted for 50.7% of episodes, particularly among preschool children. These findings are consistent with other cohorts, in which caustic exposure follows a bimodal pattern: young adults in suicide attempts and children in accidental exposures.¹¹

The high proportion of accidental cases reinforces the need to intensify preventive measures in the household setting, particularly regarding health education and safe storage of caustic products.¹⁵ Conversely, the other half of patients presented after intentional ingestion. This group requires different preventive strategies focused on early detection of psychiatric disorders or suicidal behavior. Asking family members or others in the patient's environment about the availability or accessibility of these products should form part of routine assessment.¹⁶ Several studies have reported an increase in intentional ingestions during and after the COVID-19 pandemic,¹⁷ within the broader increase in suicidal behavior observed during lockdown and the subsequent months.¹⁸

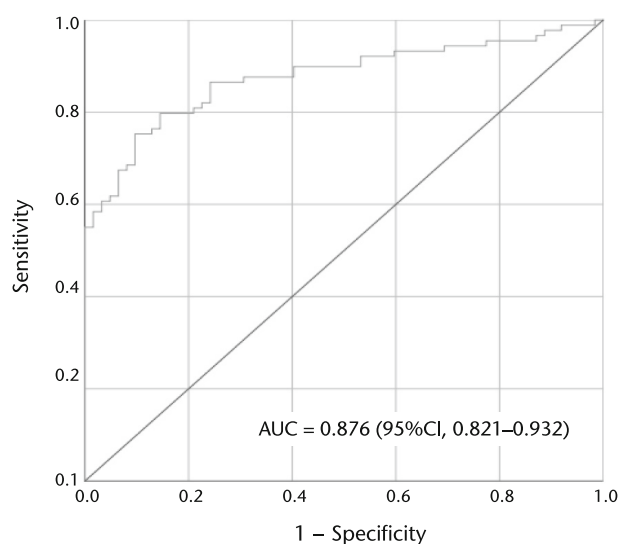


Figure 2. Receiver operating characteristic (ROC) curve for the final predictive model. The area under the curve was 0.876 (standard error, 0.028; 95%CI, 0.82–0.93). AUC: area under the curve; CI: confidence interval.

In this study, the signs and symptoms listed in Table 1 were associated with greater severity and enabled early identification of patients at risk of complications. The mean interval from ingestion to medical assessment was 2.2 hours, although with considerable variability. The literature emphasizes the importance of some of these initial signs, such as tachypnea, a vital sign that is frequently underrecorded.¹⁹

The increasing availability of blood gas analyzers in advanced life-support ambulances has enabled early measurement of parameters such as pH and bicarbonate, which were included in Table 1 as markers of greater severity. Other parameters more specific to the hospital setting, such as leukocytosis or renal dysfunction, also demonstrated prognostic value in this series (Table 2).²¹

Although elevated lactate is recognized as a marker of worse outcomes in toxicology and emergency medicine,²² this association was not confirmed in the present study. One possible explanation is that, in caustic ingestion, the initial injury is usually localized and systemic metabolic abnormalities may appear later, even in severe cases, unlike other critical conditions characterized by early hypoperfusion.

Regarding the causative agent, sodium hypochlorite (bleach) was the caustic substance most frequently involved in this series, probably because of its widespread availability in households.⁸ However, ingestion of more aggressive products such as hydrochloric acid and ammonia was associated with a significantly worse prognosis. This finding may be explained by their greater potential for mucosal injury and the deep necrosis they can cause even in small amounts.²³

In the multivariable analysis, intentionality of ingestion, type of substance (hydrochloric acid or ammonia), presence of tongue lesions and epigastric pain or early respiratory symptoms, as well as low bicarbonate levels and elevated leukocyte counts, were independently as-

Table 3. Factors associated with poor prognosis in gastrointestinal caustic injury according to multivariable models

Parameter	Value	95% CI
Sensitivity (%)	82.61	64.94–100
Specificity (%)	63.16	38.84–87.48
Accuracy (%)	73.81	59.32–88.30
Positive predictive value (%)	73.08	54.10–92.05
Negative predictive value (%)	75.00	50.66–99.34
Prevalence (%)	54.76	38.52–71.01
Youden index	0.46	0.19–0.72
Positive likelihood ratio	2.24	1.21–4.16
Negative likelihood ratio	0.28	0.11–0.72

95% CI: 95% confidence interval.

sociated with greater severity. These findings indicate that certain clinical and laboratory variables available during the initial assessment can act as early prognostic markers of severe injury. Former studies have described similar associations both for factors related to the ingested substance and for specific clinical and laboratory parameters, supporting their prognostic value.^{24,25}

In recent years, diagnostic strategies for the initial management of these patients have undergone important changes, driven by the emergence of CT as an early diagnostic investigation. This technique has acquired a key role in severe injuries because it can identify signs of transmural gastrointestinal necrosis and select patients who may require emergency surgery.¹¹ Moreover, this trend has been influenced by limitations in performing EGD, particularly in the most severe cases because of the risk of complications during the procedure, as well as by the fact that not all centers have round-the-clock access to this technique. Both factors have encouraged the search for safer and more accessible diagnostic methods, such as CT.²⁶

Despite these advances, important questions remain unresolved, including the optimal timing of CT.^{6,27} The recent study by Chen *et al.*¹² proposes that, in severe cases, initial signs and symptoms should guide selection of the complementary diagnostic test. Furthermore, it indicates that CT cannot yet definitively replace EGD when moderate or mild injuries are suspected, as confirmed in the present series, in which CT in patients with initially mild or moderate lesions ($Ryu \leq 2$) should be regarded only as a complementary technique rather than a substitute for EGD.

Consistent with this concept, which we share, we consider it appropriate to propose a clinical management algorithm for gastrointestinal caustic injury (Figure 3). Its application should be adapted to each clinical situation and level of care. In prehospital settings or centers without EGD availability, it allows early identification of cases requiring primary or secondary transfer to centers with greater diagnostic resources. At referral centers, it can help establish priorities when deciding which diagnostic investigations should be performed. Because it is based on clinical and laboratory variables that are available early, systematic implementation may reduce variability in care and optimize clinical decision-making.

The extent and severity of GI injury determine both short- and long-term outcomes. Therefore, only pa-

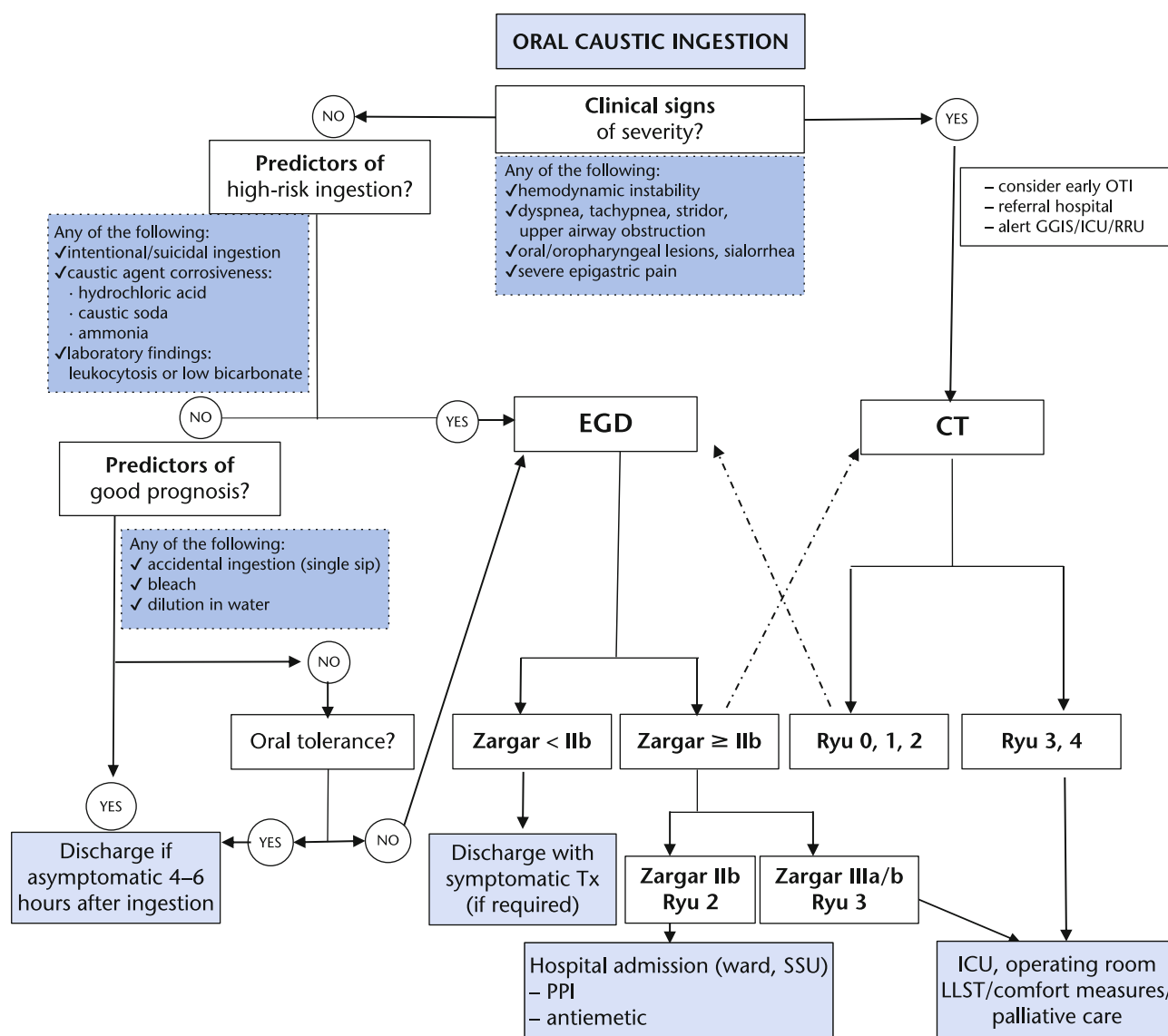


Figure 3. Management algorithm for GI caustic injury.

When computed tomography (CT) is indicated as the initial investigation, it should be performed upon the patient's arrival at the hospital, as soon as possible. When esophagogastroduodenoscopy (EGD) is the initial investigation of choice, it should be performed within the first 3 hours. When both CT and EGD are used to complement the initial assessment, both investigations should be completed within the first 12 hours.

Airway: airway management; OTI: orotracheal intubation; GGIS: general and GI surgery; ICU: intensive care unit; RRU: resuscitation/recovery unit; Tx: treatment; SSU: short-stay unit; PPI: proton pump inhibitors; LLST: limitation of life-sustaining therapy; ICU: intensive care unit.

tients with high-grade lesions (Zargar ≥ IIb or Ryu > 2) would require hospital admission because of the greater risk of complications, together with close outpatient follow-up to monitor clinical progress and development of sequelae.²⁸ The remaining patients generally have a favorable course and, in the absence of symptoms, do not require specific follow-up after hospital discharge.²⁹

This study has several methodological limitations. Selection bias may have led to overestimation of case severity because only patients presenting to EDs and meeting the inclusion criteria were included. Heterogeneity between centers in protocols, resources, and data recording may have introduced variability in lesion assessment and clinical management. Furthermore, the study was based on retrospective clin-

ical records and therefore has the limitations inherent to observational analyses of this type. Nevertheless, this multicenter series provides valuable information on caustic ingestion in Spain.

In conclusion, intentional ingestion with suicidal intent involving highly corrosive caustic substances such as hydrochloric acid or ammonia, together with the presence of tongue lesions, epigastric pain, low bicarbonate levels, and an elevated leukocyte count, suggests a poor prognosis in patients with gastrointestinal caustic injury. In general, CT can be useful for detecting severe lesions, but it does not routinely replace EGD, particularly in patients with mild or moderate ingestion. Its usefulness should be assessed according to the clinical setting and the availability of diagnostic resources at each center.

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