Original article

Risk factors for fatal outcome in surgical patients with postoperative aspiration pneumonia

Peter Studer[1], Genevieve Räber[1], Daniel Ott[2], Daniel Candinas[1], Beat Schnüriger[1]

[1]Department of Visceral Surgery and Medicine, Bern University Hospital, Bern, Switzerland

[2]Department of Radiology, Bern University Hospital, Bern, Switzerland

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Running title: Risk factors for fatal outcome after aspiration pneumonia

Corresponding Author:

PD Dr. med. Beat Schnüriger

Staff Surgeon

Department of Visceral Surgery and Medicine

Bern University Hospital, Bern, Switzerland

beat.schnuriger@gmail.com

Highlights

- Postoperative aspiration pneumonia is a rare complication, however, remains a severe disease with a significant mortality of 27% in this series.
- Increasing age, the need for intraoperative blood component transfusion and bilateral pulmonary infiltrates are independent risk factors for fatal outcome after aspiration pneumonia.
- The identification of those patients at increased risk for death after aspiration may help to further improve patients outcome.

Abstract

Methods: Aspiration pneumonia in hospitalized surgical patients has been associated with a mortality of approximately 30%. The aim of this study was to assess pre-, intra- and postoperative risk factors for mortality in patients suffering aspiration pneumonia after abdominal surgery. Retrospective study from 01/2006-12/2012 of patients with clinically and radiologically confirmed aspiration pneumonia after abdominal surgery.

Results: A total of 70 patients undergoing abdominal surgery and postoperative aspiration pneumonia were identified. There were 53 (76%) male patients, the mean age was 71±12 years and the mean ASA score was 3±1. The surgical procedures included 32 colorectal or small bowel resections, 10 partial liver resections, 9 gastric surgeries, 8 esophageal resections, 5 pancreatic surgeries, and 6 hernia repairs. Aspiration pneumonia occurred at mean postoperative day 7±10. Overall, 53% (n=37) of patients required re-intubation, with 4±5 days of additional mechanical ventilation. Mean hospital and ICU length of stay was 32±25 days and 6±9 days, respectively. Overall mortality was 27% (n=19). Forward logistic regression revealed older age [OR 7.41 (95% CI: 1.29-42.62)], bilateral aspiration pneumonia [OR 7.39 (95% CI: 1.86-29.29)] and intraoperative requirement of blood component transfusion [OR 5.09 (95% CI: 1.34-19.38)] as independent risk factors for mortality (overall R^2=0.336).

Conclusion: Postoperative aspiration pneumonia remains a severe complication with significant mortality. Increasing age, the need for intraoperative blood component transfusion and bilateral pulmonary infiltrates are independent risk factors for fatal outcome after aspiration pneumonia. Therefore, these patients suffering aspiration pneumonia require special attention and increased monitoring.

Keywords: Aspiration pneumonia, abdominal surgery, complication, critical care.

1. Introduction

Aspiration pneumonia is a precarious and well-known complication of hospitalized patients, with a high mortality rate of around 30%[1], or historically of up to 90%[2]. Moreover, it may cause re-admission to the intensive care unit as well as prolonged hospital length of stay, with significant increases in the costs of hospital care[3].

Surgical patients requiring general anesthesia and abdominal surgery with potential consequent bowel paralysis have an increased risk of pulmonary aspiration and aspiration pneumonia. Furthermore, patients with altered levels of consciousness, neurological disorders, history of pulmonary disease, older age and gastroesophageal reflux disease are at risk of aspiration pneumonia[4, 5]. The 30° elevation of the upper body has been shown to reduce the risk of aspiration pneumonia in the intensive care unit (ICU)[6]. Routine nasogastric decompression tubes[7] or percutaneous feeding tubes instead of nasogastric feeding tubes have not been shown to reduce the risk of pulmonary aspiration[8].

While guidelines and recommendations to identify patients at risk of aspiration pneumonia have been studied and published, risk factors for lethal outcome after diagnosed aspiration pneumonia have not been studied so far. However, identification of risk factors for fatal outcome may help to improve the management of this severe complication.

In this retrospective study, we opted to identify independent risk factors for mortality in patients suffering postoperative aspiration pneumonia. Therefore, pre-, intra- and postoperative parameters were analyzed of patients undergoing major abdominal surgery with postoperatively confirmed aspiration pneumonia. The early identification of those patients at increased risk for death after aspiration may help to further improve patients outcome.

2. Materials and Methods

A retrospective study of patients from 01/2006-12/2012 with clinically and radiologically confirmed aspiration pneumonia *after* abdominal surgery was performed at Bern University Hospital, which is a tertiary academic medical center in central Switzerland. All patients who undergo abdominal surgical procedures received antibiotic prophylaxis. Insertion of nasogastric tubes was at the discretion of the attending surgeon. At Bern University Hospital, protocoled measures to prevent pulmonary aspiration are in place through the pre-, intra-, and postoperative phases.

Patients with aspiration pneumonia were identified through the institutional digital patients' chard system, using the keywords "aspiration" AND/OR "pneumonia". Subsequently, all patients were carefully reviewed by one investigator (GR). To reduce heterogeneity, patients who aspirated *before or during* the surgical procedure were excluded from the study. Aspiration pneumonia was diagnosed by witnessed aspiration and subsequent confirmation by a conventional X-ray or computed tomography (CT) scan of the chest. All X-rays and CT scans were reviewed by one independent attending radiologist (DO).

Patient characteristics were collected using a computerized spreadsheet (Microsoft Access 2003, Microsoft Corporation, Redmond, WA). The collected demographic and pre-operative variables were: age, gender, main diagnosis, as well as co-morbidities, prior surgical procedures (thoracic, cardiovascular, abdominal), preoperative insertion of nasogastric tube, smoking history, alcohol abuse, drugs administered preoperatively (proton pump inhibitors, antibiotics, sedatives, opiates, neuroleptic agents), chronic pulmonary disease, gastro-esophageal reflux disease (GERD), and American Society of Anesthesiologists (ASA) physical status classification. Intraoperative variables collected included: type of surgery performed, ileostomy, colostomy, respiratory global insufficiency, amount of blood loss, operation time, transfusion of fresh frozen plasma (FFP), red blood cell (RBC) transfusion, and episodes of

intraoperative hypotension [mean arterial pressure (MAP)≤55mmHg]. Postoperative parameters collected included: postoperative day of pulmonary aspiration, days on intensive care unit (ICU), days on intermediate care (IMC), ICU readmission, length of mechanical ventilation, the need for re-intubation, nasogastric tube postoperatively, re-insertion of nasogastric tube, feeding jejunostomy, nausea, vomiting, first bowel movement, day of first mobilization, patient controlled analgesia, peridural analgesia, postoperative medication, and hospital length of stay (HLOS).

2.1 Statistics

Continuous and categorical variables are reported as mean ± standard deviation (SD), or median ± range and percentages. In order to identify risk factors for fatal outcome after aspiration pneumonia, all parameters were compared between the survivor and non-survivor group. Proportions and continuous variables were compared using the Fisher exact and the Mann-Whitney U test, respectively. Potential risk factors were identified using a p-value <0.2. Moreover, those variables of special interest were forced into the equation. Forward logistic regression analysis was used in order to identify independent risk factors for mortality.

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Windows©), version 21.0 (SPSS Inc., Chicago, IL). A p-value of <0.05 was considered statistically significant.

3. Results

From 01/2006-12/2012, a total of 70 patients with aspiration pneumonia after abdominal surgery were detected and included in the study. There were 53 (76%) male patients, the mean age was 71±12 years and the mean ASA score was 3±1. The following surgical intervention were performed in the entire study population: 32 colorectal or small bowel resections, 10 partial liver resections, 9 gastric surgeries, 8 esophageal resections, 5 pancreatic surgeries, and 6 hernia procedures. Fifty (71.4%) interventions were elective operations, and 20 (28.6%) cases were emergency interventions, including 16 (22.8%) patients preoperatively presenting with clinical signs of an ileus. According the inclusion criteria, all patients arrived in the normal ward postoperatively without a history of aspiration, but subsequently sustained aspiration pneumonia.

3.1 Incidence and outcome of postoperative aspiration pneumonia

Patients with esophageal resection, partial liver resections and pancreatic resections presented with an incidence of aspiration pneumonia of 6.5% (8/124), 2.0% (10/499), and 2.3% (5/221), respectively. For the remaining surgical procedures, the incidence of aspiration pneumonia was <1%.

Aspiration pneumonia occurred on average postoperative day 7.0±10.0, in survivors on day 6.5±9.6 and in the non-survivors on day 8.4±11.1 (*p=0.595*). Overall mortality was 27.1% (n=19). A total of 39 (55.7%) patients were admitted to the ICU after aspiration pneumonia. Of those, 37 (52.9%) patients had to be re-intubated, with an additional average length of mechanical ventilation of 4.1±4.9 days and an additional ICU length of stay of 5.7±9.5 days.

Non-survivors were intubated longer than the survivors (3.4±4.5 vs. 6.2±5.7 mechanical ventilation days, *p=0.059*). Total HLOS of the entire study population was 31.9±24.8 days.

3.2 Risk factors for mortality

Table 1 shows the detailed *preoperative* parameters obtained. A high incidence of patients with a history of previous surgical interventions was found (n=54, 77.1%). A history of alcohol abuse or smoking was present in 22 (31.3%) and 21 (30.0%) patients of the study population. Moreover, sixteen 16 (22.9%) patients suffered from GERD and fifteen (21.4%) patients were diagnosed with pre-existing chronic pulmonary disease. Patients in the non-survivor group were statistically significant older than the survivors (77.1±7.1 vs. 69.2±13.3 years, *p*=0.019). The remaining preoperative variables showed no statistical differences between the two groups (Table 1).

The comparisons of *intraoperative* variables between the survivor and non-survivor group is presented in Table 2. Operation time and intraoperative blood loss were similar in the groups, however, a trend was found for a higher number of blood component transfusions (FFP and/or RBC) for the non-survivor group than for the survivors [31.4% vs. 57.9%, *p*=0.056]. The different surgical procedures performed were not associated with an increased risk of death. Interestingly, patients receiving a colostomy tended to die more often after aspiration pneumonia than patients without colostomy (26.3% vs. 7.8%, *p*=0.054). However, those patients who required a colostomy significantly more often had a preoperative diagnosis of ileus (66.7% vs. 16.4%, *p*=0.003), with a gastric tube more often inserted preoperatively (33.3% vs. 4.9%, *p*=0.025).

Postoperative variables obtained are shown in Table 3. The non-survivors presented significantly more often with bilateral infiltrates detected in the radiological exams compared to the survivor group (68.4% vs. 39.2%, p=0.035). Of note, 76.0% of patients suffered from prolonged postoperative nausea and vomiting with re-insertion of a nasogastric tube performed in 41 (58.6%) patients of the entire study population (Table 3). Antiemetic drugs were administered in 56 (80.0%) patients. Forty patients (57.1%) received more than one sedative, with an overall number of 2.6±1.6 sedative drugs per patient. However, when comparing surviving to non-surviving patients, no statistically significant difference in the number of administered sedative drugs was found between survivors and non-survivors. Interestingly, survivors tended to be treated longer with a Patient Controlled Analgesia (PCA) system than non-survivors (5.5±3.9 days vs. 2.2±0.5 days, *p=0.117*).

Forward logistic regression revealed older age [OR 7.41 (95% CI: 1.29-42.62)], bilateral aspiration pneumonia [OR 7.39 (95% CI: 1.86-29.29)] and intraoperative requirement of blood component transfusion [OR 5.09 (95% CI: 1.34-19.38)] as independent risk factors for mortality (overall R^2=0.336). Variables entered into the equation included: age≥65 years, requirement for blood component transfusion (FFP and/or PRBC), bilateral aspiration pneumonia, at least one episode of MAP≤55mmHg intraoperatively, emergency surgery, preoperative insertion of gastric tube, preoperative ileus, type of operation (liver, colorectal, small bowel, pancreas, stomach, esophagus), preoperative intake of neuroleptic drugs, history of chronic pulmonary disease, and history of neuropsychiatric disease.

4. Discussion

Despite advances in airway management, intensive care medicine and anesthesiology, the incidence of aspiration pneumonia has been reported and is confirmed in our study to occur in approximately 1% of patients undergoing abdominal surgery, resulting in a high mortality rate of up to 30%[1, 3]. Risk factors for fatal outcome after aspiration have not been studied so far. Therefore, we opted to characterize patients who suffered postoperative aspiration pneumonia after abdominal surgery, with an attempt to identify risk factors for fatal outcome. The identification of those patients at increased risk for death after aspiration may help to further improve patients outcome.

In accordance with the literature, the current study population that suffered aspiration pneumonia comprised elderly patients with multiple co-morbidities and rather high ASA scores. The current analysis showed that older age is independently associated with mortality. Therefore, close observation and strict application of preventive measures to avoid pulmonary aspiration is of paramount importance in elderly patients.

Surprisingly, preoperative ileus as well as emergency surgery had no statistically significant impact on the mortality of patients after aspiration pneumonia. In addition, the type of surgery performed did not correlate with either the incidence or the mortality of this pulmonary complication. Interestingly, patients undergoing esophageal resection presented with the highest incidence of aspiration pneumonia (6.5%), but no fatal outcome occurred in this subgroup. However, the limited number of patients may have resulted in non-significant results. Nevertheless, this observation might be explained by the fact that, after esophageal resection, these patients receive the maximum available monitoring during the postoperative course, due to the known high potential for complications after this type of surgery.

Interestingly, in the current study group, intraoperative administration of blood components was identified as an independent risk factor for mortality after pulmonary aspiration. This effect could be explained by the increased risk of pulmonary complications and pulmonary susceptibility to additional inflammatory mediators (e.g. gastric content) after transfusions of either RBC or FFP[9] (i.e. TRALI (Transfusion-related acute lung injury) and TACO (Transfusion-related circulatory overload)). TRALI is defined as the onset of respiratory distress after blood transfusion due to donor antibody mediated and non-antibody mediated events and has long been regarded as a rare complication of transfusion medicine. Today the US Food and Drug Administration recognizes the syndrome as the leading cause of transfusion-related mortality[10]. Transfusion related complications are likely to pronounce and aggravate the clinical course of aspiration pneumonia[11]. With the risk of TRALI or TACO in mind, as suggested by other investigators, we recommend a 'patient-tailored transfusion policy' with a transfusion threshold of 70 g/l or below, with a target hemoglobin range of 70–90 g/l, unless specific co-morbidities or acute illness-related factors modify the clinical decision making[12].

As expected, a high rate of re-intubation (52.9%) and ICU admission (55.7%) was observed in the current population. In line with the extent of aspiration pneumonia, non-survivors were intubated longer than survivors (6.2±5.7 vs. 3.4±4.5 days, p=0.059). Not surprisingly, the non-survivors presented more frequently with bilateral infiltrates in the conventional radiological exam compared to the survivor group (68.4% vs. 39.2%, p=0.035).

As expected, the use of gastric tubes did not influence the clinical course of patients with aspiration pneumonia[7]. Together with the fact that nasogastric tubes do not protect patients from pulmonary aspiration, we support the recommendations in the current literature to abandon routine nasogastric decompression tubes in elective surgical patients[7].

We were surprised by the frequent use of sedative drugs, with 57.1% of patients receiving more than one drug (2.6±1.5) with known sedative effect. It is known that sedatives have the potential to suppress the swallowing reflex and other reflexes, thus increasing the risk for pulmonary aspiration; the clinician should be aware of this potentially life-threatening side-effect[13]. However, according to our knowledge, no study is currently available that explicitly examines the impact of sedative drugs on the rate of pulmonary aspiration after abdominal surgery. Interestingly, the use of patient-controlled analgesia (PCA) with dose-dependent, sedative effects tended to be applied longer in the survivor group than to the non-survivors (5.5±3.8 vs. 2.2±0.5 days, p=0.117).

5. Conclusion

Aspiration pneumonia is a rare complication in patients after abdominal surgery, but with a persistent high mortality rate. Older age, intraoperative blood component transfusion, and bilateral infiltrates on routine radiological examination are independent risk factors for mortality. After pulmonary aspiration, early identification and close monitoring and treatment of patients at increased risk for lethal outcome are crucial in further reducing postoperative mortality.

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Table 1: Comparison between survivors and non-survivors with aspiration pneumonia: Demographics and preoperative parameters

	All (n=70)	Survivors (n=51)	Non-survivors (n=19)	*p*
Gender (male)	53 (75.7%)	37 (72.5%)	16.0 (84.2%)	0.367
Age (years)	71.4±12.4	69.2±13.3	77.2±7.1	0.019
Pulmonary disease	15 (21.4%)	12 (23.5%)	3 (15.8%)	0.744
GERD	16 (22.9%)	12 (23.5%)	4 (21.1%)	1.000
History of smoking	21 (30.0%)	18 (35.3%)	3 (15.8%)	0.148
Alcohol abuse	22 (31.4%)	17 (33.3%)	5 (26.3%)	0.399
Sedatives	27 (38.6%)	18 (35.3%)	9 (47.4%)	0.414
Neuroleptic drugs	10 (14.3%)	6 (11.8%)	4 (21.1%)	0.443
Opiates	14 (20.0%)	8 (15.7%)	6 (31.6%)	0.181
PPI	28 (40.0%)	20 (39.2%)	8 (42.1%)	1.000
Pre-existing neuropsychiatric disease	16 (22.9%)	11 (21.6%)	5 (26.3%)	0.752
Emergency surgery	20 (28.6%)	13 (25.5%)	7 (36.8%)	0.383
Preoperative ileus	16 (22.8%)	9 (17.6%)	7 (36.8%)	0.114
Preop. gastric tube	6 (8.6%)	3 (5.9%)	3 (15.8%)	0.334
History of previous surgery:				
- total	54 (77.1%)	40 (78.4%)	14 (73.7)	0.752
- abdominal	45 (64.3%)	32 (62.6%)	13 (68.3%)	0.782
- cardiovascular	22 (31.3%)	18 (35.3%)	4 (21.1%)	0.386
- thoracic	5 (7.1%)	4 (7.7%)	1 (5.3%)	1.000

GERD = Gastroesophageal Reflux, PPI = Proton Pump Inhibitors.

Table 2: Comparison between survivors and non-survivors with aspiration pneumonia: Type of surgery and intraoperative parameters

	All (n=70)	Survivors (n=51)	Non-survivors (n=19)	*p*
Surgery performed:				
- large bowel	20(28.6%)	14 (27.5%)	6 (31.6%)	0.771
- small bowel	12 (17.1%)	9 (17.6%)	3 (15.8%)	1.000
- hepatobiliary	10 (14.3%)	6 (11.8%)	4 (21.1%)	0.265
- gastric	9 (12.9%)	6 (11.8%)	3 (15.8%)	0.696
- esophageal resection	8 (11.4%)	8 (15.7%)	0	0.097
- hernia repair	6 (8.6%)	4 (7.8%)	2 (10.5%)	0.660
- pancreatic	5 (7.1%)	4 (7.8%)	1 (5.3%)	1.000
Ileostomy	8 (11.4%)	5 (9.8%)	3 (15.8%)	0.674
Colostomy	9 (12.9%)	4 (7.8%)	5 (26.3%)	0.054
Bloodloss (mL)	716±893	801±999	486±461	0.371
OR time (min)	260±140	277±149	213±107	0.132
Blood component transfusion (PRBC and/or FFP)	27 (38.8%)	16 (31.4%)	11 (57.9%)	0.056
Respiratory failure	2 (2.9%)	2 (3.9%)	0	1.000
ASA Score	3.06 ± 0.634	3.08±0.627	3.00±0.667	0.651
Intraoperative hypotension	59 (84.3%)	43 (84.3%)	16 (84.2%)	1.000
Intraoperative hypotension (min)	49.1± 49.9	51.1±50.5	43.9±49.4	0.671

ASA Score = American Society of Anesthesiology Score, FFP = Fresh Frozen Plasma, PRBC = Packed Red Blood Cells

Table 3: Comparison between survivors and non-survivors with aspiration pneumonia: Postoperative parameters

	All (n=70)	Survivors (n=51)	Non-survivors (n=19)	*p*
Aspiration postop. day	7.0±10.0	6.5±9.6	8.4±11.1	0.595
Bilateral aspiration pneumonia on radiological exam	32 (45.7%)	19 (37.3%)	13 (68.4%)	0.030
IMC to ICU readmission	39 (55.7%)	26 (51.0%)	13 (68.4%)	0.280
IMC to ICU day	8.5±10.5	9.9±12.4	5.8±4.1	0.219
Total ICU (days)	5.7± 9.5	5.4± 9.7	6.4± 8.9	0.506
Re-intubation	37 (52.9%)	27 (52.9%)	10 (52.6%)	1.000
Additional mechanical ventilation [n (days)]	53 (4.1 ± 4.9)	40 (3.4±4.5)	13 (6.2±5. 7)	0.059
Respiratory failure	24 (34.3%)	16 (31.4%)	8 (42.1%)	0.412
PCA	22 (31.4%)	17 (33.3%)	5 (26.3%)	0.773
PCA days	4.7±3.7)	5.5±3.9)	2.2±0.5)	0.117
PDA	37 (52.9%)	28 (54.9%)	9 (48.4%)	0.601
PDA days	4.9±2.6	4.7±2.1	5.4±3.9	0.900
Prokinetic agents	16 (22.9%)	12 (23.5%)	4 (21.1%)	1.000
Antiemetics	56 (80.0%)	43 (84.3%)	13 (68.4%)	0.181
Opiates	64 (91.4%)	46 (90.2%)	18 (94.7%)	1.000
Neuroleptic drugs	34 (48.6%)	22 (43.1%)	12 (63.2%)	0.181
# of Sedatives	60 (2.58±1.63)	46 (2.59±1.62)	14 (2.57±1.69)	0.993
PPI	66 (94.3%)	47 (92.2%)	19 (100%)	0.568
Gastric tube	40 (57.1%)	27 (52.9%)	13 (68.4%)	0.287
Gastric tube reinsertion	41 (58.6%)	29 (56.9%)	12 (63.2%)	0.786
Gastric tube postoperative (days)	9. 8±14.0	11.3±16.2	6.5±7.4	0.117
Enteral feeding tube	31 (44.3%)	24 (47.1%)	7 (36.8%)	0.590
Nausea	53 (75.7%)	41 (80.4%)	12 (63.2%)	0.208
Vomiting	55 (78.6%)	43 (84.3%)	12 (63.2%)	0.098
Vomiting (day)	9.3±16.0)	9.1±16.8	9.8±12.9	0.473
First bowel movement (day)	4.4±3.5	4.7±3.6	3. 6±3.4	0.145
First mobilization from bed (day)	1.9±2.4	1. 8±2.0	2.1±3.2	0.409
Known psychiatric/ neurologic disease	16 (22.9%)	11 (21.6%)	5 (26.3%)	0.752

IMC = Intermediate Care, ICU = Intensive Care Unit, PCA = Patient Controlled Analgesia, PDA = Peridural Anesthesia, PPI = Proton Pump Inhibitors.