

## The Role of Second-look Endoscopy in Severe Esophageal Caustic Injury

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### Abstract

Severe caustic ingestion often leads to multiple complications and high mortality rate. Esophagogastroduodenoscopy is recommended during the first 24 hours for severity and extent evaluation, but it seems insufficient to guide further managements in severe caustic injury patients due to rapid progression and variable clinical conditions. Therefore, we tried to evaluate the safety and role of second-look endoscopy in these patients in 1-2 weeks later.

We retrospectively collected severe esophageal caustic injury (grade 2b, 3a, 3b) adults with and without second-look endoscopy in subacute stage (6<sup>th</sup>-14<sup>th</sup> days after caustic injury) in Linkou Chang Gung Memorial Hospital during 2011/1-2014/11. They were divided in to once endoscopy group and second-look endoscopic group according to the patients with second-look endoscopy or not. They were further matched with the same cause of caustic injury, corrosive properties, injury grading, and then selected with Excel RAND function. There were 26 patients in both groups.

The average timing of second-look endoscopy was 10.23 ± 3.166 (mean ± SD) days after caustic ingestion. The hospital stay was significantly shorter in the second-look endoscopy group (24.92 ± 17.50 days, 54.38 ± 43.73 days, P=0.002). However, the complication rate was not statistically significant between these two groups.

In conclusion, second-look endoscopy is safe and might shorten the hospital stay. However, prospective, randomized and larger sample size studies are needed to support the finding.

**Keywords:** Caustic injury; Caustic ingestion; Second-look endoscopy

### Introduction

Caustic ingestion brings severe complications and heavy burden to health care system [1,2]. The severity of damage depends on corrosive properties, amount, concentration, physical form and duration of contact with the mucosa [3,4]. In terms of severity evaluation, symptoms and signs alone are unreliable [5]. Early esophagogastroduodenoscopy (EGD) is recommended within the 24-48 hours to evaluate the severity and extent of damage, establish prognosis, and guide therapy [6-8]. Many endoscopic grading systems have been purposed [8-10].

However, Zargar's classification is mostly wide used and accepted: grade 0 is normal; grade 1 is mucosal edema and hyperemia; grade 2a is superficial ulcers, bleeding, exudates; grade 2b is deep focal or circumferential ulcers; grade 3a is focal necrosis; and grade 3b is extensive necrosis [8]. At least 70% patients with grade 2b and 3a injury leads to esophageal stricture [8,11]. The patients with grade 3b injury have 65% early mortality rate, and most of them need

esophageal resection with colonic or jejunal interposition [8,11]. Therefore, the patients with severe esophageal caustic injury (grade 2b, 3a, 3b) have variable clinical condition, rapid progression and poor outcome.

Recent study mentioned conservative management of severe caustic injury during acute phase leads to superior long-term nutritional and quality of life outcome [12]. In this way, precisely clinical decision making, esp. timing of surgical intervention is critical.

Only once endoscopic exam within 24-48 hours seems insufficient to guide the treatment because the endoscopic grade at that time not actually reflects the most severe status, especially in alkali ingestion. Some researches mentioned it's safe to repeat endoscopy up to 3 weeks after caustic injury in expert hands [13,14]. Although upper gastrointestinal series plays the role in clinical evaluation, it's not as precise as endoscopic examination.

Therefore, some clinical physicians prefer second-look endoscopy to help them deciding the timings of initiating feeding, operation, and etc. in sub-acute stage (6<sup>th</sup>-14<sup>th</sup> days after caustic injury). No study mentioned the role of second-look endoscopy in severe esophageal caustic injury patients till now. We try to clarify its safety and benefit.

## Materials and Methods

Under the approval of the Chang Gung Medical Foundation Institutional Review Board (104-2662B), we retrospectively collected severe caustic ingestion (Zagar grade 2, 3a, 3b) adults from electronic endoscopic report system in Linkou Chang Gung Memorial Hospital during 2011/01-2014/11. The patients who had unknown corrosive properties or no first endoscopy result within 24 hours were excluded. The rest patients were divided into once endoscopic group (only once EGD within first 24 hours) and second-look endoscopy group (first EGD within 24 hours of caustic ingestion and second EGD during 6<sup>th</sup>-14<sup>th</sup> days). The second-look endoscopy was performed when patients had improved clinical condition, including less pain and stable vital sign, and we considered to try oral intake to confirm the endoscopic grade in subacute stage. If the Zagar's score of second-look endoscopy was the same or improved, patients would go ahead to starting intake. On the other hand, surgical evaluation and prolonged fasting were indicated. In once endoscopic group, there was much higher proportion of the patients with Zagar grade 3a, 3b, and they could not receive second-look endoscopy due to worse clinical condition in subacute stage. Therefore, we matched these two group patients with the same Zagar grading, cause of caustic injury (suicide or accident), corrosive properties and injury grading in maximum case number, and then selected by Excel RAND function if we got several candidates.

The initial managements, including stabilizing vital sign, intravenous fluid and nutrition support, intensive care unit admission, fasting, serial chest and abdominal film follow-up were proved in all patients. The indications for emergency surgery were clinical signs or image evidence of perforation, mediastinitis, peritonitis or highly suspected impending perforation by clinicians or endoscopic finding. Receiving second-look endoscopy or not and the timing were decided by clinical physicians, patients' agreements, clinical symptoms and signs in subacute stage. All the endoscopic exams were performed with room air by the same experienced endoscopic doctor.

We analyzed the hospital stay duration, systemic complications (aspiration pneumonia, respiratory failure, disseminated intravascular coagulation (DIC), acute hepatitis, acute kidney injury), gastrointestinal (GI) complications (perforation, fistula formation, bleeding, stricture) and the need of further treatment (dilatation, esophagectomy) to evaluate the safety and benefits of second-look endoscopy in these cases.

We used Microsoft Excel 2013 RAND function to select patients after matched the same cause of caustic injury, corrosive properties and endoscopic severity grading. The  $\chi^2$  test was used for group comparisons involving binary data and independent samples. Numerical data were evaluated by Student ttest. The results were considered to indicate a statistically significant difference when  $P < 0.05$ . Statistical calculations were performed using SPSS, 18.0 software (SPSS, Inc., Chicago, IL, USA).

## Results

In this study, we finally enrolled 52 severe esophageal caustic injury (Zagar grade 2b, 3a, 3b). In these patients, suicide was the major cause of caustic ingestion (84.62%), and acid ingestion was more than alkali ingestion (57.69%, 42.31%). The average age was  $50.48 \pm 19.08$  years old, and men were predominant (51.92%, 48.08%). The distribution of endoscopic severity were grade 2b (11.54%), grade 3a (23.08%) and grade 3b (65.38%). There were 26 patients in each group.

As we showed in Table 1, the cause of caustic injury (suicide/accident), corrosive property and endoscopic severity were matched equally in both groups, but the age of second-look endoscopy group is older than once endoscopy group ( $55.81 \pm 17.45$  y/o,  $45.15 \pm 19.47$  y/o,  $P=0.043$ ). All patients in the study had first time endoscopic exam within 24 hours, and the average timing of second-look endoscopy was  $10.23 \pm 3.17$  days after caustic ingestion in second-look endoscopy group.

Characteristics	Overall (n=52)	Once endoscopy (n=26)	Second-look endoscopy (n=26)	P-value
Timing of second-look endoscopy (days after event)	-	-	10.23 ± 3.17	-
Sex	-	-	-	0.405
Male	27(51.92%)	12(46.15%)	15(57.69%)	-
Female	25 (48.08%)	14(53.85%)	11 (42.31%)	-
Age (y/o)	50.48 ± 19.08	45.15 ± 19.47	55.81 ± 17.45	0.043*
Suicide	44(84.62%)	22(84.62%)	22(84.62%)	1
<b>Corrosive property</b>				
Alkali	22(42.31%)	11(42.31%)	11(42.31%)	1
Acid	30(57.69%)	15(57.69%)	15(57.69%)	1
<b>Endoscopic severity</b>				
Grade 2b	6(11.54%)	3(11.54%)	3(11.54%)	1
Grade 3a	12(23.08%)	6(23.08%)	6(23.08%)	1
Grade 3b	34(65.38%)	17(65.38%)	17(65.38%)	1
Data are presents as mean ± standard deviation or number (%) of subjects *P<0.05				

**Table 1:** Demographic features analysis.

In Table 2, we could find the overall patients had 65.38% GI complication rate and 67.31% systemic complication rate. 59.62% patients needed esophageal balloon dilatation and 25% received esophagectomy due to perforation, progressive endoscopic severity score with highly suspected impending rupture.

The overall mortality rate was 5.77%. The average hospital stay was  $39.65 \pm 36.18$  days, but it was significantly shorter in the second-look endoscopy group ( $24.92 \pm 17.50$  days,  $54.38 \pm 43.73$  days,  $P=0.002$ ). The systemic (65.38%, 69.23%,  $P=0.768$ ) and GI (53.85%, 76.92%,  $P=0.080$ ) complication rates seemed lower in this group, but not reached statistically significant.

The two cases with perforation in second-look endoscopy group were not procedure related according to clinical symptoms and serial chest film follow-up. No endoscopy related complications, including fetal arrhythmia, bleeding, pneumomediastinum, pneumoperitoneum, aspiration or respiratory failure was observed during or immediately after endoscopic exam in these patients.

Diseases	Overall	Once endoscopy(n=26)	Second-look endoscopy (n=26)	P-value
GI complication	34(65.38%)	20(76.92%)	14(53.85%)	0.08
Bleeding	5(9.62%)	4(15.38%)	1(3.85%)	0.158
Perforation	7(13.46%)	5(19.23%)	2(7.69%)	0.223
Stricture	31(59.62%)	17(65.38%)	14(53.85%)	0.397
Fistula	0(0.00%)	0(0.00%)	0(0.00%)	1
Systemic complication	35(67.31%)	18(69.23%)	17(65.38%)	0.768
Respiratory failure	16(30.77%)	10(38.46%)	6(23.08%)	0.229
Aspiration pneumonia	18(34.62%)	12(46.15%)	6 (23.08%)	0.08
DIC	6(11.54%)	5(19.23%)	1(3.85%)	0.083
Acute hepatitis	1(1.92%)	1(3.85%)	0(0.00%)	0.313
Acute kidney injury	1(1.92%)	0(0.00%)	1(3.85%)	0.313
<b>Advanced treatment</b>				
Dilatation	31(59.62%)	17(65.38%)	14(53.85%)	0.397
Operation	13(25%)	6(23.08%)	7(26.92%)	0.749
Hospital stay (day)	39.65 ± 36.18	54.38 ± 43.73	24.92 ± 17.50	0.002*
Death	3(5.77%)	3(11.54%)	0(0.00%)	0.074
Data are presents as mean ± standard deviation or number (%) of subjects; GI: Gastrointestinal; DIC: Disseminated Intravascular Coagulation; *P< 0.05				

Table 2: Outcome analysis in once endoscopy and second-look endoscopy groups.

Characteristics	Alkali (n=22)	Acid (n=30)	P-value
<b>Sex</b>	-	-	0.424
Male	10(45.45%)	17(56.67%)	-
Female	12(54.55%)	13(43.33%)	-
Age (y/o)	52.14 ± 19.03	49.27 ± 19.35	0.597
Suicide	16(72.72%)	28(93.33%)	0.042*
<b>Times of endoscope</b>			
Once	11(50%)	15(50%)	1
Second-look	11(50%)	15(50%)	1
<b>Endoscopic severity</b>			
Grade 2b	2(9.09%)	4(13.33%)	0.636
Grade 3a	8(36.36%)	4(13.33%)	0.051
Grade 3b	12(54.55%)	22(73.33%)	0.159
GI complication	16(72.73%)	18(60.00%)	0.341
Bleeding	1(4.55%)	4(13.33%)	0.288
Perforation	3(13.64%)	4(13.33%)	0.975

Stricture	16(72.73%)	15(50.00%)	0.099
Fistula	0(0.00%)	0(0.00%)	-
Systemic complication	17(77.27%)	18(60.00%)	0.19
Respiratory failure	6(27.27%)	10(33.33%)	0.64
Aspiration pneumonia	9(40.91%)	9(30.00%)	0.414
DIC	3(13.64%)	3(10.00%)	0.685
Acute hepatitis	1(4.55%)	0(0.00%)	0.238
Acute kidney injury	0(0.00%)	1(3.33%)	0.387
<b>Advanced treatment</b>			
Dilatation	16(72.73%)	15(50.00%)	0.099
Operation	6(27.27%)	7(23.33%)	0.746
Hospital stay (day)	37.23 ± 20.66	41.43 ± 44.55	0.683
Death	2(9.09%)	1(3.33%)	0.379
Data are presents as mean ± standard deviation or number (%) of subjects; Abbreviations: GI: Gastrointestinal; DIC: Disseminated Intravascular Coagulation; *P<0.05			

**Table 3:** Demographic features and outcome analysis in alkali and acid ingestion groups.

As far as corrosive property was concerned, acid ingestion group had higher suicide rate (93.33%, 72.72%, P=0.042) in Table 3. It seems to have higher GI and systemic complication rates and longer hospital stay in acid ingestion group, but there was no statistical significance.

## Discussion

Unlike caustic ingestion in children, adults usually ingest strong corrosives with suicidal intent and lead to severe, life-threatening injuries with multiple long-term complications, including stricture, fistula formation and malignancy [7,15]. In the study, we found most caustic injury adults were also suicide intent with acid caustic agents (detergent or insecticides) at middle to older age in Taiwan. Therefore, this kind of injury is heavy burn to family and health care system [16]. How to improve the survival rate, shorten the hospital stay and decrease long-term complications are important issues. There is no specific treatment guideline for caustic ingestion injury because the corrosive property, amount, concentration, physical form, duration of contact with the mucosa, and patients' comorbidity should be taken into consideration of clinical care and affect the clinical outcome. It's not difficult to provide general management, including urgent resuscitation with correction of fluid and electrolyte and acid-base abnormalities to every caustic injury patients and immediate surgical exploration in those patients with signs of perforation [17]. How about further individual management in severe caustic injury patients? In such complicated and variable situation, EGD grading is most subject way to evaluate the severity of the injury and then guided the treatment. Therefore, early EGD is generally suggested during the first 24-48 hours after ingestion [6-8], although some doctors thought it might be unnecessary in mild injury [18].

However, the condition of severe caustic injury might change fatly and get worst injury grading after first 24 hours. We need an objective reference to guide further treatment in the subacute stage (6<sup>th</sup>-14<sup>th</sup> days), and second-look endoscopy would be the reliable tool.

Although upper gastrointestinal series is alternative, but not objective and comparable to first time endoscopic result. In our study, second-look endoscopy was performed at 10.23 ± 3.17 days after the caustic event to confirm endoscopic grading under stable clinical condition. In this way, hospital stay was shorter without increased the complications. Second-look endoscopy might play the role in shorten hospital stay in the patients with severe caustic injury. The dynamic change of endoscopic severity grade helping clinical physicians to decide the adequate timing of intake might explain the result.

With regard to safety, it was no endoscopic related complication noted in the study. According to previous studies, it was safe up to 96 hours after caustic ingestion, and even dilatation have been performed without consequences from 5 to 15 days after corrosive event. They also mentioned passage of the scope should be limited to the level of the first signs of a circumferential second or third degree esophageal injury to prevent possible adverse event [13,19-22]. Besides, we thought gentle insufflation, delicate manipulation, great caution and carbon dioxide use might further improve the safety and decrease complications.

However, second-look endoscopy could not statistically decrease gastrointestinal and systemic complication rate, the needs of balloon dilation and surgical intervention, and mortality rate in this study. The severity and extent were mostly destined by initial caustic event and primary management, so second-look endoscopy could not significantly change the outcome. However, it helped clinicians to make more precise therapeutic plan to shorten the hospital stay. It decrease family's economic burden, and let patients back to family and society earlier.

## Conclusions

Second-look endoscopy in subacute stage is safe in severe esophageal casutic injury. It might shorten the hospital stay, but not

improve other clinical outcomes. Because of limited case number and no comparison of twice endoscopic results, we needed prospective, randomized and larger sample size studies to support the finding.

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