Nosocomial infections after aneurysmal subarachnoid hemorrhage: time course and causative pathogens

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Background **Nosocomial infections after aneurysmal subarachnoid hemorrhage (aSAH) are associated with prolonged length of stay and poor functional outcome. It remains unclear if infections result in prolonged length of stay or, vice versa, if prolonged length of stay results in more infections. Before strategies can be designed to reduce infections after aneurysmal subarachnoid hemorrhage, more data are needed on time course and causative pathogens of infections.**

Aim **To investigate the time course of infection onset and bacterial microorganisms that cause nosocomial infections after aSAH.**

Methods **In consecutive patients with aneurysmal subarachnoid hemorrhage admitted to the University Medical Center Utrecht between 2009 and 2011, we analyzed the proportion of patients with infections, day of infection onset, and culture results.**

Results **Of the 291 included patients, 107 (37%) patients developed 115 nosocomial infections. Fifty-six patients (19%) developed an infection within the first week. Median day of infection onset was for pneumonia ($n = 49$; 17%) day 4 (interquartile range 3–9), respiratory tract infection ($n = 16$; 6%) day 4 (interquartile range 1–7), urinary tract infection ($n = 27$; 9%) day 11 (interquartile range 7–14), and meningitis/ventriculitis ($n = 10$; 3%) day 19 (interquartile range 9–33). Cultures of infections mostly yielded *Staphylococcus aureus* (20%), *Haemophilus influenzae* (15%), and *Escherichia coli* (14%),**

Conclusion **Nosocomial infections after subarachnoid hemorrhage are common and mostly occur in the first week after ictus. Future studies should investigate if general hygienic measures, infection awareness, minimizing the duration of mechanical ventilation and use of catheters/drains, or prophylactic antibiotics reduce infections and improve functional outcome.**

Key words: aneurysm, infection, meningitis, pneumonia, subarachnoid hemorrhage, urinary tract infection

Introduction

Patients with aneurysmal subarachnoid hemorrhage (aSAH) often develop infections such as pneumonia and urinary tract infection during hospitalization after the hemorrhage (1–3). Nosocomial infections after aSAH are associated with poor functional outcome and case fatality (2–4). Risk factors for infections after SAH include higher age, gender, poor clinical condition on admission, intensive care unit (ICU) admission, endotracheal intubation, tracheostomy, urinary cathether, and extraventricular drain (3,5,6). Although infections after aSAH are associated with prolonged length of stay (2,3), it remains unclear if infections result in prolonged length of stay or, vice versa, if prolonged length of stay results in more infections. Before strategies can be designed that reduce the risk of infections after aSAH, more data are needed on the time course of infection onset and bacterial microorganisms that cause nosocomial infections after aSAH.

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Received: 3 September 2014; Accepted: 6 January 2015; Published online 20 April 2015

Conflict of interest: None declared.

DOI: 10.1111/ijs.12494

Methods

This study was conducted at the University Medical Center Utrecht, the Netherlands, which is a tertiary referral center for patients with aSAH. Approval was obtained from the Institutional Research Ethics Board. From a prospective database of consecutive patients, we included all patients with aSAH admitted between January 1, 2009 and January 1, 2011. Patients were excluded if no aneurysm was identified. All patients received treatment according to our institutional subarachnoid hemorrhage (SAH) protocol, including antibiotic treatment in case of infection. Patients were initially admitted to a medium care unit (MCU). Patients in need of mechanical ventilation were admitted or transferred to an ICU. Also, after aneurysm surgery, patients were admitted for at least one-day to the ICU. No prophylactic antibiotics were given, except for patients admitted to the ICU with an expected ICU stay longer than 48 h. These patients received treatment with selective decontamination of the digestive tract (SDD) consisting of intravenous cefotaxime, and/or selective oropharyngeal decontamination (SOD) consisting of topical application of tobramycin, colistin, and amphotericin B in the oropharynx and stomach.

The following variables were extracted: age, gender, clinical condition on admission by means of the Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage (PAASH) scale (7), (type of) nosocomial infection, day of infection onset, microorganisms found at bacterial cultures, treatment with SDD/SOD and duration of SDD/SOD treatment, aneurysm treatment modality, ICU admission, length of stay at ICU, and total length of stay.

Definitions

Infections [pneumonia, respiratory tract infection (RTI), urinary tract infection (UTI), and bacterial meningitis/ventriculitis] were defined according to previously defined international criteria from the Centers for Disease Control and Prevention (appendix 1) (8). Because the Centers for Disease Control and Prevention did not give definitions for phlebitis, cellulitis, and staphylococcal scalded skin infection, we used the diagnoses of the attending physicians for these infections. Day of infection

onset was defined as the day after aSAH when the criteria for the diagnosis of infection were met. Day of ictus was considered day 0.

Outcome measures and analyses

We analyzed the proportion of patients with an infection, the day of infection onset, and causative bacterial microorganisms. Values are presented in means with standard deviations (SD), or medians with interquartile ranges (IQRs). We calculated crude odds ratios (ORs) with 95% confidence intervals (CIs) to investigate potential relationships between several interventions [intubation, tracheostomy, bladder catheterization, external ventricular drain (EVD) use] and infections after the introduction of these interventions. Subsequently, we performed multivariable logistic regression analyses with adjustments for age, gender, and clinical condition on admission.

Results

Patient characteristics are shown in Table 1. In total, 259 patients (89%) were admitted on the day of ictus. Of the 291 included patients, 107 patients (37%) had 115 nosocomial infections. Pneumonia was the most prevalent infection ($n = 49$; 17%), followed by UTI ($n = 27$; 9%), RTI ($n = 16$; 5%), and bacterial meningitis/ventriculitis ($n = 10$; 3%) (Table 2). In total, 199 patients (68%) were admitted to the ICU at some point during hospitalization, with a median day of admission at day 1 (IQR 0–3). Of the 58 patients with limitation of care, 39 (67%) died within three-days and 15 (26%) developed an infection.

Day of infection onset

Time course of infection onset is shown in Figs 1–3. Twenty-five (9%) patients developed an infection within the first three-days after ictus, and 56 (19%) patients developed an infection within the first week after aSAH. Median day of pneumonia onset was at day 4 (IQR 3–9), RTI onset was at day 4 (IQR 1–7), UTI onset was at day 11 (IQR 7–14), and bacterial meningitis/ventriculitis onset was at day 19 (IQR 9–33). Infection onset was at the MCU or general ward in 78 (68%) infections, and at the ICU in 37 (32%) infections.

Causative pathogens

Of 115 infections, 83 cultures (72%) yielded positive results. Culture results per infection are summarized in Table 2. Overall, the most prevalent microorganisms were *Staphylococcus aureus* ($n = 23$; 20%), *Haemophilus influenzae* ($n = 17$; 15%), and *Escherichia coli* ($n = 16$; 14%).

Potential iatrogenic etiologies

Relationships between several interventions and infections occurring after the introduction of these interventions are shown in Table 3. Of 203 patients who were intubated during hospitalization, 43 patients (21%) developed pneumonia and 15 patients (7%) had RTI following intubation. Of the 21 patients with tracheostomy, four patients (19%) later on developed pneumonia

Table 1 Demographics and clinical characteristics

Baseline characteristics	All patients *N* = 291	With infection *N* = 107	Without infection *N* = 184
Mean age in years (SD)	57 (13)	59 (13)	56 (13)
Female, no. (%)	214 (74)	74 (69)	140 (76)
PAASH score on admission			
PAASH 1 (GCS = 15), no. (%)	112 (38)	36 (34)	76 (41)
PAASH 2 (GCS = 11–14), no. (%)	98 (34)	36 (34)	62 (34)
PAASH 3 (GCS = 8–10), no. (%)	15 (5)	8 (8)	7 (4)
PAASH 4 (GCS = 4–7), no. (%)	39 (13)	19 (18)	20 (11)
PAASH 5 (GCS = 3), no. (%)	27 (9)	8 (8)	19 (10)
WFNS score on admission			
WFNS 1, no. (%)	112 (39)	36 (34)	76 (41)
WFNS 2, no. (%)	64 (22)	20 (19)	44 (24)
WFNS 3, no. (%)	11 (4)	7 (7)	4 (2)
WFNS 4, no. (%)	51 (18)	26 (24)	25 (14)
WFNS 5, no. (%)	53 (18)	18 (17)	35 (19)
Hijdra score, median (IQR)	20 (11–27)	22 (14–29)	19 (10–26)
Aneurysm treatment			
Endovascular, no. (%)	108 (37)	47 (44)	61 (33)
Clipping, no. (%)	120 (41)	44 (41)	76 (41)
None, no. (%)	65 (22)	16 (15)	49 (27)
ICU admission at any moment during clinical course, no. (%)	199 (68)	83 (78)	116 (63)
Duration ICU admission in days, median (IQR)	2 (1–4)	4 (1–9)	1 (1–2)
SDD/SOD Treatment, no. (%)	104 (36)*	61 (57)	43 (23)
Length of stay in days, median (IQR)	15 (9–22)	21 (14–29)	14 (4–18)

*In 49 patients, SDD/SOD was started after infection onset.

ICU, intensive care unit; IQR, interquartile range; *N*, number; PAASH, Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage scale; SD, standard deviation; SDD, selective decontamination of the digestive tract; SOD, selective oropharyngeal decontamination; WFNS, World Federation of Neurosurgical Societies.

Table 2 Results of cultures in patients with infection. Since cultures may yield more than one microorganism, total number of microorganisms can exceed the number of patients with infection and positive culture

Positive cultures	*N* (%)
Pneumonia (total)	49
Patients with pneumonia and positive sputum culture	32 (65)
Staphylococcus aureus	13 (27)
Haemophilus influenzae	13 (27)
Streptococcus pneumoniae	5 (10)
Other	11 (22)
Respiratory tract infection (RTI) (total)	16
Patients with RTI and positive sputum culture	13 (81)
Staphylococcus aureus	4 (25)
Haemophilus influenzae	4 (25)
Streptococcus pneumoniae	3 (19)
Other	6 (38)
Urinary tract infection (UTI) (total)	27
Patients with UTI and positive urine culture	22 (81)
Escherichia coli	16 (59)
Enterococcus species	8 (30)
Coagulase negative *staphylococcus*	3 (11)
Other	6 (22)
Meningitis/ventriculitis (total)	10
Patients with meningitis/ventriculitis and positive cerebrospinal fluid culture	10 (100)
Coagulase negative *staphylococcus*	6 (60)
Staphylococcus aureus	1 (10)
Staphylococcus epidermidis	1 (10)
Other	3 (30)
Phlebitis (total)	9
Staphylococcus aureus	5 (56)
Bloodstream infection not secondary to another identified infection (total)	1
Enterococcus cloaca	1 (100)
Cellulitis (no culture results)	1
Surgical site infection (no culture results)	1
Staphylococcal scalded skin infection (no culture results)	1

N, number.

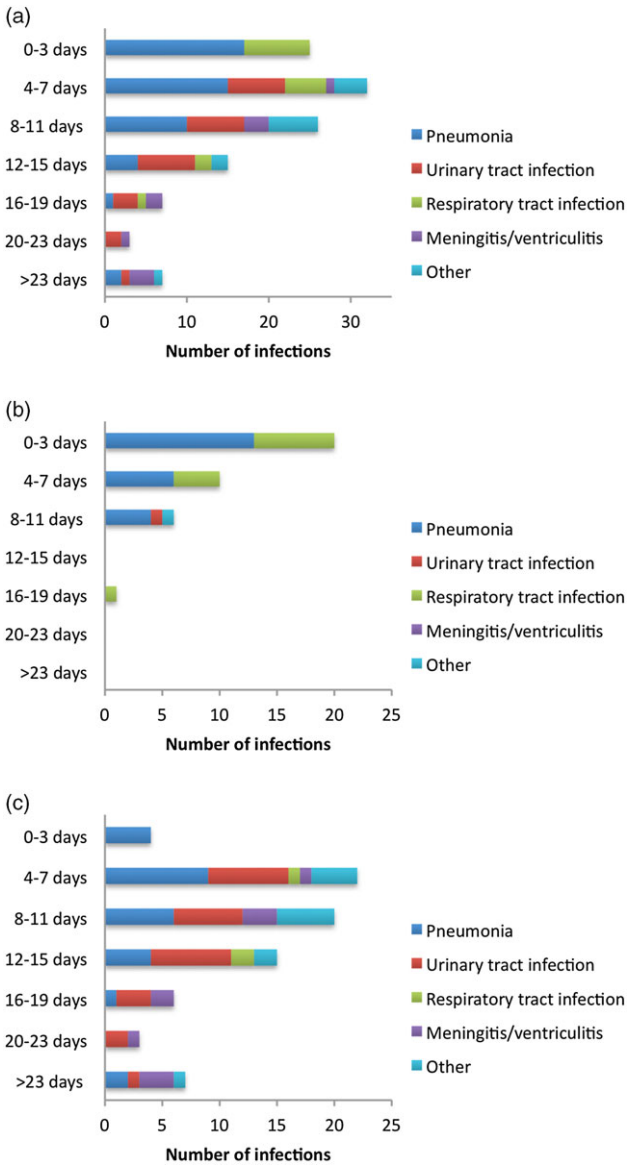

Fig. 1 (a) Time course of all nosocomial infections; (b) time course of infections diagnosed at the intensive care unit; and (c) time course of infections at the medium care unit and general ward.

and three (14%) had RTI. Meningitis/ventriculitis only occurred after EVD placement. All patients received urinary catheters on the day of admission.

Discussion

The results of our study show that more than one-third of patients with aSAH have nosocomial infections. Nineteen percent of the total SAH population developed an infection within the first week after aSAH. The most prevalent microorganisms were *S. aureus*, *H. influenzae*, and *E. coli*.

The time course of infections after aSAH has not been investigated systematically before. In one study of six patients with pneumonia after aSAH, median day of onset was day 3 (9). Four recent studies reported on culture results, but only in selected groups of aSAH patients, such as patients with pneumonia or admitted to the ICU (4–6,9). Because we investigated culture results in 291 consecutive patients with aSAH without applying exclusion criteria, our results have stronger external validity and are more useful for designing new strategies to prevent infections after SAH.

A limitation of our study is the retrospective design. Therefore, not all patients who were suspected of having an infection had a standardized workup. In addition, physicians might have given antibiotics when there was only a suspicion of infection, and hereby may have prevented the onset of an infection according to the criteria from the Centers for Disease Control and Prevention. However, because the use of antibiotics in the Netherlands is quite restricted compared with other European countries, we assume that overall the observed incidence rates are quite realistic (10).

In conclusion, nosocomial infections after SAH are common and mostly occur in the first week after SAH. Future studies should investigate if prophylactic measures, such as general hygienic measures, infection awareness, minimizing the duration

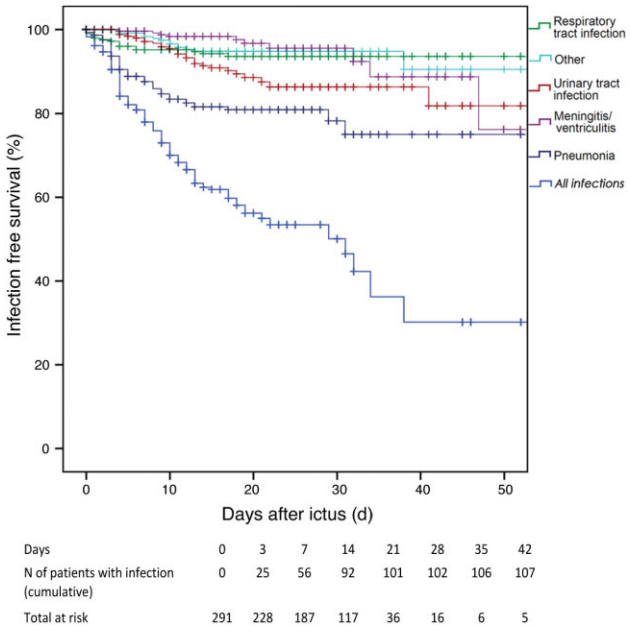

Fig. 2 Infection-free survival represented in Kaplan–Meier curve for all infections, and categorized by type of infection.

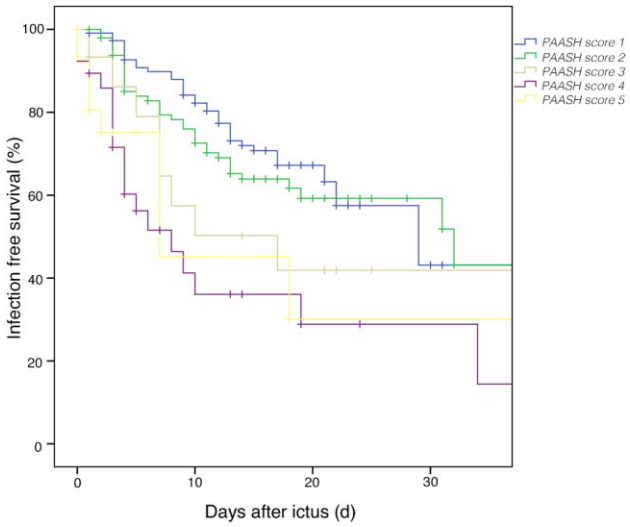

Fig. 3 Infection-free survival represented in Kaplan–Meier curves categorized by Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage (PAASH) score on admission.

of mechanical ventilation and use of catheters/drains, or prophylactic antibiotics, reduce infections and improve functional outcome.

Author contributions

M. D. I. V. and G. J. E. R. conceived and designed the study. K. G. L. performed data collection and drafted the manuscript. M. D. I. V. and G. J. E. R. contributed to its revision. All authors approved the final version.

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Table 3 Odds ratios for several interventions to develop infections following these interventions

Baseline characteristics	Crude OR (95% CI)	Adjusted OR* (95% CI)
Pneumonia		
Intubation	3·0 (1·3–7·0)	3·6 (1·5–9·2)
Intubation duration (OR per day)	1·3 (1·2–1·5)	1·3 (1·2–1·5)
Tracheostomy	2·6 (0·8–9·0)	2·5 (0·7–9·1)
Respiratory tract infection		
Intubation	6·9 (0·9–53·4)	5·8 (0·7–47·7)
Intubation duration (OR per day)	1·2 (1·1–1·4)	1·1 (1·1–1·3)
Tracheostomy	4·0 (1·03–15·6)	3·0 (0·7–12·5)
Urinary tract infection		
Foley catheter duration (OR per day)	1·04 (1·02–1·11)	1·04 (1·01–1·09)
Bacterial meningitis/ ventriculitis		
External ventricular drain (EVD)	28·8 (3·6–231·1)	33·6 (4·0–282·9)
EVD duration (OR per day)	1·2 (1·1–1·3)	1·2 (1·1–1·3)

*Adjusted for age, gender, and clinical condition on admission [Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage (PAASH) score].
CI, confidence interval; OR, odds ratio.

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