

Prophylactic Endotracheal Intubation Prior to Urgent Endoscopy in Patients with Suspected Variceal Hemorrhage: An Evaluation of Outcomes and Complications

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ABSTRACT

AIM: There is limited evidence that suggests prophylactic intubation improves patient outcomes despite wide utilization. Our study aims to evaluate outcomes and complications related to prophylactic intubation through a retrospective comparison.

METHODS: Urgent esophagogastroduodenoscopy (EGD) for suspected variceal hemorrhage were included in the study and categorized into two cohorts, one with prophylactic intubation

and one without. Primary outcomes for the study were immediate aspiration, post EGD pneumonia, death, and other complications. Secondary outcomes included post EGD intensive care unit (ICU) stay, total ICU stay and total hospital stay. Retrospective comparison between cohorts was performed.

RESULTS: Total 110 occurrences of urgent EGD were included. Prophylactic intubation was performed in 65 occurrence. Demographics, clinical background and significant comorbidities were similar in both cohorts. Immediate aspiration, post EGD pneumonia, and mortality were similar in both cohorts. Complications other than cardiac and pulmonary related were higher in prophylactic intubation group than no intubation group (40% vs 17.78%, $p = 0.02$). Overall average hospital stay of both cohorts and overall average ICU stay were similar. Average ICU stay post EGD was significant longer in prophylactic intubation group than no intubation group (4.7 ± 3.9 days vs 2.6 ± 2.6 days, $p = 0.002$).

CONCLUSION: Our study revealed that prophylactic intubation prior to urgent EGD for variceal hemorrhage (VH) did not improve clinical outcomes. Our finding would suggest against routine prophylactic intubation in patients having VH with only mild encephalopathy and no ongoing hemorrhage.

Key words: Variceal hemorrhage (VH); endoscopic variceal ligation (EVL); esophagogastroduodenoscopy (EGD); medical intensive care unit (MICU); model for end-stage liver disease (MELD); standard deviation (SD); upper gastrointestinal bleeding (UGIB)

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INTRODUCTION

Variceal hemorrhage (VH) is the worst consequence of portal

hypertension, which represents the leading cause of death of cirrhotic patients^[1]. Despite the development in diagnostic and therapeutic measures, mortality of VH remains high at 15-20%^[2]. Endoscopic variceal ligation (EVL) is current first line treatment for VH^[3]. It's recommended to perform endoscopy urgently (within 12 hours of admission) for suspected VH^[3].

Urgent endoscopy for upper gastrointestinal bleeding has been associated more than 10 times higher complication rates (8%) comparing to non-urgent endoscopy (0.7%)^[4,5]. It's found that in this situation, cardiopulmonary complications constitute 23-50% of all adverse events and are responsible for 50-60% of deaths^[4,6]. Aspiration during endoscopy and consequent aspiration pneumonia are considered major problems in cardiopulmonary complications. Large volumes of blood located in the stomach and proximal to the lower esophageal sphincter is considered as the potential risk of aspiration during urgent esophagogastroduodenoscopy (EGD) for variceal hemorrhage.

In attempt to prevent aspiration, prophylactic intubation is more commonly adopted in nowadays prior to EGD^[6,7]. However, despite wide utilization, there is limited evidence that reveals prophylactic intubation improves patient outcomes^[5-8]. Our study is aiming to evaluate effects and complications related to prophylactic intubation prior to urgent endoscopy for VH through comparison between group of patients who underwent prophylactic intubation and group who did not undergo intubation in our institution.

MATERIALS AND METHODS

Data collection

Institutional review board approval for the study protocol was obtained before data collection. We reviewed the medical records of patients who underwent urgent bedside EGD within 12 hours of admission for suspected VH in the medical intensive care unit (MICU) at the University Hospital of Rutgers-New Jersey Medical School, Newark from 1/1/2008 to 12/31/2013. Inclusion criteria included known cirrhosis and hematemesis with EGD findings of active variceal bleeding or blood in stomach plus presence of varices with high risk stigmata. Exclusion criteria included (1) hematemesis due to other cause than variceal bleed; (2) intubation for other pre-existing conditions before EGD, such as respiratory distress, unstable cardiopulmonary status, warranted airway protection due to large volume blood in proximal GI tract; (3) the presence of hepatic encephalopathy of grade 3 or above; (4) signs of pneumonia or chest X-ray abnormalities before EGD. The West Haven Grading System staging scale was used to justify the grade of hepatic encephalopathy. EGD usually was performed by a fellow trainee under supervision of a staff gastroenterologist. Prophylactic endotracheal intubation was requested by the gastroenterologist performing procedure. Intubation was done by staff anesthesia providers. Patients were usually sedated with propofol. Decisions of intubation for reasons other than EGD were usually made by MICU providers or primary medical providers. Patients undergoing EGD without intubation had conscious sedation (midazolam, fentanyl and diphenhydramine) given by a registered nurse under supervision of performing gastroenterologist without anesthesia involvement.

A retrospective cohort study was performed to all cases which met the inclusion and exclusion criteria. A computerized database was designed to extract data from chart review. The variables of patient's background included patient demographics, etiology of cirrhosis, Child-Pugh score, Model for end-stage liver disease (MELD) score, presence of ascites, and grade of encephalopathy. The variables of patient's significant comorbidities included history of substance

abuse, acute infection other than pneumonia, active pneumonia, cardiac condition, chronic pulmonary condition, renal condition, diabetes, malignancy, neurologic condition other than hepatic encephalopathy, or gastroenterology condition other than cirrhosis. Primary outcomes for the study were immediate aspiration, post EGD pneumonia, death, or other complications. Secondary outcomes included post EGD ICU stay, total ICU stay and total hospital stay. Pneumonia was defined as new infiltrate on chest X-ray plus two the following findings within 48 hours after EGD: fever (temperature > 100.8 Fahrenheit), leukocytosis (white blood cells count > 10,000/mm³) or purulent sputum.

Data analysis

Categorical data were expressed in proportions. Continuous data were summarized as mean \pm standard deviation (SD). Student *t*-test was used for comparison between two groups of continuous data. Fisher exact test was used for comparison between two groups of categorical data. Statistical significance was considered achieved with a *p* value <0.05 (two tails).

RESULTS

A total of 190 EGD (171 patients) for suspected VH were reviewed. 110 occurrences of EGD met the inclusion criteria for the study. 65 occurrences of EGD were performed with prophylactic intubation, and 45 cases were done without intubation. 11 cases were excluded because the post procedure diagnosis was not variceal bleeding. 20 cases were excluded due to severe hepatic encephalopathy (grade 3-4). 49 cases were excluded because patients had been intubated for other reasons before endoscopy. Figure 1 displayed how cases were enrolled in the study.

Two cohorts of prophylactic intubation and no intubation had similar demographic features. Prophylactic intubation group had

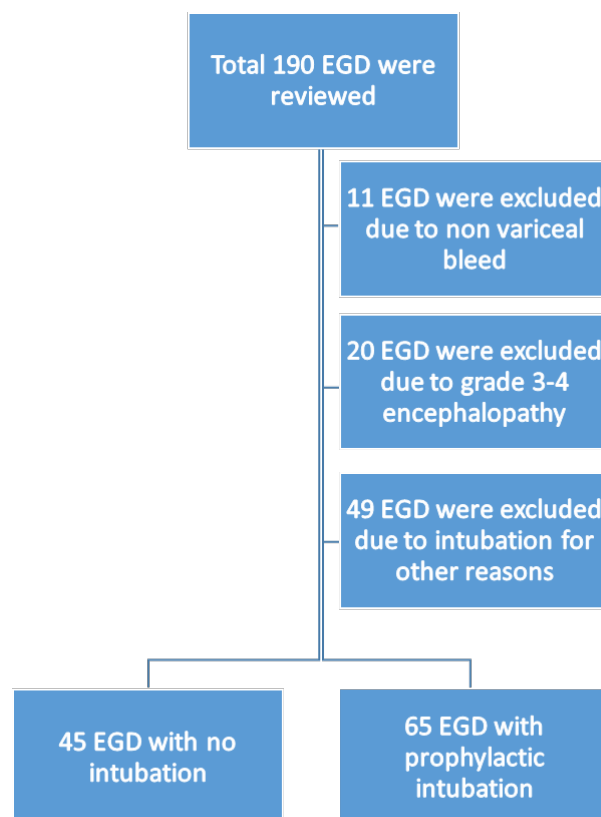


Figure 1 EGD inclusions and exclusion flow chart.

a mean age of 53.2 ± 12.2 years with 70.8% males. No intubation group has a mean age of 55.9 ± 9.1 years with 64.4% males. In both groups, alcohol is the most frequent etiology of cirrhosis (63.8% vs 44.4%, P = 0.074), followed by hepatitis C (44.6% vs 51.1%, p = 0.56), then hepatitis B (15.4% vs 13.3%, p = 1.001).

Medical comorbidities are similar between the two cohorts, with respect to active substance abuse, acute infection, active pneumonia, cardiac condition, pulmonary condition, diabetes, malignancy, neurological condition and gastroenterological condition.

Clinical severity at admission is similar in both groups. Child-Pugh score was 10 ± 3 for prophylactic intubation group, and 9 ± 2 for no intubation group (p = 0.053). MELD score was 19 ± 9 for prophylactic intubation group and 18 ± 7 for intubation group (p = 0.536). Ascites was presented in 53.9% of patients in prophylactic intubation group and 46.7% in the no intubation group (p = 0.813). All patients with greater than grade 3 encephalopathy are considered not able to protect airway and were excluded from study. In the patients included in study, grade 2 encephalopathy was presented in 21.5% patients in prophylactic intubation group and 8.9% patients in no intubation group (p = 0.117). Table 1 summarized demographics, clinical features and comorbidities of two cohorts.

Primary outcomes were found similar in two cohorts. Incidence of death less than 24 hours is considered procedure related mortality. Within 24 hours after procedure, 3 of 65 patients died in prophylactic intubation group and 1 of 45 patients died in no intubation group (4.6% vs 2.2%, p = 0.643). Mortality after 24 hours was 18.5% in prophylactic intubation group and 6.7% in no intubation group (p = 0.097). Total mortality was similar in both groups. All death were found cardiac related. Immediate aspiration was only found in one case in prophylactic intubation group. Pneumonia developed in 7 of 65 cases in prophylactic intubation group and 1 of 45 cases in no intubation group (10.77% vs 2.2%, p = 0.142). The only exception were overall complications other than cardiac and pulmonary, which were found 40% in prophylactic intubation group and 17.78% in no intubation group (p = 0.02).

Length of stay was the secondary outcome of this study. We found overall average hospital stay of both cohorts were similar (10.6 ± 7.9 days vs 8.8 ± 7.5 days, p = 0.233). The overall average ICU stay was also similar in both groups (5.3 ± 4.0 days vs 4.3 ± 3.3 days, p = 0.170). It's interesting to find that average ICU stay post EGD in significant longer in prophylactic intubation group (4.7 ± 3.9 days) than no intubation group (2.6 ± 2.6 days, p = 0.002). Table 2 summarized primary and second outcomes of the study.

DISCUSSION

VH is known to be related to large volume of blood in upper gastrointestinal track and high risk of aspiration. In the meantime, concurrent hepatic encephalopathy worsen patient's ability of airway protection, which reasonably concerns clinician about EGD induced aspiration. Both AASLD (American Association for the Study of Liver Diseases) and ASGE (American Society for Gastrointestinal Endoscopy) postulated in their practice guidelines that intubation before EGD is highly recommended for aspiration prevention^[3,9]. However, the level of recommendation is very weak due to lack of strong evidence. There are only a few small studies examining the assumption of prophylactic intubation can prevent aspiration. The results are controversial. Lipper and et al found 20% of 30 patients with severe UGIB (upper gastrointestinal bleeding) without intubation developed new pulmonary infiltrate and none in the intubated patients^[10]. In contrast, Rudolph and et al found in his study that 15.5% low risk patient developed infiltrates without intubation

Table 1 Demographics, etiology of cirrhosis and comorbidities of patients.

Variable	Prophylactic Intubation	No Intubation	P Value
N	65	45	
Age	53.2 ± 12.2	55.9 ± 9.1	0.213
Male	70.8%(46)	64.4%(29)	0.534
Hepatitis B	15.4%(10)	13.3%(6)	1.001
Hepatitis C	44.6%(29)	51.1%(23)	0.565
Alcohol	63.8%(41)	44.4%(20)	0.074
Other etiology	20.0%(13)	22.2%(10)	0.813
Ascites	53.9%(35)	46.7%(21)	0.568
Encephalopathy (grade 2)	21.5%(14)	8.9%(4)	0.117
Child-Pugh score	10 ± 3	9 ± 2	0.053
MELD	19 ± 9	18 ± 7	0.536
Substance abuse	27.7%(18)	11.1%(5)	0.055
Acute infection	24.6%(16)	24.4%(11)	1
Active pneumonia	4.6%(3)	0.0%(0)	0.268
Cardiac condition	12.3%(8)	11.1%(5)	1
Pulmonary condition	7.7%(5)	4.4%(2)	0.698
Renal condition	18.5%(12)	15.6%(7)	0.8
Diabetes	21.5%(14)	31.1%(14)	0.274
Malignancy	18.5%(12)	26.7%(12)	0.352
Neurology condition	9.2%(6)	4.4%(2)	0.468
Gastroenterology condition	6.15%(4)	4.4%(2)	1

†P values are from student t-test for continuous data and fisher exact test for categorical data.

Table 2 Length of stay and clinical outcomes of patients.

Variable	Prophylactic Intubation	No Intubation	P Value
Death < 24 hours	4.6%(3)	2.2%(1)	0.643
Death >24 hours	18.5%(12)	6.7%(3)	0.097
Total death	23.1%(15)	8.9%(4)	0.072
Cardiac complications < 24 hours	4.6%(3)	2.2%(1)	0.643
Cardiac complications > 24 hours	18.5%(12)	6.7%(3)	0.097
Immediate Aspiration after intubation	1.5%(1)	0.0%(0)	1
Pneumonia	10.77%(7)	2.2%(1)	0.142
Other complication	40.0%(26)	17.78%(8)	0.020*
Hospital stay	10.6±7.9	8.8±7.5	0.233
ICU stay	5.3±4.0	4.3±3.3	0.17
ICU stay post EGD	4.7±3.9	2.6±2.6	0.002*

†P values are from student t-test for continuous data and fisher exact test for categorical data.

but 48% high risk patients with intubation still had new infiltrates^[6]. A few other studies found intubation may only prevent aspiration in selected group, i.e., with altered mental status or massive hemorrhage^[7,11].

It's noted that utilization of prophylactic intubation for EGD were more prevalent in nowadays. Rodolph and *et al* found that in his institution significantly fewer patients underwent intubation before EGD in 1988 than in 1992 despite the proportion of overall intubations during hospitalization did not change^[6]. Koch and *et al* also found more patients with intubation were available to include in his retrospective study than patients without intubation^[5]. Our findings are consistent with above. Between 2008 and 2013, 65 case were done with prophylactic intubation and only 45 cases were done without prophylactic intubation in our institution.

Four small scale retrospective studies on value of prophylactic intubation before EGD have been published till present. Three of them studied the EGD for UGIB with any causes^[6,8,12] and one study examined EGD for VH^[5]. Only one large scale retrospective study was done recently, which studied procedure associated mortality by using national Danish patients' registry (enrolled 3580 cases)^[8]. This study consistently showed no significant difference in mortality between intubation and no intubation cohorts. Our study found similar results. Mortality within 24 hours, which was considered death related to procedure, and mortality after 24 hours were both similar in two cohorts.

Only one case was observed to have immediate aspiration in intubation group. No aspiration was observed in no intubation group. There was no significant difference between two groups. Rehman and Rudolph both studied cohorts of UGIB with all causes, which revealed no difference in aspiration^[6,12]. Koch's study used similar cohorts like ours, which was only stable patients with VH excluded severe altered mental status and massive hemorrhage. However, he discovered that prophylactic intubation was associated with higher risk of aspiration pneumonia^[5]. It's interesting to note that Koch's study only enrolled patients with grade 1 encephalopathy or less. Our study enrolled patients with grade 1 and 2 hepatic encephalopathy. Our results may suggest that prophylactic intubation does not protect patient from aspiration. In the other word, intubation's own risk of aspiration may override its benefits in stable patients with VH.

Most EGD related complications are cardiopulmonary in nature^[13,14]. We found no difference in immediate procedure related cardiac complications and delayed cardiac complications in both groups. This finding is consistent with Reham, Rudolph and Koch's study^[5,6,12]. Pneumonia is the other major EGD related complications, which was also found similar in our study. We were able to detect complications other than pulmonary and cardiac related, majorly including infection, kidney failure and shock, were significantly higher in the group getting prophylactic intubation. This finding was not reported in any prior studies.

Overall length of hospital stay were reported no difference in all four prior studies. Our findings is consistent with prior studies. We also found similar length of intensive care unit (ICU) stay in both groups. We found patients underwent prophylactic intubation had significant longer length of ICU stay after intubation, which may relate to delayed extubation after procedure.

There are a few strengths of our study. One is that it's so far the largest study looking at outcome of prophylactic intubation in specific population with variceal bleeding. Our study excluded patients with severe altered mental status or ongoing hemorrhage who demanded prophylactic intubation for airway protection and focused on a subgroup having variceal bleed with relative stable mental and hemodynamic status which intubation may be overused. The other strength is that we evaluated the hospital stay and ICU stay as secondary outcome, which were never studied in prior study. We found significant prolonged post intubation ICU stay in the group of intubation, which may lead to higher health care cost.

The limitation of our study is due to the nature of small retrospective design, such as self-inherent selection bias, unable to control confounding factors and low statistical power. A larger scale controlled prospective design will study this topic better. However, VH is considered a life threatening condition, the patient population need to be carefully selected to exclude high risks patients.

Our study revealed that prophylactic intubation prior to urgent EGD for VH did not improve clinical outcomes. It also showed the trend of higher complications rate other than cardiopulmonary

and longer length of post procedure ICU stay. We would suggest against routine prophylactic intubation in patients having VH with mild encephalopathy and no ongoing hemorrhage because routine prophylactic intubation is lack of benefits and is not cost-effective in proper utilization of healthcare resources.

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