Published in final edited form as:

Neurocrit Care. 2018 February ; 28(1): 77–82. doi:10.1007/s12028-017-0431-6.

Men experience higher risk for pneumonia and death after intracerebral haemorrhage

Sandro Marini, MD^{1,2}, Andrea Morotti, MD^{1,2,3}, Umme K.Lena, BA¹, Joshua N. Goldstein, MD, PhD^{2,4}, Steven M. Greenberg, MD, PhD^{2,4}, Jonathan Rosand, MD, MSc^{1,2,4}, and Christopher D. Anderson, MD, MMSc^{1,2,4}

¹Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA

²J. P. Kistler Stroke Research Center, Massachusetts General Hospital, Boston, MA, USA

³Stroke Unit and Department of Emergency Neurology, C. Mondino National Neurological Institute, Pavia, Italy

⁴Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Massachusetts General Hospital, Boston, MA, USA

Abstract

Background and aim—Infectious complications worsen outcome after intracerebral haemorrhage (ICH). We investigated the impact of sex on post-ICH infections and mortality.

Methods—Consecutive ICH patients (admitted to a single hospital between 1994 and 2015) were retrospectively assessed via chart review to ascertain the following in-hospital infections: urinary tract infection, pneumonia, and sepsis. Adjusted logistic regression was performed to identify associations between sex, infection, and mortality at 90 days.

Results—2004 patients were investigated, 1071 (53.7 %) male. Men were more likely to develop pneumonia (21.9%, VS 15.5 % $p<0.001$) and sepsis (3.4% VS 1.6%, $p=0.009$) whereas women had higher risk of UTI (19.9% VS 11.7% $p<0.001$). Multivariate analyses confirmed association between male sex and pneumonia (Odds Ratio (OR) 1.37, 95% confidence interval (CI) 1.08 – 1.74, $p=0.011$). Male sex (OR 1.40; CI 1.07–1.85; $p=0.015$) and infection (OR 1.56; CI 1.11–1.85; $p=0.011$) were independently associated with higher 90-day mortality.

Conclusions—Types and rates of infection following ICH differ by sex. Male sex independently increases pneumonia risk, which subsequently increases 90-day mortality. Sex-specific preventive strategies to reduce the risk of these complications may be one strategy to improve ICH outcomes.

Keywords

infections; intracerebral haemorrhage; sex; pneumonia; sepsis; mortality

Corresponding author: Sandro Marini, MD, Center for Genomic Medicine, 185 Cambridge Street, Boston, MA 02114. Office: (617) 726-5942, smarini1@mgh.harvard.edu.

Conflicts of interest
None.

Introduction and aims

Intracerebral haemorrhage (ICH) carries a mortality of 40%–50% and remains the most fatal form of stroke [1,2]. Complications of ICH, both related to the haemorrhage itself as well as secondary medical problems, can heavily influence outcome and account for more than 1/3 of the overall mortality [3,4]. Among those, infections are common, with pneumonia and UTI affecting 43% and 38% of patients, respectively [5–7]. The occurrence of these infections is associated with a fourfold increased risk of a poor functional outcome[8,9].

Sex is associated with ICH outcome, but the mechanisms underlying this association remain poorly understood[10]. We recently found an association between male sex and hematoma expansion after ICH, but this association does not fully explain the overall excess of mortality in men compared to women [11]. Given prior evidence that sex impacts rates of infectious complications in traumatic brain injury and ischemic stroke[12,13] we sought to test the hypothesis that excess ICH mortality in men could be partially explained by an excess in infectious complications. If present, sex-specific infectious risks after ICH could highlight future strategies to deploy interventions aimed at reducing complication risks in patient populations most likely to derive benefit.

We used an observational single centre cohort of ICH subjects, screening for pneumonia, UTI, and sepsis during the acute post-ICH hospitalization. We then explored the relationship between infection risk and sex, as well as the compound associations between infection risk, sex, and 90-day mortality.

Methods

Participants

We used data from the Massachusetts General Hospital (MGH) ICH Longitudinal Study, an ongoing single-centre cohort study of patients with primary ICH[14], censored at a predetermined data freeze in April 2015. Initial criteria for inclusion in this study were: 1) age ≥ 18 years and 2) admission to MGH between January 1994 to April 2015 with primary ICH confirmed by neuroimaging. Exclusion criteria included other presumed causes of the hemorrhage, namely: traumatic intracranial bleeding, intracranial tumor, aneurysm or other vascular malformation, or hemorrhagic conversion of acute brain infarction. For the present analyses, patients were further excluded in case of missingness of clinical variables, lack of data to include or exclude the presence of infection, and absence of information on mortality at 90 days. All aspects of the study were approved by the Institutional Review Board (IRB). Informed written or verbal consent was obtained by patients or family members or was explicitly waived by the IRB.

Clinical Variables

Dedicated study staff collected demographic and clinical data via structured standardized in-person interview and review of existing medical records. Survival data were obtained via follow up by phone whenever possible, or updated from hospital records supplemented by the Social Security Death Index. We collected data including sex, age, history of hypertension, diabetes mellitus, and coronary artery disease (CAD), alcohol consumption,

smoking, and oral anticoagulant treatment. Prior functional dependence was defined as requiring assistance at least in one instrumental activity of daily living (IADL)[15]. For the index hospital stay, we collected the following data: Glasgow Coma Scale (GCS) at presentation, intubation, any surgical procedure, length of hospitalisation (days) and any limitation of care (defined as presence of “do-not-resuscitate/do-not-intubate” code status or a “comfort measures only” order). We also recorded recurrence of primary ICH in the studied period. Finally, participants self-identified race and ethnicity at enrollment, choosing from the options recommended by the Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity[16].

Infectious Complications

The incidence of pneumonia, urinary tract infections, and sepsis during the immediate post-ICH hospital stay were established through a retrospective review of: hospital charts, laboratory and radiological tests, and discharge reports by two investigators (SM, AM). The presence of an infection during the hospital stay was assessed according to previously published criteria[17–19]. Specifically, pneumonia was diagnosed on the combination of typical clinical presentation with confirmatory chest X-ray changes[17]. A positive urine culture was required for the diagnosis of urinary tract infection[18]. Sepsis was diagnosed in the setting of a documented source of infection associated with evidence of acute end organ dysfunction[19].

Computed Tomography (CT) image acquisition and analysis

Non-contrast CT (NCCT) (performed with an axial technique and 5 mm thickness slices, 120–140 kVp, 10–500 mA) was reviewed by researchers blinded to all clinical and laboratory variables for presence of intraventricular extension of the hematoma (IVH) and determination of ICH location (deep, lobar or infratentorial). Hematoma volume was calculated on NCCT images with Analyze Direct 11.0 software, a semi-automated computer assisted technique, and natural-log transformed to approximate normality[14].

Statistical Analyses

Age at index ICH, GCS, volume of ICH and blood pressure values were analysed as a continuous variable, expressed as median (interquartile range, IQR) or mean (standard deviation, SD) as appropriate, and compared with the Mann-Whitney test. All other variables were analysed as static categorical variables, expressed as count (%) and compared using the χ^2 test. Multivariate logistic regressions analysis was performed to assess the role of sex as a predictor of infection after ICH. We performed a first regression including established predictors of infection[20,21] (model 1: sex, intubation, age, ICH Location, ICH volume, GCS, IVH), followed by a more comprehensive model including all variables differing in the univariate comparison between male and female (p value <0.05) and the period of enrolment (model 2: sex, intubation, age, ICH Location, ICH volume, GCS, IVH, diabetes, CAD, hypertension, smoking, alcohol, warfarin, prior dependence, expansion, ethnicity, and enrolment epoch).

Similarly, we used multivariate logistic regression to test associations between sex, infections, and 90-day mortality, using known determinants of ICH mortality as covariates

(model 3: ICH location, GCS, IVH, age, ICH volume, length of stay, UTI) as well as a larger model including variables differing between patients with and without infection (model 4: model 3 + intubation, surgery). All analyses were performed using the statistical package SPSS v. 21, 2012 (www.spss.com). We considered results statistically significant for p -values < 0.05 .

Results

A total of 2004 patients met the eligibility criteria (median age 75 y/o, 53.4 % males). Of 2403 enrolled patients with ICH, 399 were excluded due to lack of information on clinical variables ($n=351$) and presence or absence of infection ($n=48$). Compared to the cohort studied, patients excluded from the analysis did not differ for age, race, sex, hematoma expansion or mortality (all p values > 0.10).

Impact of sex on infections

Table 1 shows differences between sexes: women were older (average 78 vs. 72 years), more likely to be functionally dependent prior to their index ICH ($p=0.008$) and more likely to suffer from lobar ICH ($p<0.001$). Men had a higher burden of coronary artery disease, hypertension, diabetes, warfarin exposure, and alcohol and tobacco use. Univariate analysis [Table 1] showed that men, were more likely to develop pneumonia and sepsis, whereas women were more likely to develop urinary tract infections. Both multivariable models in logistic regression showed independent association between male sex and risk of pneumonia, after controlling for prespecified covariates [Table 2].

Multivariable analyses for UTI showed that female sex was independently associated in both models. Male sex was independently associated with sepsis in model 1 but not model 2.

Impact of infections on death

Table 3 shows the relationship between infection and 90-day mortality. Given the low impact of UTI on mortality [female excess for 90-day mortality: OR 0.72; 95% CI 0.5–1.04, $p=0.08$ (model 3)], we restricted our analysis to pneumonia and sepsis, combined into one infection endpoint. Patients with these infections were more likely to be men, had higher rates of intubation, surgical procedures, IVH, and UTI, as well as a lower GCS ($p<0.001$), and longer length of stay (all $p<0.001$) (Supplemental: Table I).

Both male sex and infections were independent predictors of mortality at 90 days [Table 3] (all variance inflation factors < 2.0). To better prove the effect of sex we run a sex-stratified analysis for factors associated with mortality: males have a higher risk of 90 mortality whether female do not (Supplement table II). Interaction sex*infection analysis was not significant.

Finally, sensitivity analysis including only patients with pneumonia, using model 3, showed comparable results for male sex (OR 1.42; 95%CI 1.08–1.86, $p=0.012$) and pneumonia (OR 1.43; 95%CI 1.01–2.02, $p=0.046$) as a predictor of death at 90 days.

Discussion

Our study demonstrates a higher risk of pneumonia after ICH among men, independent of known risk factors for infection. Our findings support existing literature for female sex as a risk factor for UTI. Analysis of mortality shows that male sex and infection represent independent risk factors for death at 90 days. Taken together, these data suggest that male sex is a risk factor for pneumonia and sepsis, and that these infections may drive the observed excess in 90-day mortality.

Previous literature has identified male sex as a risk factor for the development of pneumonia[12,22–24] following stroke, but these studies have primarily focused on ischemic stroke which carries an overall more favourable prognosis. Ji and colleagues [25] recently developed a score to predict hospital-acquired pneumonia after ICH that included male sex, but this study was based exclusively on Asian populations and did not assess the effect of pneumonia or sepsis on mortality.

The present analysis expands observations specifically to ICH, where brain injury-related immunosuppression plays a larger and more unpredictable role in comparison to ischemic stroke[26,27]. Our results also explicitly link the observed increased risk of pneumonia and sepsis to sex-specific 90-day mortality.

Sex-based differences of the outcome of various infections are well reported, with men showing weaker cellular and humoral immune responses compared to women. Several mechanisms for these observations have been suggested, including X chromosome-related gene expression, influences of sex steroids on the immune system, and sex interactions with behaviours predisposing to susceptibility to infection [28–30].

The underlying mechanisms driving the observed differences between men and women are not discernible from our available data. Nonetheless, these results may help to explain observed differences in stroke outcomes between sexes. While we have previously demonstrated the role of sex in hematoma related complications [11]; here we provide evidence of its role in a secondary adverse outcome. Both observations highlight the potential promise of sex-specific precision strategies to at least partially mitigate the high overall mortality of ICH.

The strengths of this analysis include our use of a large representative dataset, which allowed us to adjust for potential confounders related to ICH severity. This permitted a more unbiased estimation of mortality effects specifically related to infection. Additionally, linking prospectively-collected data at patient enrolment with retrospectively-collected data from the electronic health record allowed us to accurately apply criteria for each type of infection in all included patients.

Our study has limitations. First, our observations are derived retrospectively from a single tertiary care referral centre. Our results may therefore be susceptible to selection bias due to severity of disease at presentation. Second, most the patients self-identified as white, leaving us with very limited power to determine whether associations between male sex, infections, and mortality are preserved across other relevant races and ethnicities. Finally, our data are

derived from a long recruitment period, with likely baseline changes in ICH management over the time. We controlled for recruitment epoch during our analyses, but unmeasured time-dependent confounds could still exist.

Conclusion

Pneumonia and other infection are common in ICH patients. Sex based differences seem to affect types and rate of infection complications, and subsequently drive differences in the 90-day mortality. Further investigation is needed to confirm our results, but sex-specific interventions to reduce infectious complications may be one strategy to attenuate ICH-related mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of funding

This study was supported by the following awards from the NINDS: K23NS086873, R01NS059727, R01AG26484, P50NS061343

None of the funding entities had any involvement in study design; data collection, analysis, and interpretation; writing of the manuscript; or decision to submit the study for publication.

References

1. van Asch CJJ, Luitse MJA, Rinkel GE, van der Tweel I, Algra A, Klijn CJM. Incidence, case fatality, and functional outcome of intracerebral haemorrhage overtime, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *LANCET Neurol.* 2010; 9:167–76. [PubMed: 20056489]
2. Feigin VL, Lawes CMM, Bennett DA, Barker-Collo SL, Parag V. Review Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol.* 2009; 8:355–69. [PubMed: 19233729]
3. Balami JS, Buchan AM. Complications of intracerebral haemorrhage. *Lancet Neurol.* 2012;101–18. [PubMed: 22172625]
4. Koennecke H-C, Belz W, Berfelde D, Endres M, Fitzek S, Hamilton F, et al. Factors influencing in-hospital mortality and morbidity in patients treated on a stroke unit. *Neurology [Internet].* 2011; 77:965–72. Available from: <http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2011-23180-011&site=ehost-live%5Cnhans-christian.koennecke@vivantes.de>.
5. Rumbach L, Sablot D, Berger E, Tatu L, Vuillier F, Moulin T. Incidence and prognostic significance of fever following intracerebral hemorrhage. *Neurology [Internet].* 2000; 54:350–4. Available from: <http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=10668695&retmode=ref&cmd=prlinks%5Cnpapers2://publication/uuid/C8F705C5-181C-4891-AE81-9885583AE746>.
6. Davenport RJ, Dennis MS, Wellwood I, Warlow CP. Complications after acute stroke. *Stroke.* 1996; 27:415–20. [PubMed: 8610305]
7. Ingeman A, Andersen G, Hundborg HH, Svendsen ML, Johnsen SP. Processes of care and medical complications in patients with stroke. *Stroke.* 2011; 42:167–72. [PubMed: 21148436]
8. Rocco A, Pasquini M, Cecconi E, Sirimarco G, Ricciardi MC, Vicenzini E, et al. Monitoring after the acute stage of stroke: A prospective study. *Stroke.* 2007; 38:1225–8. [PubMed: 17322080]

9. Kimura K, Minematsu K, Kazui S, Yamaguchi T. Mortality and cause of death after hospital discharge in 10,981 patients with ischemic stroke and transient ischemic attack. *Cerebrovasc Dis* [Internet]. 2005; 19:171–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15644630>.
10. Gokhale S, Caplan LR, James ML. Sex differences in incidence, pathophysiology, and outcome of primary intracerebral hemorrhage. *Stroke*. 2015; 46:886–92. [PubMed: 25657181]
11. Marini, S., Morotti, A., Ayres, AM., Crawford, K., Kourkoulis, CE., Lena, UK., et al. *J Neurol Sci* [Internet]. Vol. 379. Elsevier; 2017. Sex differences in intracerebral hemorrhage expansion and mortality; p. 112–6. Available from: <http://dx.doi.org/10.1016/j.jns.2017.05.057>
12. Aslanyan S, Weir CJ, Diener HC, Kaste M, Lees KR. Pneumonia and urinary tract infection after acute ischaemic stroke: A tertiary analysis of the GAIN International trial. *Eur J Neurol*. 2004;49–53. [PubMed: 14692888]
13. Angele MK, Ayala A, Cioffi WG, Bland KI, Chaudry IH. Testosterone: the culprit for producing splenocyte immune depression after trauma hemorrhage. *Am J Physiol* [Internet]. 1998; 274:C1530–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9696695>.
14. Falcone GJ, Biffi A, Brouwers HB, Anderson CD, Battey TWK, Ayres AM, et al. Predictors of hematoma volume in deep and lobar supratentorial intracerebral hemorrhage. *JAMA Neurol* [Internet]. 2013; 70:988–94. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3808840&tool=pmcentrez&rendertype=abstract>.
15. Lawton MP, Brody EM. Assessment of Older People: Self-Maintaining and Instrumental Activities of Daily Living. *Gerontologist* [Internet]. 1969; 9:179–86. Available from: http://gerontologist.oxfordjournals.org/cgi/doi/10.1093/geront/9.3_Part_1.179.
16. Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity [Internet]. [cited 2016 Nov 19]. Available from: https://www.whitehouse.gov/sites/default/files/omb/assets/information_and_regulatory_affairs/re_app-a-update.pdf
17. Smith CJ, Kishore AK, Vail A, Chamorro A, Garau J, Hopkins SJ, et al. Diagnosis of Stroke-Associated Pneumonia: Recommendations From the Pneumonia in Stroke Consensus Group. *Stroke*. 2015; 46:2335–40. [PubMed: 26111886]
18. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. *Clin Infect Dis* [Internet]. 2004; 38:1150–8. Available from: <http://cid.oxfordjournals.org/content/38/8/1150.full>.
19. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Jama* [Internet]. 2016; 315:801–10. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26903338>.
20. Lord AS, Langefeld CD, Sekar P, Moomaw CJ, Badjatia N, Vashkevich A, et al. Infection after intracerebral hemorrhage: Risk factors and association with outcomes in the ethnic/racial variations of intracerebral hemorrhage study. *Stroke*. 2014; 45:3535–42. [PubMed: 25316275]
21. Murthy SB, Moradiya Y, Shah J, Merkler AE, Mangat HS, Iadacola C, et al. Nosocomial Infections and Outcomes after Intracerebral Hemorrhage: A Population-Based Study. *Neurocrit Care*. 2016; 25:178–84. [PubMed: 27350549]
22. Katzan IL, Cebul RD, Husak SH, Dawson NV, Baker DW. The effect of pneumonia on mortality among patients hospitalized for acute stroke. *Neurology* [Internet]. 2003; 60:620–5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12601102>.
23. Kwon HM, Jeong SW, Lee SH, Yoon BW. The pneumonia score: A simple grading scale for prediction of pneumonia after acute stroke. *Am J Infect Control*. 2006; 34:64–8. [PubMed: 16490608]
24. Kammergaard LP, Jørgensen HS, Reith J, Nakayama H, Houth JG, Weber UJ, et al. Early infection and prognosis after acute stroke: The Copenhagen Stroke Study. *J Stroke Cerebrovasc Dis*. 2001; 10:217–21. [PubMed: 17903827]
25. Ji R, Shen H, Pan Y, Du W, Wang P, Liu G, et al. Risk score to predict hospital-acquired pneumonia after spontaneous intracerebral hemorrhage. *Stroke*. 2014; 45:2620–8. [PubMed: 25028448]
26. Boehme AK, Hays AN, Kicielinski KP, Arora K, Kapoor N, Lysterly MJ, et al. Systemic Inflammatory Response Syndrome and Outcomes in Intracerebral Hemorrhage. *Neurocrit Care*. 2016; 25:133–40. [PubMed: 26920909]

27. Meisel C, Schwab JM, Prass K, Meisel A, Dirnagl U. Central nervous system injury-induced immune deficiency syndrome. *Nat Rev Neurosci*. 2005; 6:775–86. [PubMed: 16163382]
28. Muenchhoff M, Goulder PJR. Sex differences in pediatric infectious diseases. *J Infect Dis* [Internet]. 2014; 209(Suppl):S120–6. Available from: http://jid.oxfordjournals.org/content/209/suppl_3/S120.short.
29. Fish EN. The X-files in immunity: sex-based differences predispose immune responses. *Nat Rev Immunol* [Internet]. 2008; 8:737–44. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18728636><http://www.nature.com/nri/journal/v8/n9/pdf/nri2394.pdf>.
30. Klein SL. The effects of hormones on sex differences in infection: From genes to behavior. *Neurosci Biobehav Rev*. 2000; 24:627–38. [PubMed: 10940438]
31. Ayala C, Croft JB, Greenlund KJ, Keenan NL, Donehoo RS, Malarcher AM, et al. Sex differences in US mortality rates for stroke and stroke subtypes by race/ethnicity and age, 1995–1998. *Stroke* [Internet]. 2002; 33:1197–201. Available from: <http://stroke.ahajournals.org/cgi/doi/10.1161/01.STR.0000015028.52771.D1><http://www.ncbi.nlm.nih.gov/pubmed/11988590>.
32. Zia E, Engström G, Svensson PJ, Norrving B, Pessah-Rasmussen H. Three-year survival and stroke recurrence rates in patients with primary intracerebral hemorrhage. *Stroke* [Internet]. 2009; 40:3567–73. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19729603>.
33. Sheikh K, Bullock CM. Effect of measurement on sex difference in stroke mortality. *Stroke*. 2007; 38:1085–7. [PubMed: 17255545]

Table 1

clinical characteristic of the studied cohort and the differences between sexes.

	Female (933)	Male (1071)	p
Age (median, IQR)	78(68–84)	72(62–80)	0.001
Race, n (%)			0.108
White	809(86.7)	901(84.0)	
Black	51(5.5)	62(5.8)	
Asian	19(5.3)	60(5.6)	
other/unknown	24(2.6)	49(4.6)	
Hispanics/Latinos, n (%)	715(95.5)	782(92.1)	0.007
Hypertension, n (%)	708(76.1)	864(80.9)	0.010
Diabetes, n (%)	155(16.6)	274(25.6)	<0.001
Warfarin, n (%)	186(20.0)	258(24.1)	0.031
Alcohol, n (%)	73(10.3)	231(28.4)	<0.001
Smoking, n (%)	319(43.8)	543(63.3)	<0.001
Coronary artery disease, n (%)	149(16.0)	285(26.7)	<0.001
Intubation, n (%)	293(31.4)	391(36.5)	0.018
Surgery, n (%)	60(6.4)	69(6.4)	1.0
ICH Location, n (%)			<0.001
lobar	433(46.4)	393(36.7)	
deep	398(42.7)	558(52.1)	
infratentorial	102(10.9)	121(11.3)	
IVH, n (%)	459(49.2)	556(51.9)	0.244
Expansion, n (%)	78/617(12.6)	143/751(19.0)	<0.001
Mortality 90 days, n (%)	340(36.4)	407(38.0)	0.488
Pneumonia, n (%)	145(15.5)	235(21.9)	<0.001
Sepsis, n (%)	15(1.6)	36(3.4)	0.009
Urinary tract infection, n (%)	186(19.9)	125(11.7)	<0.001
Prior Dependence, n (%)	146/746(19.5)	124/871 (14.2)	0.008
Limitation of care, n (%)	322(39.2)	348(35.9)	0.156
GCS (median, IQR)	14(8–15)	14(7–15)	0.733
Length of stay(median, IQR)	3(3–11)	6(3–12)	0.576
ICH volume*	1.2(0.7–1.7)	1.3 (0.8–1.7)	0.341

Table 2

logistic regression of sex (male excess) and the three infective complications

	OR (CI 95%) and p value		
Model 1	Pneumonia	UTI	Sepsis
	1.37 (1.08–1.74), p=0.011	0.59 (0.46–0.77), p<0.001	2.31 (1.20–4.44), p<0.012
Model 2	1.53 (1.07–2.19), p=0.021	0.60 (0.42–0.88) p=0.008	1.74 (0.68–4.47), p=0.251

Model 1

(variables entered in the model: ICH location, GCS, IVH, age, ICH volume^{*}, intubation)

Model 2

(Variables entered in the model: model 1 + HTN, DM, CAD, alcohol, smoking, warfarin, prior dependence, ethnicity, expansion)

ICH: intracerebral haemorrhage; GCS: Glasgow coma scale; IVH: intraventricular haemorrhage; DM: diabetes mellitus; CAD: coronary artery disease; HTN: hypertension, UTI: urinary tract infection.

Model2 is based on patients with follow-up NCCT data available (n 1368)

^{*} ICH volume is log10 transformed

Table 3

logistic regression of infection and sex (male excess) on mortality at 90 days

		OR (CI 95%)	p value
Model 3	infection (pneumonia or sepsis)	1.56 (1.11–1.85)	0.011
	Sex	1.40 (1.07–1.85)	0.015
Model 4	infection (pneumonia or sepsis)	1.61 (1.13–2.29)	0.008
	Sex	1.38 (1.05–1.83)	0.023

Variables entered in model 3: ICH location, GCS, IVH, age, ICH volume*, length of stay

Variables entered in model 4: model 3 + intubation, surgery, UTI

ICH: intracerebral haemorrhage; GCS: Glasgow coma scale; IVH: intraventricular haemorrhage; DM: diabetes mellitus; CAD: coronary artery disease; HTN: hypertension. *ICH volume is log10 transformed