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Characteristics and Outcomes of Patients Hospitalized Following Pulmonary Aspiration

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BACKGROUND: Pulmonary aspiration is an important recognized cause of ARDS. Better characterization of patients who aspirate may allow identification of potential risks for aspiration that could be used in future studies to mitigate the occurrence of aspiration and its devastating complications.

METHODS: We conducted a secondary analysis of the Lung Injury Prediction Score cohort to better characterize patients with aspiration, including their potential risk factors and related outcomes.

RESULTS: Of the 5,584 subjects at risk for ARDS and who required hospitalization, 212 (3.8%) presented with aspiration. Subjects who aspirated were likely to be male (66% vs 56%, $P < .007$), slightly older (59 years vs 57 years), white (73% vs 61%, $P = .0004$), admitted from a nursing home (15% vs 5.9%, $P < .0001$), have a history of alcohol abuse (21% vs 8%, $P < .0001$), and have lower Glasgow Coma Scale (median, 13 vs 15; $P < .0001$). Aspiration subjects were sicker (higher APACHE [Acute Physiology and Chronic Health Evaluation] II score), required more mechanical ventilation (54% vs 32%, $P < .0001$), developed more moderate to severe ARDS (12% vs 3.8%, $P < .0001$), and were twofold more likely to die in-hospital, even after adjustment for severity of illness (OR = 2.1; 95% CI, 1.2-3.6). Neither obesity nor gastroesophageal reflux was associated with aspiration.

CONCLUSIONS: Aspiration was more common in men with alcohol abuse history and a lower Glasgow Coma Scale who were admitted from a nursing home. It is independently associated with a significant increase in the risk for ARDS as well as morbidity and mortality. Findings from this study may facilitate the design of future clinical studies of aspiration-induced lung injury.

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ABBREVIATIONS: ACE = angiotensin-converting enzyme; APACHE = Acute Physiology and Chronic Health Evaluation; CDC = Centers for Disease Control and Prevention; GCS = Glasgow Coma Scale; GERD = gastroesophageal reflux disease; IQR = interquartile range; LIPS = Lung Injury Prediction Score; LOS = length of stay; PPI = proton pump inhibitor

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The Lung Injury Prediction Score (LIPS) study identified aspiration as among the leading risk factors for ARDS.[1-7] However, most of our knowledge on aspiration and its associated risks and outcomes is based on observational studies where aspiration is determined retrospectively or concurrent to the clinical consequence (eg, ARDS).[8,9] We systematically and prospectively characterized patients who aspirated and required hospitalization from the LIPS cohort, with the goal of identifying the burden of illness, consequences of aspiration, and risk factors associated with aspiration. Findings from this study are meant to be descriptive and hypothesis-generating to support the design of future clinical trials on aspiration, with long-term goals to identify potential therapeutic targets to mitigate aspiration-induced lung injury and its other consequences.

Materials and Methods

This is an a priori planned secondary analysis of the LIPS1[7] cohort to characterize patients who aspirated and required hospitalization. The LIPS1 study developed and validated the LIPS to facilitate clinical trials aimed at preventing ARDS. Because only deidentified clinical data were collected and aggregated, a formal informed consent was waived per each center's institutional review board.[7] This secondary analysis was approved under Mayo Clinic institutional review board #08-008726. Subjects were enrolled prospectively at 19, and retrospectively at three, centers over 6 months (starting March 2009), and were followed to hospital discharge or death.

Every patient admitted with a predisposing condition (e-Appendix 1) for ARDS,[7] including those with aspiration, was identified.[7] We aimed to further characterize this subgroup in-depth, including an analysis of risks for aspiration, its associations, and outcomes specific to aspiration that were not reported in the primary study. Aspiration was defined as "witnessed or suggestive history of inhalation of food or regurgitated gastric contents"[10] and was determined along with all baseline covariates from review of medical documentation and clinically obtained tests, within 6 h of hospital. Principal outcomes included acute lung injury ($Pao_2/Fio_2 < 300$) and ARDS ($Pao_2/Fio_2 < 200$) per the prevailing definition[11] and mortality. Given the interval update in the definition,[12] henceforth, ARDS will refer to $Pao_2/Fio_2 < 300$, and moderate to severe ARDS to $Pao_2/Fio_2 < 200$. Covariates and outcomes were predefined and systematically captured: demographics, ARDS "risk modifiers" (e-Appendix 1), medications, APACHE (Acute Physiology and Chronic Health Evaluation) II at admission, LIPS,[7] ventilator settings, length of hospital and ICU stay, and costs of hospitalization. Comparisons were done between patients who aspirated ("aspirators") vs those who did not aspirate ("nonaspirators"), as well as between those who aspirated (with or without pneumonia) vs those who met Centers for Disease Control and Prevention (CDC) criteria for pneumonia[13] (without aspiration).

This is primarily a descriptive report, and all analytic statistics should be considered exploratory. Descriptive statistics are summarized as medians and interquartile ranges (IQRs), and exploratory statistical hypothesis testing was performed using nonparametric assumptions: Mann-Whitney or Fisher exact tests. ORs with 95% CI are reported as appropriate. Bivariate analyses distinguishing aspirators from nonaspirators were the primary hypothesis-generating aim of the report. Particular hypotheses of interest included whether aspirators would have more gastroesophageal reflux disease (GERD) and be on agents that suppress consciousness (eg, benzodiazepines, opiates, alcohol). Multivariate logistic regression models were used to identify independent predictors of aspiration from baseline covariates (e-Appendix 1). We also analyzed whether medications that affect acid reflux, the cough reflex, and host response to aspiration would influence outcomes (invasive ventilation, ARDS, death). Statistical analyses were completed using JMP10 (SAS Institute Inc).

Results

The LIPS1 cohort enrolled 5,584 subjects and has been previously described.[7] The mean age was 56 years, and 57% were men, with 5.1% overall mortality. ARDS developed in 377 (6.8%).[7]

Aspiration was identified in 212 patients (3.8%) at admission, 41% of whom also met CDC criteria for pneumonia (Fig 1). Aspirators were more likely to be male, older, white, and admitted from nursing home, compared with nonaspirators (Table 1). There was no difference in BMI or smoking status, but aspirators had more excessive alcohol use than nonaspirators. Aspiration was also associated with both higher APACHE II score and base risk for ARDS (modified LIPS) at hospital admission. The Glasgow Coma Scale (GCS) was slightly lower among aspirators (Table 1).

Among the predefined ARDS risk modifiers, prior chest radiation was the only preexisting condition that was more common among aspirators, while active immunosuppression was less common (Table 2). Despite more aspirators taking proton pump inhibitors (PPIs), there was no difference in the frequency of clinically documented GERD. The prehospital use of opiates and benzodiazepines were no more common among aspirators than nonaspirators, but antipsychotics were more common in univariate though not adjusted analyses (Table 3).

Independent predictors significantly associated with aspiration in the multivariate logistic regression model included male sex (OR = 1.5), white (OR = 2.0), admission from a nursing home (OR = 2.9), excessive alcohol use (OR = 2.8), and prior history of chest radiation (OR = 3.7). GCS (OR = 0.77), admission for sepsis (OR = 0.57), and high-risk trauma (OR = 0.13) were inversely associated with likelihood of being diagnosed with aspiration.