

# Use of Early Bronchoscopy in Mechanically Ventilated Patients with Aspiration Pneumonitis

Mohammed M Megahed<sup>1</sup>, Ahmed M El-Menshaway<sup>2</sup>, Ahmed M Ibrahim<sup>3</sup>

## ABSTRACT

**Background and objectives:** Aspiration-induced lung injury accounts for a significant proportion of acute pulmonary dysfunction. Few studies were conducted to study the use of early bronchoscopy in mechanically ventilated patients with aspiration pneumonitis. This study aimed at assessing the clinical impact of early bronchoscopy for removal of gastric fluid and solid particles in the first 24 hours of mechanical ventilation (MV) on the progression of aspiration, MV days, intensive care unit (ICU) stay, development of pneumonia, and ICU mortality.

**Materials and methods:** The study was an open-label randomized control trial and included 76 adult subjects mechanically ventilated due to aspiration pneumonitis, half the subjects received early bronchoscopy in the first 24 hours after aspiration for removal of aspirated material and bronchoalveolar lavage sampling, the other half received standard treatment.

**Results:** The intervention group had a significant reduction in the rate of development of pneumonia at 60.5 vs 81.6%,  $p = 0.043$  through the first week of admission, the intervention group has a significantly better hypoxic index (HI), white blood count, clinical pulmonary infection score, lung injury score, and sepsis-related organ failure assessment (SOFA) score compared to the control group. Although there was a reduction in mechanical ventilation days and ICU mortality in the intervention group vs control group that difference did not reach statistical significance.

**Conclusions:** Early bronchoscopy in mechanically ventilated patients with aspiration pneumonitis can be beneficial in improving respiratory functions and decreasing the incidence of development of aspiration pneumonia and may guide the de-escalation of antibiotic therapy.

**Keywords:** Acute lung injury, Aspiration, Critical care, Flexible bronchoscopy, Mechanical ventilation, Pneumonia.

**CTRI/Trial Reg No.:** PACTR201909915486179

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## INTRODUCTION

Aspiration is defined as the inhalation of foreign material into the airways beyond the vocal cords. Aspiration-induced lung injury is often underdiagnosed in the clinical setting in the care of the critically ill and accounts for a significant proportion of acute pulmonary dysfunction.<sup>1</sup> Moreover, it is recognized as an independent risk factor for subsequent development of pneumonia or acute lung injury, or acute respiratory distress syndrome (ALI/ARDS).<sup>1</sup> The lack of well-designed, randomized clinical studies on this subject has led to several generalizations that can be misleading.<sup>1,2</sup>

Aspiration events can be categorized as aspiration pneumonitis (chemical pneumonitis) or aspiration pneumonia (infectious process secondary to an aspiration event), though the differentiation between these two processes can be very difficult and they very often overlap.<sup>1-4</sup>

Aspiration pneumonitis refers to a condition that shows immediate hypoxia, fever, tachycardia, and abnormalities on a chest radiograph, which is caused by macroaspiration of noxious fluids. The noxious fluids are mostly sterile gastric contents; although they may also be bile or other agents introduced through the stomach.<sup>1,4,5</sup>

Aspiration pneumonia implies acute lung infection that occurs after aspiration of oropharyngeal or upper gastrointestinal contents. The aspirated contents are often not acidic enough (likely a pH greater than 2.5) to induce chemical pneumonitis.<sup>1,4,5</sup>

There is a degree of overlap between aspiration pneumonia and pneumonitis. Gastric contents are sterile under normal conditions. However, changes in gastric pH to inhibit bacterial growth through the use of antacids, H<sub>2</sub>-receptor antagonists, or proton-pump inhibitors may result in an environment where

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potentially pathogenic organisms can grow.<sup>6</sup> Additionally, gastric colonization due to gram-negative bacteria can occur in patients under enteral feeding or patients with gastroparesis or small-bowel obstruction.<sup>6,7</sup> If gastric aspiration occurs under these circumstances, lung infection from bacterial load in gastric contents can occur in addition to the inflammation due to acid or food particles; this is one case explaining the overlap between aspiration pneumonia and aspiration pneumonitis.<sup>3</sup>

Another condition for overlap between the two syndromes is the possible subsequent infection added on top of aspiration pneumonitis at a later stage of the inflammatory process.<sup>8,9</sup> Aspiration-induced lung injury is a clear risk factor for the development of pneumonia, the incidence of progression to pneumonia and whether the aspiration of bacteria occurs at the initial period or is a result of altered host-bacterial interaction is currently not well understood.<sup>2-4,9,10</sup>

Management of aspiration pneumonitis is mainly supportive; positioning and aggressive pulmonary care with the possibility of intubation and mechanical ventilation depending on the clinical situation,<sup>11</sup> the use of antibiotics is a controversial issue due to the difficulty of differentiating aspiration pneumonia from pneumonitis, a recent survey suggested that a vast majority of intensivists were prescribing antibiotics in patients with suspected aspiration events.<sup>12</sup>

The main use of bronchoscope in patients with aspiration events is the sampling of the lower respiratory tract. The quantitative bacteriology obtained from the bronchoalveolar lavage (BAL) samples can not only direct definitive therapy and de-escalation of antibiotics but also can result in discontinuation of antibiotics if cultures do not show significant bacterial growth.<sup>2,3</sup>

In the current practice, the therapeutic use of bronchoscopy is preserved for the event that the aspirate is predominantly particulate with clear radiographic evidence of lobar collapse or major atelectasis where a therapeutic bronchoscopy may be helpful.<sup>2,3</sup>

Studies have shown a potential diagnostic and therapeutic role for bronchoscopes in patients with aspiration.

A case series by Campinos et al. described the use of bronchoscopy to identify airway lesions caused by aspiration pneumonitis and the use of bronchoscopes to relieve the airway obstruction and atelectasis in these patients.<sup>13</sup>

Deng et al. studied the effect of early bronchoscopic sputum suction in elderly patients with acute heart and lung failure due to aspiration pneumonia. Patients receiving bronchoscopic suction showed faster recovery of normal central venous pressure and left ventricular ejection fraction and more rapid increment of the arterial partial pressure of oxygen than those without the suction.<sup>14</sup>

Lee et al. performed a retrospective cohort study to compare the clinical outcome between mechanically ventilated aspiration pneumonia patients who underwent fiber-optic bronchoscopy (FB) and BAL in the first 24 hours and those who had delayed FB. Their study showed that the early bronchoscopy group had significantly lower mortality.<sup>15</sup>

To date, no clinical trials were carried to investigate the clinical impact of the use of early bronchoscopy in patients with acute lung injury following aspiration. This study was designed to assess the use of early bronchoscopy for removal of gastric fluid and solid particles in the first 24 hours after aspiration on the progression of respiratory functions, mechanical ventilation days, intensive care unit (ICU) stay, development of pneumonia, and ICU mortality.

## MATERIALS AND METHODS

### Trial Design

The study was an open-label randomized controlled single-center trial conducted in ICUs of Alexandria Main University Hospital, a tertiary referral hospital with over 100 ICU beds, from March to September 2019. The study was registered at the Pan African Clinical Trials Registry trial no. PACTR201909915486179. The study was approved by the medical ethics committee of Alexandria Faculty of Medicine and informed consent from the subject or their next of kin was taken before enrollment to the study.

### Study Population

Depending on a previous similar study<sup>15</sup> sample size was calculated using Fleiss method assuming mortality rate difference of 20%,

power of study 80%, and alpha 5%, 35 subjects were to be included in each arm of the study.

A total of 98 subjects were considered for enrollment based on inclusion criteria; adults age > 18 years, intubated and ventilated, presented with acute aspiration evident by gastric contents in the oropharynx leading to some or all of the following; fever, dyspnea, wheezes, crackles, and cough in a subject with risk factors for aspiration. Patients with signs and symptoms suggestive of pneumonia prior to the event of aspiration and those with preexisting pulmonary diseases were excluded from the study.

Of these 98 subjects 22 were excluded; 14 due to previous pulmonary illness preceding the aspiration event, 6 with chronic obstructive pulmonary disease, and 8 with symptoms suggestive of pneumonia.

Eight subjects were excluded due to contraindication to perform bronchoscopy,<sup>16</sup> four were hemodynamically unstable despite vasopressors and inotropes, and four were severely hypoxic despite mechanical ventilation and delivery of FiO<sub>2</sub> 1.0.

Seventy-six subjects were enrolled in the study and were randomly assigned—using computer-generated sequence—within 24 hours of aspiration into the study group undergoing flexible bronchoscopy ( $n = 38$ ) and the control group receiving conventional management ( $n = 38$ ).

All subjects enrolled in this study were subjected to complete physical examination together with chest X-ray or chest computed tomography (CT) for identification of diagnosis and inclusion criteria.

Clinical scores were recorded including Glasgow coma score (GCS), acute physiology and chronic health evaluation score II on admission,<sup>17</sup> sepsis-related organ failure assessment (SOFA) score,<sup>18</sup> lung injury score (LIS),<sup>19</sup> and clinical pulmonary infection score (CPIS).<sup>20</sup>

All the subjects received standard treatment; mechanical ventilation, positioning, bronchodilators, and empirical antibiotics if seemed appropriate, the decision to start antibiotics and the choice of empirical antibiotics were decided by the attending intensivists according to the unit's protocol.

The intervention group underwent flexible bronchoscopy in the first 24 hours after aspiration.

Bronchoscopy was done by an experienced intensivist, sedation with midazolam or propofol was used, inspired oxygen fraction was increased to 100%, tidal volume increased by 50%, positive end-expiratory pressure was removed for selected subjects, flexible bronchoscope AMBU®aSCOPE™ 3 Large 5.8/2.8 produced by Ambu A/S, Denmark was introduced through an adaptor, connected to the endotracheal tube for airway clearance by saline instillation and suction of secretions, and sampling bronchoalveolar lavage for bacteriological culture.

For the control group, chest physiotherapy and blind suctioning were used for airway clearance and miniBAL was sampled in the first 24 hours.

### Study Outcomes

Both groups were followed for the development of pneumonia defined as persistent leukocytosis, fever, and infiltrates, >48 hours after aspiration,<sup>1,21</sup> the progression of respiratory functions by follow up of SOFA score,<sup>18</sup> LIS,<sup>19</sup> and CPIS<sup>20</sup> at admission, day 3 and day 7, days of mechanical ventilation, length of ICU stay, and ICU mortality.

## Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. The Kolmogorov–Smirnov test was used to verify the normality of the distribution. The significance of the obtained results was judged at the 5% level. The *t*-test was used for normally distributed continuous variables, the Mann–Whitney *U*-test for non-normal continuous variables, and the chi-square test for categorical variables. *F*-test (ANOVA) and Friedman test were used to compare between repeated measures within groups.

## RESULTS

### Baseline

The trial profile describing subjects flow is shown in [Flowchart 1](#). The baseline characteristics of the 78 subjects included in the study are shown in [Table 1](#).

The age of studied cases ranged from 18.0 to 87.0 years with a mean of  $53.63 \pm 18.8$  years. A total of 27% of the subjects were already hospitalized for another reason and the event of aspiration occurred in-hospital ( $n = 21$ ), the others presented to the ER with aspiration.

The most common diagnosis was ischemic cerebrovascular stroke ( $n = 13$ ), intracranial hemorrhages were collectively as common ( $n = 13$ ) with subarachnoid hemorrhage the most common type of hemorrhage among subjects of our study ( $n = 5$ ). A table describing the main diagnoses of study subjects is available in supplementary materials.

All but one of the study subjects started antibiotics before the results of BAL or miniBAL ( $n = 75$ ), one-third of them started on antibiotic monotherapy ( $n = 25$ ), two-thirds started combination therapy of two or more antibiotics. Most of the subjects, 64.5% started antibiotics directly after ICU admission with aspiration ( $n = 49$ ), 26% of the subjects were already on antibiotics for other indications on admission to ICU, mainly the group of in-hospital aspiration ( $n = 20$ ), only a minority 5.3%, started antibiotics after symptoms of pneumonia started ( $n = 4$ ), two subjects (2.6%) started antibiotics after bronchoscopy revealed purulent discharge and signs of infection.

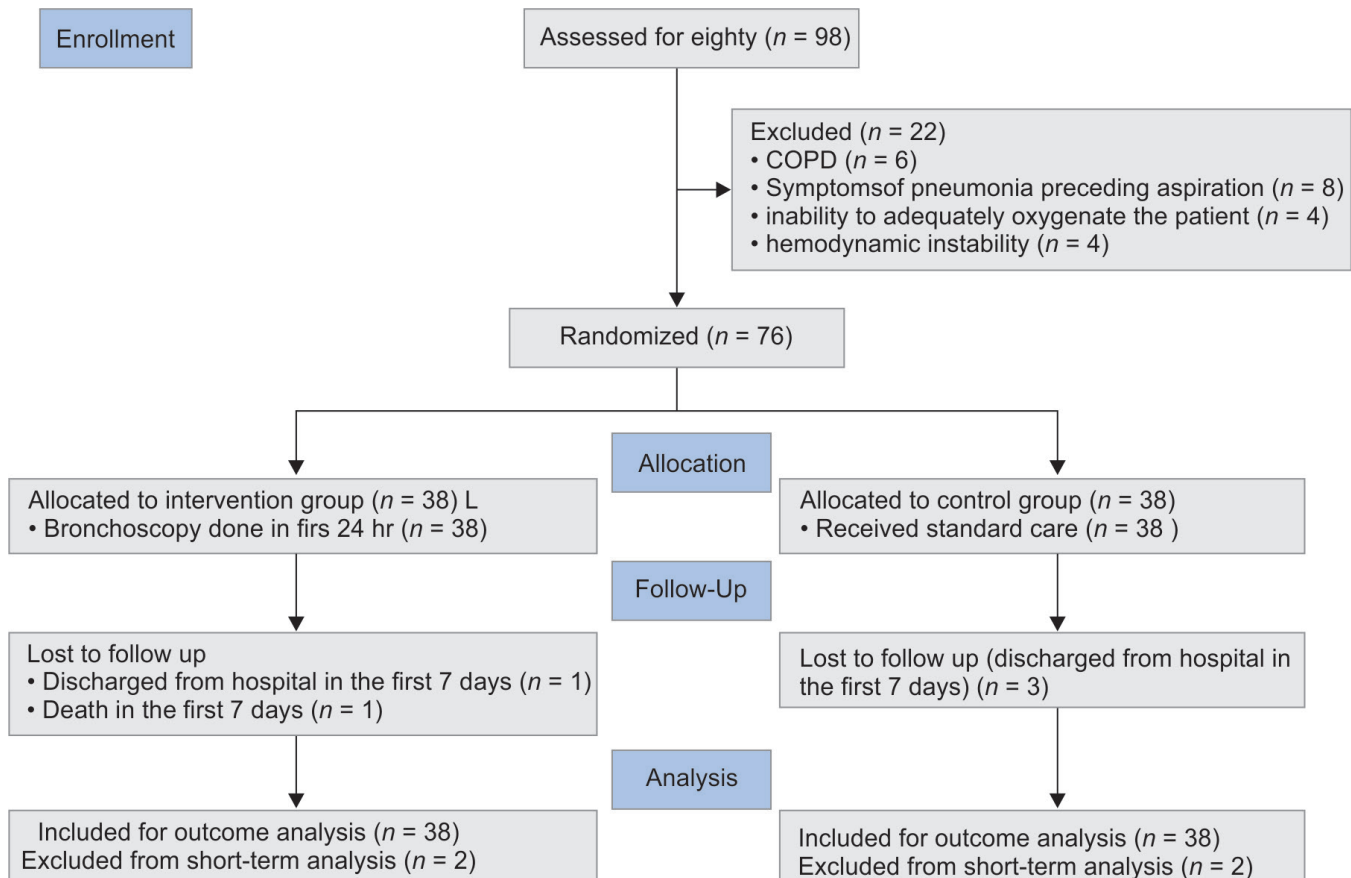
### Progression of Respiratory Functions

At admission and by day 3 there was no significant difference with regard to GCS, Tmax, SOFA, and CPIS between the intervention and control groups. Although the intervention group showed more improvement with regard to hypoxic index (HI), lung injury score, and white blood cell counts (WBC) than the control group by day 3, this improvement did not reach statistical significance.

By day 7, the bronchoscopy intervention group showed significant improvement with regard to HI, WBC count, CPIS, LIS, and SOFA score than the control group.

The mean HI of the intervention group at day 7 was  $343.21 \pm 100.77$  compared to  $278.47 \pm 90.29$ ,  $p < 0.01$ . Mean WBC count on day 7 in the intervention group was  $13.34 \pm 3.55$  vs  $15.05 \pm 3.25$  among the control group,  $p = 0.038$ . LIS was significantly lower among the intervention group than the control group  $0.81 \pm 0.73$  vs  $1.22 \pm 1.67$ ,

**Flowchart 1:** Flow of participants through the trial



**Table 1:** Comparison between the two studied groups at baseline

| Baseline                     | Intervention (n = 38) | Control (n = 38)   | Test of sig.     | p-value |
|------------------------------|-----------------------|--------------------|------------------|---------|
| <b>Sex</b>                   |                       |                    |                  |         |
| Male (%)                     | 22 (57.9%)            | 19 (50%)           | $\chi^2 = 0.477$ | 0.49    |
| <b>Age (years)</b>           |                       |                    |                  |         |
| Mean $\pm$ SD.               | 53.21 $\pm$ 17.89     | 54.05 $\pm$ 19.91  | t = 0.194        | 0.85    |
| <b>Setting of aspiration</b> |                       |                    |                  |         |
| In-hospital                  | 10 (26.3%)            | 11 (28.9 %)        | $\chi^2 = 0.066$ | 0.79    |
| Out-of-hospital              | 28 (73.7 %)           | 27 (71.1%)         |                  |         |
| <b>Main diagnosis</b>        |                       |                    |                  |         |
| CNS disorders                | 18 (47.4%)            | 17 (44.7%)         | $\chi^2 = 0.095$ | 0.95    |
| Metabolic and sepsis         | 13 (34.2%)            | 13 (34.2%)         |                  |         |
| Drug induced                 | 7 (18.4%)             | 8 (21.1%)          |                  |         |
| <b>GCS</b>                   |                       |                    |                  |         |
| Mean $\pm$ SD                | 6.32 $\pm$ 2.19       | 6.11 $\pm$ 1.90    | U = 666.50       | 0.56    |
| <b>APACHE II score</b>       |                       |                    |                  |         |
| Mean $\pm$ SD                | 24.68 $\pm$ 6.78      | 25.05 $\pm$ 5.60   | t = 0.258        | 0.79    |
| <b>WBCs</b>                  |                       |                    |                  |         |
| Mean $\pm$ SD                | 15.64 $\pm$ 4.12      | 15.50 $\pm$ 3.70   | t = 0.161        | 0.87    |
| <b>HI</b>                    |                       |                    |                  |         |
| Mean $\pm$ SD                | 182.62 $\pm$ 56.41    | 180.50 $\pm$ 38.45 | t = 0.191        | 0.85    |
| <b>Temperature</b>           |                       |                    |                  |         |
| Mean $\pm$ SD                | 38.20 $\pm$ 0.56      | 37.98 $\pm$ 0.78   | U = 568.50       | 0.11    |
| <b>LIS</b>                   |                       |                    |                  |         |
| Mean $\pm$ SD                | 1.80 $\pm$ 1.51       | 1.84 $\pm$ 0.38    | U = 695.0        | 0.77    |
| <b>SOFA</b>                  |                       |                    |                  |         |
| Mean $\pm$ SD                | 10.26 $\pm$ 2.51      | 10.45 $\pm$ 2.38   | U = 692.50       | 0.76    |
| <b>CPIS</b>                  |                       |                    |                  |         |
| Mean $\pm$ SD                | 7.32 $\pm$ 2.16       | 7.18 $\pm$ 2.0     | U = 680.50       | 0.66    |

$\chi^2$ , chi-square test; t, Student's t-test; U, Mann-Whitney test; p-value for comparing between the two groups; CNS, central nervous system; GCS, Glasgow coma score; WBC, white blood cells; HI: hypoxic index; LIS: lung injury score; SOFA: sepsis-related organ failure assessment; CPIS, clinical pulmonary infection score

$p = 0.018$ . Mean CPIS was lower in the intervention group  $4.17 \pm 3.51$  compared to the control group  $5.94 \pm 3.67$ ,  $p = 0.035$ . SOFA score was also lower among the intervention group than the control group  $6.5 \pm 4.19$  vs  $8.97 \pm 4.84$ ,  $p = 0.02$ . There was no significant difference with regard to GCS or Tmax.

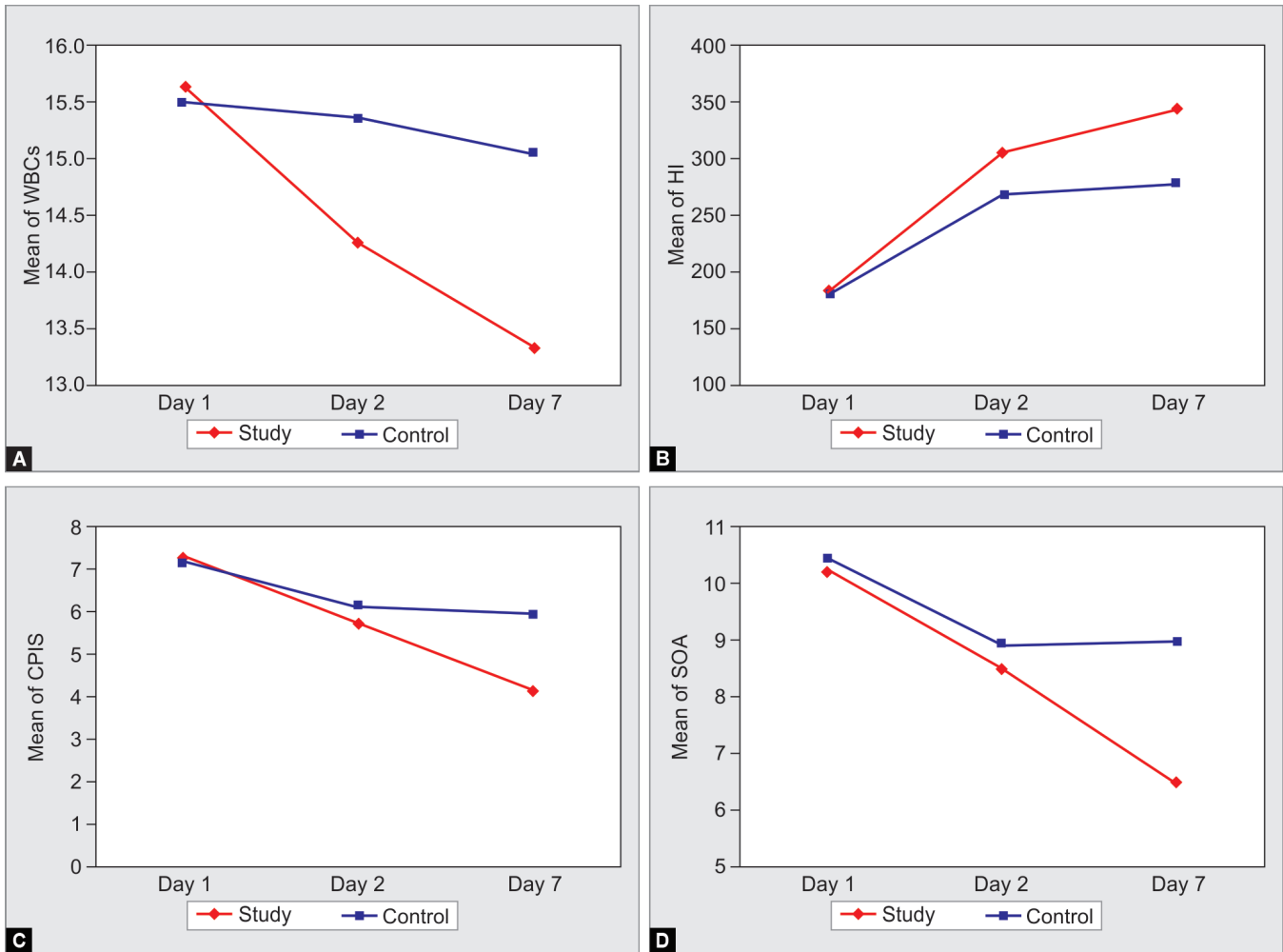
The intervention group had a significant reduction of WBCs count when comparing readings from admission day, day 3, and day 7;  $15.64 \pm 4.12$ ,  $14.26 \pm 4.23$ , and  $13.34 \pm 3.55$ ,  $p < 0.01$ . The control group did not show a significant reduction of WBCs during the same period.

Both groups had significant improvement of HI over the 7 days, mean HI for the intervention group at admission, day 3, and day 7 was  $182.62 \pm 56.41$ ,  $305.25 \pm 110.72$ , and  $343.21 \pm 100.77$ ,  $p < 0.001$  while for the control group  $180.50 \pm 38.45$ ,  $267.76 \pm 84.53$ , and  $278.47 \pm 90.29$ ,  $p < 0.001$ . Although both are statistically significant, the improvement of the intervention group was more clinically significant than the control group.

Both groups had significant improvement of LIS over the 7 day period, mean HI for the intervention group at admission, day 3, and day 7 was  $1.80 \pm 1.51$ ,  $1.13 \pm 0.74$ , and  $0.81 \pm 0.73$ ,  $p < 0.001$  while for the control group  $1.84 \pm 0.38$ ,  $1.36 \pm 0.53$ , and  $1.22 \pm 1.67$ ,  $p < 0.001$ . Although both are statistically significant, the improvement of the intervention group was more clinically significant than the control group.

The intervention group had a significant reduction of SOFA score when comparing readings from admission day, day 3, and day 7;  $10.26 \pm 2.51$ ,  $8.53 \pm 3.90$ , and  $6.50 \pm 4.19$ ,  $p < 0.001$ . The control group did not show a significant reduction in SOFA score during the same period.

The intervention group had a significant reduction of CPIS count when comparing scores from admission day, day 3, and day 7;  $7.32 \pm 2.16$ ,  $5.76 \pm 2.88$ , and  $4.17 \pm 3.51$ ,  $p < 0.001$ . The control group did not show a significant reduction of CPIS during the same period.



**Fig. 1A to D :** Progress of both groups over first 7 days. WBCs, white blood cells in  $10^3$ , HI, hypoxic index, CPIS, clinical pulmonary infection score, SOFA: sepsis related organ failure score

The progression of both groups over the first 7 days period is presented in [Figure 1](#).

Tables of GCS, LIS, HI, WBCs, Tmax, and CPIS at admission, day 3, and day 7 are provided in supplementary materials.

### MiniBAL and BAL Results

A total of 43.4% of all the cultures showed no growth ( $n = 33$ ) whereas 56.6% showed growth of bacteria ( $n = 43$ ), the most common bacterial cultures were *Pseudomonas aeruginosa* in 9 subjects (5 cases and 4 controls) and *Klebsiella pneumoniae* in 9 subjects (3 cases and 6 controls), staphylococci were isolated in 8 subjects (4 cases and 4 controls) with 2 cultures revealing methicillin-resistant staphylococcus (1 case and 1 control). Two cultures showed the growth of two different organisms. A total of 48.8% of the isolated organisms ( $n = 21$ ) were multidrug-resistant, 47.6% of BAL cultures ( $n = 10$ ) vs 50% of miniBAL cultures ( $n = 11$ ), organisms from cultures were defined as multidrug resistance (MDR) if they are non-susceptibility to at least one agent in three or more antimicrobial categories.<sup>22</sup>

Cultures from in-hospital aspiration subjects revealed no growth in 5 subjects (3 cases and 2 controls), *K pneumoniae* in 6 subjects (1 case and 5 controls), *Acinetobacter* in 6 subjects

**Table 2:** Comparison between two groups according to the appropriateness of initial antibiotics

|   | Intervention<br>( $n = 38$ ) |      | Control<br>( $n = 38$ ) |      | Test of sig.     | p-value |
|---|------------------------------|------|-------------------------|------|------------------|---------|
|   | No.                          | %    | No.                     | %    |                  |         |
| <b>Appropriateness of initial antibiotics</b> |                              |      |                         |      |                  |         |
| No growth                                     | 17                           | 44.7 | 16                      | 42.1 | $\chi^2 = 0.070$ | 0.97    |
| Sensitive                                     | 12                           | 31.6 | 13                      | 34.2 |                  |         |
| Resistant                                     | 9                            | 23.6 | 9                       | 23.6 |                  |         |

$\chi^2$ , chi-square test; p-value for comparing between the two groups

(3 cases and 3 controls), *Pseudomonas aeruginosa* in 2 subjects (1 case and 1 control), one subject *Escherichia coli* (a case), and another *Enterococcus faecalis* (a case).

The sensitivity of initial empirical antibiotics was similar between the intervention and control group as presented in [Table 2](#).



**Table 3:** Comparison between the two studied groups according to the outcome

| Outcome                         | Intervention<br>(n = 38) |      | Control<br>(n = 38) |      | Test of sig.       | p-value |
|---------------------------------|--------------------------|------|---------------------|------|--------------------|---------|
|                                 | No.                      | %    | No.                 | %    |                    |         |
| <b>Development of pneumonia</b> |                          |      |                     |      |                    |         |
| No                              | 15                       | 39.5 | 7                   | 18.4 | $\chi^2 = 4.094^*$ | 0.043*  |
| Yes                             | 23                       | 60.5 | 31                  | 81.6 |                    |         |
| <b>Extubation</b>               |                          |      |                     |      |                    |         |
| Failed                          | 6                        | 15.8 | 11                  | 28.9 | $\chi^2 = 2.860$   | 0.24    |
| Successful                      | 25                       | 65.8 | 18                  | 47.4 |                    |         |
| Tracheostomy                    | 7                        | 18.4 | 9                   | 23.7 |                    |         |
| <b>Days of MV</b>               |                          |      |                     |      |                    |         |
| Min.–Max.                       | 1.0–23.0                 |      | 1.0–25.0            |      | $U = 543.50$       | 0.063   |
| Mean $\pm$ SD                   | 7.39 $\pm$ 5.67          |      | 10.13 $\pm$ 6.92    |      |                    |         |
| Median                          | 5.0                      |      | 8.0                 |      |                    |         |
| <b>ICU days</b>                 |                          |      |                     |      |                    |         |
| Min.–Max.                       | 3.0–28.0                 |      | 3.0–28.0            |      | $U = 606.0$        | 0.23    |
| Mean $\pm$ SD                   | 11.16 $\pm$ 5.77         |      | 12.63 $\pm$ 6.31    |      |                    |         |
| Median                          | 9.50                     |      | 10.0                |      |                    |         |
| <b>Outcome</b>                  |                          |      |                     |      |                    |         |
| Discharge                       | 28                       | 73.7 | 20                  | 52.6 | $\chi^2 = 3.619$   | 0.057   |
| Death                           | 10                       | 26.3 | 18                  | 47.4 |                    |         |

\*Statistically significant at  $p \leq 0.05$ ;  $\chi^2$ , chi-square test;  $U$ , Mann–Whitney test,  $p$ -value for comparing between the two groups

### Findings of Bronchoscopic Examination

The most common finding was airway hyperemic lesions encountered in 68% of the subjects ( $n = 26$ ) commonly on the surface of trachea and carina and more common on the surface of right bronchus than left. The second most common finding was purulent secretions in 52.6% of the cases ( $n = 20$ ). Blood clots were found in 23.7% of the cases ( $n = 9$ ). A partial or complete bronchial obstruction was noted in 15.8% of the cases ( $n = 6$ ).

### Outcome

Table 3 summarizes the comparison between the outcomes of the two groups.

There was a significant reduction in the rate of progression of pneumonitis into pneumonia in the intervention group compared to the control group 60.5 vs 81.6%,  $p = 0.043$ .

Although there was also a reduction in mechanical ventilation days 7.39  $\pm$  5.67 in the intervention group vs 10.13  $\pm$  6.92 in a control group that difference did not reach statistical significance,  $p = 0.063$ .

There was no statistically significant difference in the ICU stay duration between the two groups, 11.16  $\pm$  5.77 for the intervention group vs 12.63  $\pm$  6.31 for the control group,  $p = 0.23$ .

The mortality rate was lower in the intervention group than the control group 26.3 vs 47.4% but this difference did not reach statistical significance,  $p = 0.057$ .

## DISCUSSION

This study shows a beneficial role of early bronchoscopy in the prevention of progression of aspiration pneumonitis into pneumonia and improvement of respiratory functions in addition to its previously studied diagnostic role for identifying causative organisms that were found comparable to miniBAL.

In our study, 20 subjects were on antibiotics when the aspiration event happened, 49 of the rest 56 subjects (87%) started empirical antibiotics after the confirmed aspiration event, in a study by Kane-Gill et al.,<sup>23</sup> a similar percentage 87% of aspiration pneumonitis patients started empirical antibiotics.

Almost 50% of the BAL and miniBAL samples revealed no growth, initial antibiotics were appropriate in about one-third of the study subjects and the isolated organism was resistant to the initial empirical antibiotic in 23% of the subjects.

The baseline characteristics of both the study and intervention subjects were similar with regard to diagnoses, risk factors, and clinical scores. The rate of positive bacterial growth, the distribution of MDR, and the appropriateness of the initial antibiotics were similar between the study and the control groups. This would indicate that the clinical improvement is a therapeutic effect of early bronchoscopy rather than a diagnostic benefit.

The rate of development of pneumonia subsequent to aspiration-induced lung injury decreased in the intervention group from 81 to 60%. Animal studies showed that pneumonitis prime the lung tissue for superadded bacterial infection through exaggerated inflammatory response or impaired bacterial clearance both factors were shown to decrease after washing with saline.<sup>8,9</sup> To the best of our knowledge, there was no clinical trial to show the effect of flexible bronchoscopy on the progression of aspiration pneumonitis to aspiration pneumonia.

Previous studies have shown beneficial rule for bronchoscopic suction of secretions in preventing the development of pneumonia; Vejdani and Khosravi demonstrated in their clinical trial that the use of FB and BAL to clear airway secretions in head trauma patients who needed tracheostomy decreased the risk of nosocomial pneumonia from 35 to 14% and can even shorten the ICU stay time.<sup>24</sup>

Another possible beneficial rule for FB is the removal of airway obstruction and prevention of atelectasis; a case series of 26 subjects with aspiration pneumonitis undergoing bronchoscopy described the use of bronchoscopy to relieve airway obstruction in seven subjects of the study.<sup>13</sup> In our study purulent secretions were found in 52.6% of the cases, blood clots were found in 23.7% of the subjects and partial or complete bronchial obstruction was noted in 15.8% of the cases.

Our study has shown clinical improvement in the early bronchoscopy group when compared to the control group with regard to oxygenation, SOFA, CPIS, and WBCs. This is in concordance with the study by Lee et al. that also showed that LIS, CPIS, and SOFA scores decreased more rapidly in the group of aspiration pneumonia patients undergoing early bronchoscopy than the group of delayed bronchoscopy.<sup>15</sup>

Improvement of HI, LIS, and CPIS also comes in agreement with the study by Deng et al.; as patients receiving bronchoscopic suction showed faster recovery of the arterial partial pressure of oxygen and reduction of carbon dioxide partial pressure than the control group.<sup>14</sup>

Our study showed a reduction in ICU mortality rate, mechanical ventilator days, and ICU stay among the intervention group but this reduction did not reach the level of statistical significance, unlike

Lee et al. study where the early bronchoscopy group showed significantly lower in intensive care unit (ICU) mortality and 90-day mortality.<sup>15</sup>

The difference between the two studies may explain the failure of our study to reach statistical significance is the sample size; 76 subjects were included in our study vs 154 in the other study and the higher mortality rate in our study.

The results of the study support performing early bronchoscopy in patients with acute aspiration presented with lung injury as it can decrease the incidence of development of aspiration pneumonia and leads to more rapid improvement in respiratory functions. Bronchoscopy and miniBAL showed comparable results in diagnosing causative organisms and titrating the antibiotic therapy. Further multicenter trials with a larger sample size are needed to confirm the therapeutic role of early bronchoscopy in such patients.

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