Selling vs Non-Selling Clinical Research Manuscripts

Grumpy Reviewer’s Critical View

Juha E Jääskeläinen
Professor / UEF Neurosurgery
Chairman / Neurosurgery / KUH NeuroCenter
Member of 3 Research Grant Boards
Chairman of Clinical Cancer Research Board / Cancer Society of Finland
Editorial Board / Acta Neurochirurgica (>480)
Evidence Based Clinical Medicine – Käypä hoito
Best Evidence Clinical Medicine

Class I (A) evidence

- Meta-Analysis
- Systematic Review
- Randomized Controlled Trial
- Cohort studies
- Case Control studies
- Case Series/Case Reports
- Animal research/Laboratory studies
Clinical research data are published

- to be verified by research community
  - by peer reviewal
  - by anonymous reviewers of medical journals

- to add to the big picture of clinical medicine

- to become PhD / Post Doc / Docent / Professor

- publish or perish …
  - publish = get research money
  - high impact factor of journal = more money
  - high H-index of researcher = more money
from manuscript to published article

most clinical research manuscripts are sh..
many published clinical research articles are also sh..

avoid open access predatory journals with no peer reviewal!
Long-term Excess Mortality of 244 Familial and 1502 Sporadic One-Year Survivors of Aneurysmal Subarachnoid Hemorrhage Compared With a Matched Eastern Finnish Catchment Population

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Mikael von und zu Fraunberg, MD, PhD*
Timo Koivistoo, MD, PhD*
Antti Ronkainen, MD, PhD*
Jaakko Rinne, MD, PhD*
Risto Sankila, MD, PhD†
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Results: 5

1. Increased relative risk of lung cancer in 2,904 patients with saccular intracranial aneurysm and in eastern Finland.
   PMID: 22343186 [PubMed - indexed for MEDLINE]
   Related citations

2. Long-term excess mortality of 244 familial and 1502 sporadic one-year survivors of subarachnoid hemorrhage compared with a matched Eastern Finnish catchment population.
   Huttunen T, von und Zu Fraunberg M, Koivistoo T, Ronkainen A, Rinne J, Sankila R, Jääskeläinen JE.
   PMID: 21099703 [PubMed - indexed for MEDLINE]
   Related citations

3. Saccular intracranial aneurysm disease; distribution of site, size, and age suggests etiologies for aneurysm formation and rupture in 316 familial and 1454 sporadic patients.
• read read read / listen / think / talk / write English
• read carefully previous articles and reviews from your area
• adopt words / phrases / sentences …
  ▪ Thesaurus
  ▪ phrase dictionaries
• spell correctly
  ▪ Medical Dictionary
• avoid grammatical errors
Lousy English Finnglish Maitolaituriglish Piglish …

Dull prose vs Ilta-Sanomat / Iltalehti ?
Common errors in typography

- define the question
- gather Information ja resources
- form the hypotheses
- perform experiment and collect data
- analyze data
- interpret data and draw conclusions
  - reject /accept the hypotheses
  - form new hypotheses
- publish the results.
Methods to point out your message in texts

1. (a)  nnnnnnnn

2. (b)  nnnnnnnn

1. (a)  nnnnnnn

2. (b)  nnnnnnnn
Harvey Cushing 1869-1939
Father of neurosurgery
1926 Pulitzer Prize for Biography of Sir William Osler (1.371 pages)

* wrote over 10.000 words per day

’The pen is more difficult than the scalpel’
Structure of manuscript

- Title
- Authors
- Affiliations of authors
- Contact person
- Short title
- Key words
- Disclosures
- Grants & Acknowledgements
- Abstract
- Introduction
- Materials and Methods
- Results
- Discussion
- Conclusions
- References
- Tables
- Figures + Figure Legends

Guidelines to Preparation of Manuscripts

Please prepare your manuscript in accordance with the following instructions and send it as printed copy together with an electronic file saved on an floppy disk (3.5 inches) or CD-ROM (ISO9660) to:

PNS2006@MEDACAD.ORG

Authors must guarantee that their paper has not been published in another journal nor will be submitted for publication in another journal.

Manuscripts must not exceed 6 typewritten double spaced pages (max. 30 lines), including summaries, references, tables and figure legends. All pages should be numbered consecutively. Figures and illustrations must not exceed 3 per manuscript.

Manuscripts will be reviewed by experienced colleagues who can do minor revisions and small corrections. Final acceptance of manuscripts is subject to the decision of the Editors. Please be informed that a manuscript may be rejected if several of the above mentioned criteria are not met or if their content is too far outside the scope of the volume.
How others can find Your article in PubMed and what can they easily read from it?

- Title words
- Authors’ surnames and initials
- Affiliations of authors
- Contact person
- Short title
- Key words
- Disclosures
- Grants & Acknowledgements

Abstract words

BACKGROUND: Saccular intracranial aneurysms (sIAs) develop in 2% of the population. Rupture of the sIA wall causes almost all cases of aneurysmal subarachnoid hemorrhage (aSAH).

OBJECTIVE: We analyzed the long-term excess mortality of 244 familial and 1502 sporadic 1-year survivors of aSAH from sIA compared with a matched Eastern Finnish catchment population.

METHODS: The Kuopio Neurosurgery Database contains 1746 one-year survivors of aSAH (1980-2007) from a defined population. The median follow-up time, until death (n = 494) or the end of 2008, was 12 years. Relative survival ratios were calculated compared with the matched (sex, age, calendar time) catchment population. Relative excess risk of death (RER) was estimated for variables known on admission for aSAH as well as Glasgow Outcome Scale score at 12 months.

RESULTS: There was 12% excess mortality at 15 years (cumulative relative survival ratio: 0.88; 95% confidence interval: 0.85-0.91). Independent risk factors were male sex (RER: 1.6), age older than 64 years (RER: 2.9), ruptured basilar tip sIA (RER: 4.5), severe hydrocephalus on admission (RER: 3.6), no occlusive therapy (RER: 6.0), and Glasgow Outcome Scale scores of 2, 3, or 4 at 12 months (RER: 23, 4.1, 2.1, respectively), but not familial sIA disease. There were lethal rebleeds from 13 of the 1440 clipped sIAs, 2 of the 265 coiled sIAs, and 2 from the 17 non-occluded sIAs, and 14 new lethal bleeds from other sIAs.

CONCLUSION: The impact of both sporadic and familial aSAH and their sequelae in the central nervous and cardiovascular systems may cause long-term morbidity and mortality. The complex sIA disease may predispose to other vascular events later in life. The causes of the long-term excess mortality are heterogeneous, and more detailed analyses are required.

KEY WORDS: Causes of death, Familial, Long-term excess mortality, Saccular intracranial aneurysm, Sporadic, Subarachnoid hemorrhage
Title is highly important / selling

- does it inspire reviewers?
  - not interesting – another lousy study?

- too long or too short
- does not match the study design
- does not clearly describe the study
- contains abbreviations

- declares the most important result?
  - Diabetes and stroke …
  - Diabetes is a risk factor for stroke …
Long-term Excess Mortality of 244 Familial and 1502 Sporadic One-Year Survivors of Aneurysmal Subarachnoid Hemorrhage Compared With a Matched Eastern Finnish Catchment Population

Long-term Mortality of One-Year Survivors of Aneurysmal Subarachnoid Hemorrhage
List of authors – competent company?

- reviewers (often) know Your research area

- what have the authors published before?
  - H-index?
  - does their expertise cover the study design?
  - missing experts?

- free rider authors? – more liberal now

- MOST IMPORTANT SITES FOR AUTHORS
  - 1. author
    - divided 1. authorship (PhD theses)
  - 2. author
  - last author
    - divided last authorship
Affiliations of authors – known groups / institutions?

internet address of study group! – www.uef.fi/nph
FinnHealth welcomes you to Finland and to the peak of health tourism to Kuopio!
Structure of manuscript – previously published data

- Title
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- Affiliations of authors
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- Figures + Figure Legends
Search carefully for Previous Literature – essential / relevant / best / latest for Introduction and Discussion – what new / improved data your study provides?
Materials and Methods – Essential previous literature search words / hits? / selection of relevant articles

**PubMed search**

A PubMed search for articles on SAH risk and DM was made from 2001 through April 2012 with the following keyword(s): subarachnoid hem(a)orrhage; stroke; diabetes; case-control. Bibliographies of the retrieved articles were examined for further relevant publications. Cross-checking was continued until no further publications in English were found. Only the studies that reported the number of patients exposed to DM, allowing recalculation of the associated SAH risk, were included. Studies restricted to
Table 1. Independent Risk Factors for Poor Outcome After Aneurysmal Subarachnoid Hemorrhage

<table>
<thead>
<tr>
<th>Series</th>
<th>Number of Patients</th>
<th>Occlusive Therapy</th>
<th>Measure and Time Point for Poor Outcome</th>
<th>Independent Risk Factors for Poor Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molyneux et al., 2005, ISAT Study (18)</td>
<td>2128</td>
<td>1055</td>
<td>1063</td>
<td>Age, WFNS, aneurysm location</td>
</tr>
<tr>
<td>Wartenberg et al., 2006 (30)</td>
<td>513</td>
<td>310</td>
<td>95</td>
<td>Fever, anemia, hyperglycemia (after adjustment for age, aneurysm size &gt; 10 mm, H&amp;H grade, rebleeding, infarct owing to vasospasm)</td>
</tr>
<tr>
<td>Rosengart et al., 2007, Tirilazad Trial (26)</td>
<td>3567</td>
<td>3567</td>
<td>0</td>
<td>Age, WFNS grade, SAH thickness on initial CT, posterior circulation saccular IA, large saccular IA size, IVH, ICH, high systolic blood pressure on admission, history of hypertension, prior SAH, myocardial infarction and liver disease, temperature on day 8 ≥ 38°C, anticonvulsant use, no therapeutic hypervolemic or induced hypertension, symptomatic vasospasm, cerebral infarction</td>
</tr>
<tr>
<td>Frontera et al., 2008 (6)</td>
<td>573</td>
<td>NA</td>
<td>NA</td>
<td>Mortality at 3 months</td>
</tr>
<tr>
<td>Stentrup et al., 2007 (27)</td>
<td>545</td>
<td>NA</td>
<td>NA</td>
<td>Bloodstream infection (after control for age, H&amp;H grade, and aneurysm size)</td>
</tr>
</tbody>
</table>
A fixed effects Mantel-Haenszel method was used in the review of the literature to estimate pooled odds ratios and confidence intervals. The appropriateness of fixed effects model was evaluated by the Cochran Q test, which indicated no heterogeneity of study effects (Q=3; df=7; p=0.7).
Saccular intracranial aneurysms (sIAs) develop in 2% of the population. Rupture of the sIA wall causes almost all cases of aneurysmal subarachnoid hemorrhage (aSAH).

Acute aSAH is a complex and critical systemic condition. Survivors of the primary bleed require

REFERENCES

Introduction – should start a detective story

- who dunnit and how and why?

- lousy Introduction does NOT
  - read well
  - define the plot / study focus / disease studied …
  - define what was published before
  - describe the purpose and objective of the study
  - describe the importance and originality of the study
Increased relative risk of lung cancer in 2 904 patients with saccular intracranial aneurysm disease in Eastern Finland

Terhi Huttunen et al.

Introduction

Some 2% of population develops during life saccular intracranial aneurysms (sIAs) at the branching sites of major intracranial extracerebral arteries.1 Rupture of the sIA wall causes almost all cases of aneurysmal subarachnoid hemorrhage (aSAH),2 but most sIAs do not rupture as the annual incidence of SAH is about 6 per 100,000.3 Acute aSAH is a critical condition, a devastating form of stroke that affects the working age population.2,4,5 The sIA disease is a complex trait. Known risk factors include age, female sex, hypertension, smoking, and excess drinking,6 and at least 10% of aSAH patients have a family history.7-9

A large multinational genomewide association study of intracranial aneurysm identified five susceptibility loci,19 among them 9p21.3,20 close to the CDKN2A and CDKN2B genes that are involved in many types of cancer.21 Furthermore, smoking is a common risk factor for both the sIA disease and cancers of the upper digestive tract (oral cavity, nasal cavity and sinuses, pharynx, larynx, oesophagus), pancreas, stomach, liver, lower urinary tract (renal pelvis and bladder), kidney and uterine cervix.18 Population-based studies of the long-term outcome of sIA patients are few10-15, and it has not been established whether the sporadic or familial sIA disease carriers are predisposed also to other phenotypes, including cancer.14-16

Neurosurgery of Kuopio University Hospital serves solely an Eastern Finnish catchment population, and Kuopio sIA Database (www.uef.fi/crc/ns) contains all sIA patients admitted since 1980 (Ref Huttunen 2010 and 2011). In the present study, we analyze the long-term incidence of cancer in 2904 sIA patients from 1980 to 2007 as compared to the KUH catchment population.
lets have a break
Structure of manuscript

- Title
- Authors
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- Abstract
- Introduction
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- Results
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- Tables
- Figures + Figure Legends
Materials & Methods – contents

- **Definitions of Study Cohort**
  - source of study cohort – *population-based*?
  - exclusion / inclusion criteria
  - Flow Chart of Study Cohort

- Methods of investigations
  - histology / biochemistry / imaging …

- Gathering of follow up / research data

- Definitions of research variables
  - Table 2. Study Cohort with variables

- Literature review

- Statistical methods

- Ethical board approvals
M & M – description of basic study cohort / registry population-based? – reduction of selection bias!

MATERIALS AND METHODS

Kuopio NPH Registry

The Neurosurgery Department at the Kuopio University Hospital (KUH) has solely served the defined catchment population in Eastern Finland. The Kuopio NPH Registry (www.uef.fi/nph) consists of 468 consecutive patients evaluated for suspected NPH clinically and neuroradiologically and by 24-hour ICP monitoring between 1991 and 2006. The primary examination was performed by a neurologist. Patients with 1 to 3 symptoms potentially related to NPH (impaired cognition, gait, or urinary continence), together with enlarged brain ventricles disproportionate to the size of sulci of cerebral convexities (Evan index > .30)\textsuperscript{26,27} in computed tomography or magnetic resonance imaging were referred for further neurosurgical examinations.
Study Population of 1657 Patients with Aneurysmal Subarachnoid Hemorrhage
The inclusion criteria were as follows:

1. Resident of KUH catchment area at the time of primary aneurysmal SAH between January 1, 1980, and December 31, 2007

2. Admission alive to KUH within 24 hours from the start of acute aneurysmal SAH, verified by computed tomography, spinal tap, or autopsy

3. Verification of saccular IA by angiography or autopsy

4. Rupture of a saccular IA
193 shunted for idiopathic NPH (iNPH) after intraventricular pressure monitoring and frontal cortical biopsy

157 responsive to shunt

146 shunt responsive iNPH patients
- 100 Aβ- HP
- 40 Aβ+ HP
- 6 Aβ+ HP

11 with inadequate follow-up data

79 no dementia at the end of follow-up

67 (46%) had dementia at the end of follow-up
- 41 Aβ- HP
- 24 Aβ+ HP
- 2 Aβ+ HP
Table 2. Characteristics of the 146 Patients With Initially Shunt-Responsive iNPH

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dementia (n = 67)</th>
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<td>17/23</td>
<td>14/25</td>
<td>.66</td>
</tr>
<tr>
<td>Age at onset of iNPH symptoms, y</td>
<td>70.6 ± 6.2</td>
<td>65.8 ± 9.4</td>
<td>68.1 ± 6.0</td>
<td>.007</td>
</tr>
<tr>
<td>Duration of symptoms before shunt</td>
<td>2.2 ± 2.6</td>
<td>3.3 ± 4.1</td>
<td>2.1 ± 3.6</td>
<td>.19</td>
</tr>
<tr>
<td>Age at shunt for iNPH, y</td>
<td>72.6 ± 5.9</td>
<td>69.2 ± 8.3</td>
<td>69.6 ± 6.8</td>
<td>.019</td>
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<tr>
<td>Symptoms at iNPH diagnosis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory deficit</td>
<td>66</td>
<td>36</td>
<td>26</td>
<td>&lt;.001</td>
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<td>Memory deficit as the first symptom</td>
<td>23 (34%)</td>
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<tr>
<td>Urinary incontinence</td>
<td>46</td>
<td>26</td>
<td>24</td>
<td>.73</td>
</tr>
<tr>
<td>MMSE score at iNPH diagnosis</td>
<td>20.6 ± 4.3</td>
<td>24.3 ± 3.3</td>
<td>25.5 ± 3.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Follow-up time, y</td>
<td>6.3 ± 3.5</td>
<td>5.7 ± 3.5</td>
<td>5.3 ± 3.8</td>
<td>.35</td>
</tr>
<tr>
<td>Deceased</td>
<td>42 (63%)</td>
<td>14 (35%)</td>
<td>15 (38%)</td>
<td>.008</td>
</tr>
</tbody>
</table>
Cognitive and Radiological Evaluation

**Immunohistochemical staining and histological evaluation of brain biopsy**

**Functional Analysis of Differentially Expressed Genes**

An overrepresentation analysis was performed for the upregulated and downregulated gene lists separately. For this enrichment analysis of gene ontology terms and Kyoto Encyclopedia of Genes and Genomes pathways, GOstats R package version 2.1 \(^{32}\) and database for annotation, visualization, and integrated discovery (DAVID) \(^{33,34}\) bioinformatics resource was used. All of the distinct 17,788 genes in the array were used as a background gene set. To avoid reporting redundant ontologies, a conditional gene ontology analysis strategy was used that reports only the most specific gene ontology terms in the hierarchy that are statistically overrepresented in the differentially expressed gene sets. \(^{32}\) The Benjamini and Hochberg \(^{31}\) false discovery rate was used to adjust for multiple testing, and adjusted values of \(P < .05\) were considered significant. The similarity of differentially expressed gene sets to genes...
M & M – gathering of clinical follow up data

- is follow up data required?
  - complications / recurrences / mortality / …

- you sell with MINIMAL SELECTION BIAS!

- start of follow up time (date)
  - date of operation / diagnosis / imaging / …

- end of follow up time (date)
  - death or last contact date

- methods of follow up
  - scheduled visits / phone interviews …
  - data from other sources
    - hospitals
    - national clinical data registries …
Variables

The variables used in the following (table 1):

(1) sIA disease carrier (general sIA patient);
(2) sIA disease (location and fistula or more sIAs);
(3) condition on admission (time peak grade; intracerebral hemorrhage; acute hydrocephalus);
(4) occlusive therapy of ruptured aSAH; admission to KUH sIA.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>1,014 (55)</td>
</tr>
<tr>
<td>Males</td>
<td>848 (45)</td>
</tr>
<tr>
<td>Member of sIA family</td>
<td>266 (14)</td>
</tr>
<tr>
<td>Multiple sIAs (≤2)</td>
<td>487 (26)</td>
</tr>
<tr>
<td>Age at aSAH</td>
<td></td>
</tr>
<tr>
<td>5–44 years</td>
<td>597 (32)</td>
</tr>
<tr>
<td>45–54 years</td>
<td>504 (27)</td>
</tr>
<tr>
<td>55–64 years</td>
<td>433 (23)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>328 (18)</td>
</tr>
<tr>
<td>Referring health care unit</td>
<td></td>
</tr>
<tr>
<td>KUH</td>
<td>444 (24)</td>
</tr>
<tr>
<td>Central hospitals at KUH area (n = 4)</td>
<td>1,083 (58)</td>
</tr>
<tr>
<td>Other</td>
<td>335 (18)</td>
</tr>
<tr>
<td>Period of aSAH</td>
<td></td>
</tr>
<tr>
<td>1980–1989</td>
<td>580 (31)</td>
</tr>
<tr>
<td>1990–1999</td>
<td>739 (40)</td>
</tr>
<tr>
<td>2000–2007</td>
<td>543 (29)</td>
</tr>
<tr>
<td>Time from aSAH to admission to KUH</td>
<td></td>
</tr>
<tr>
<td>≤24 h</td>
<td>1,171 (70)</td>
</tr>
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<td>24–48 h</td>
<td>487 (26)</td>
</tr>
<tr>
<td>49–72 h</td>
<td>204 (11)</td>
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Statistical methods

- **multiple imputations for missing data**
- distributions of variables
- univariate analyses
- survival / mortality analyses
- multivariate analyses
- recursive partitioning analysis
- usually SPSS …

**Statistical Analysis**

Continuous variables were expressed in medians. Groups were compared using Mann-Whitney U test or $\chi^2$ test as appropriate. Kaplan-Meier mortality curves were displayed with a logarithmic time scale (x-axis) to visualize better the 12-month mortality after the high acute mortality, and the log-rank test was used to compare the mortality rates. All variables with $P < 0.2$ in the **univariate analysis** were included into the **multiple logistic regression analysis** of mortality. The logistic regression analysis was used to identify the factors with independent and significant impact on the mortality. $P$ values of $\leq 0.05$ were considered significant. **SPSS 17.0** statistical software (SPSS, Inc, Chicago, Illinois, USA) was used.
Research ethical / institutional approvals

- any research concerning patients or their samples requires Ethical Board approvals !!!

**Ethical Issues**

The study was approved by the KUH Research Ethical Committee, the Finnish National Supervisory Authority for Welfare and Health, and the Finnish Ministry of Social Affairs and Health.
Structure of manuscript – Results / Tables / Figures

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Dont muddle Your Results …

- with information that belongs to Materials & Methods

- with information that is already shown in Tables or Figures
### Table 1. Characteristics of the 146 Patients With Initially Shunt-Responsive iNPH$^{a,b}$

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<td>.008</td>
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Figure 1. (A) Cumulative mortality rate of 1657 patients alive on admission within 24 hours after aneurysmal subarachnoid hemorrhage (aSAH) from ruptured saccular intracranial aneurysm (IA). The x-axis is logarithmic to visualize early mortality better. The mortality rates at 3 days, 30 days, and 365 days are given in italics. (B) Numbers of deaths related to aSAH from ruptured saccular IA and deaths from other causes are presented in 3-month time periods since admission for acute aSAH.
Subtitles / paragraphs of Results

- distribution of key/end variables
  - diagnosis / complications / death …
- how end variables associate to other variables
  - univariate analyses
  - multivariate analyses
    - independent risk factors for end variables
      - age / sex / diagnosis / therapy …
    - confounding factors
    - partitioning tree for reader?
- cumulative event analyses
  - survival / complication / recurrence rates
At the end of follow-up, 67 (46%) of the 146 shunt-responsive iNPH patients had clinical dementia, 40 (27%) were observed to have mild cognitive impairment, and only 39 (27%) were cognitively unaffected (Table 1). Their median follow-up times were 5.3, 4.6, and 4.4 years, respectively. The iNPH patients with dementia were older than those with mild cognitive decline at the onset of the symptoms ($P = .006$) and at the time of shunting ($P = .038$). They had more frequent cognitive symptoms ($P = .006$) and were more severely affected by cognitive impairment (Mini-Mental State Examination score; $P < .001$) at the time of the shunt surgery. In multivariate analysis (Table 2), the risk of subsequent dementia in the 146 shunt-responsive iNPH patients increased significantly with age ($P = .001$, odds ratio [OR] 1.17 years, confidence interval [CI] 1.07-1.3) and memory deficit as the first symptom ($P = .012$, OR 18.3 years, CI 1.9-175) at the time of shunt as well as with the length of follow-up time ($P = .027$, OR 1.20 years, CI 1.02-1.4).
Learn to perform your own SPSS statistics!
distributions / cumulative rates / univariate vs multivariate

<table>
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<th>Lung cancer/total</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
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<td>sIA patients</td>
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<td>Females</td>
<td>9/1,220</td>
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<td>Males</td>
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<td>Familial</td>
<td>4/307</td>
<td>0.9</td>
<td>0.3–2.7</td>
<td>0.87</td>
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<td>Age at aSAH</td>
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<td>≤45 years</td>
<td>5/777</td>
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<td>46–59 years</td>
<td>16/855</td>
<td>1.5</td>
<td>0.5–4.7</td>
<td>0.54</td>
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Table 3. Characteristics of aSAH patients with lung cancer, with odds ratios (ORs) from logistic regression analysis.
Partitioning Tree from Multivariate Analysis – … risk of depression after subarachnoid hemorrhage

Patients
with ≥2 purchases of ATD
after sIA-SAH
26% (185 / 701)

GOS II-IV
moderate or worse recovery
46% (92 / 200)

GOS V
good recovery
19% (93 / 501)

No epilepsy
after sIA-SAH
16% (73 / 448)

Epilepsy
after sIA-SAH
38% (20 / 53)
Figure 2. Cumulative mortality rate of 1657 patients alive on admission within 24 hours after aneurysmal subarachnoid hemorrhage (SAH). The x-axis is logarithmic to visualize early mortality better. The mortality rates are stratified by age Hunt & Hess (H&H) scale at aneurysmal SAH.
Figures must be large enough to be informative
Improve / cut / trim images – e.g. PhotoShop tools
Figures must be in colour when necessary – e.g. histology / MRI spectroscopy / PET though journals often charge for colour images
Identification data in patient’s PACS images must be absent in Figures.
Patients’s face can be published only with written permission.
Structure of manuscript – Discussion + Conclusion

- Title
- Authors
- Affiliations of authors
- Contact person
- Short title
- Key words
- Disclosures
- Grants & Acknowledgements
- Abstract
- Introduction
- Materials and Methods
- Results
- Discussion
- Conclusions
- References
- Tables
- Figures + Figure Legends
Subtitles / paragraphs for Discussion

- Essential findings in the present study
- Essential findings in the present study as compared to essential findings in relevant previous literature
- Strengths / originality of the present study
- Limitations / weaknesses of the present study
- Significance of essential findings in the present study
- Suggested further research
Main Entry: bad
Part of Speech: adjective
Definition: poor quality
Synonyms: abominable, amiss, atrocious, awful, bad news, beastly, blah*, bottom out, bummer, careless, cheap, cheesy*, crappy*, cruddy, crummy, defective, deficient, diddly, dissatisfactory, downer, dreadful, erroneous, fallacious, faulty, garbage, godawful, grody, gross*, grungy, icky, imperfect, inadequate, incorrect, inferior, junky, lousy*, not good, off, poor, raunchy*, rough, sad, slipshod, stinking, substandard, synthetic, the pits, unacceptable, unsatisfactory
Notes: badly is an adverb to describe an activity; bad is an adjective to describe a condition or state
Antonyms: good, honest, reputable, right, upright, virtuous, worthy
Lousy Discussion

- logical flow is lacking
- does not absorb / inspire / entertain
- does not read well

- too expansive / wordy / long
- includes unrelated information

- unreliable
- overstates importance of the study
- omits findings from other studies
- misinterprets data from references
- includes outdated references
**Conclusions reflect clarity of scientific thinking**

**CONCLUSION:** The novel findings were (a) a significant risk of dementia in iNPH initially responsive to cerebrospinal fluid shunt, (b) cognitive impairment most commonly due to iNPH-related a subgroup.

**Conclusion** In presumed NPH patients, \textit{APOE4} associates independently with the presence of Aβ plaques in the frontal cortical biopsy. \textit{APOE4} is not a risk.

The impact of both sporadic and familial aSAHs and their sequelae in the central nervous and cardiovascular systems may cause long-term morbidity and mortality. The complex sIA disease may lead to irreversible causes of morbidity and mortality. For more details...

Smoking is a modifiable risk factor that is important in the prevention of aSAH as well as for further understanding of the pathogenesis of sIA formation and sIA wall rupture. The long-term smoking habits of the carriers of unruptured sIAs as well as survivors of aSAH after the first diagnosis should be elucidated. Their permanent abstinence from smoking should be supported and monitored.
Electronic submission of manuscript to Clinical Medical Journal X – further communication by email

Editorial Office + Chief Editor

manuscript to Reviewers

seems acceptable if revised

Manuscript + 1-6 Reviewers’ statements back to authors for revisions

Your revised manuscript is accepted for publication!
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<th>Current Status</th>
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<th>Date Reviewer Agreed</th>
<th>Date Review Due</th>
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Reviewer’s rating of manuscript

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<td>Relevance of results</td>
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Reviewers often suggest revisions to Authors – answer politely and revise carefully point by point.

Comments to Author:

The authors analyzed their stupendously large series of 24 solitary fibrous tumours of the CNS from 2002-2010 from the Shanghai HuaShan Hospital.

Suggested revisions:
* Materials and methods lacks subtitles.
* The numbers of meningiomas and meningeal hemangiopericytomas operated on in 2002-2010 could be given to get a view of the rarity of SFT.
* Ethics Committee approval for this retrospective study is missing.
* Statistics - various methods such as Kaplan-Meier used should be mentioned - for the 24 cases medians are more appropriate than means.
* Figures - illustrative MRI figures missing - Kaplan-Meier curves for recurrence rate missing.
* The following reference should be included: Vassal F, Manet R, Forest F, Camdessanche JP, Péoc'h M, Nuti C. Solitary fibrous tumors of the central nervous system: report of five cases with unusual clinicopathological and outcome patterns. Acta
Electronic submission of manuscript to Clinical Medical Journal X – further communication by email

Editorial Office + Chief Editor

- unacceptable

manuscript to Reviewers

- seems unacceptable

seems acceptable if revised

- unacceptable

Manuscript + 1-6 Reviewers’ statements back to authors for revisions

Your revised manuscript is accepted for publication!

unacceptable