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Alcohol consumption as a risk factor for poor outcome after aneurysmal subarachnoid haemorrhage

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Abstract

Objective—To evaluate the effect of factors existing before aneurysmal subarachnoid haemorrhage on outcome of haemorrhage.

Design—Prospective follow up study.

Setting—Helsinki University Hospital.

Patients—291 consecutive patients (149 men) aged 15 to 65 years admitted within 96 hours after the bleeding.

Main outcome measures—Potential risk factors (baseline characteristics, health habits, and clinical variables) for poor outcome after haemorrhage (dependent state in the activities of daily living, or death) were studied using multiple logistic regression.

Results—One year after haemorrhage, 179 (62%) patients were independent in the activities of daily living and 28 (10%) dependent; 84 (29%) had died. Risk of poor outcome was predicted, after adjustment for sex and age, by clinical condition at admission according to the Glasgow coma scale ($p<0.0001$); occurrence of rebleeding (relative risk 7.1, 95% confidence interval 2.8 to 18.0, $p<0.0001$) or delayed cerebral ischaemia (10.3, 4.2 to 25.4, $p<0.0001$); surgery on an aneurysm (0.13, 0.05 to 0.35, $p<0.0001$); and heavy consumption of alcohol (4.5, 1.8 to 11.0, $p=0.0014$). Heavy drinking remained a significant risk factor after additional adjustment for hypertension, body mass index, and presence of intracerebral haematoma. Heavy drinkers had a more unfavourable outcome after rebleeding and delayed ischaemia than did others with rebleeding or ischaemia. Those who had salicylates in urine on admission had delayed ischaemia with fixed neurological deficits less commonly than others.

Conclusions—Heavy drinking impairs outcome mainly through severe rebleeding and delayed ischaemia and to a lesser extent through a poor initial condition and presence of intracerebral haematoma.

Introduction

Aneurysmal subarachnoid haemorrhage is a serious disease with high mortality and morbidity. Delayed cerebral ischaemia and rebleeding are the most important causes of death and disability, after the primary bleed.^{1,3} The risk of delayed ischaemia is best predicted by the amount of subarachnoid^{4,6} and intraventricular⁵ blood, as well as by previous hypertension,⁶ irrespective of clinical condition on admission or hydrocephalus. There are no uniformly accepted predictive risk factors for rebleeding except the administration of antifibrinolytic drugs, which reduce this risk.^{4,5} The overall outcome can best be predicted

by the initial clinical condition and the amount of subarachnoid blood as a poor initial condition is associated with mortality due to the primary bleed.^{4,5}

Besides these independent risk factors, which are associated with the severity of haemorrhage, there may also be pre-ictal factors other than hypertension that can impair the outcome. It is not known whether alcohol consumption, smoking, or the use of non-steroidal anti-inflammatory drugs influence outcome. Alcohol consumption, especially heavy drinking, has been shown to increase the risk of all types of stroke,⁷⁻¹¹ while smoking increases the risk of subarachnoid haemorrhage¹²⁻¹⁵ and cerebral infarction.^{10,11,15} Use of non-steroidal anti-inflammatory drugs seems to increase the risk of haemorrhagic stroke.¹⁶ Hence, these factors might also impair outcome after subarachnoid haemorrhage by making patients prone to cerebral ischaemia, rebleeding, or a severe initial bleed. Awareness of factors worsening the outcome could be important in the management of subarachnoid haemorrhage. This prospective study investigated the influence of these factors on the outcome after subarachnoid haemorrhage.

Patients and methods

From January 1985 to September 1986 a total of 291 patients with aneurysmal subarachnoid haemorrhage were admitted to the Helsinki University Hospital. After they had been admitted, I interviewed patients, their family members, and fellow workers, as appropriate, about smoking and alcohol habits, use of medicines, and previous diseases of the patient. Data were obtained solely from the patients themselves in 42 cases and from family members only in 55 cases or fellow workers only in six cases when the patient was in poor condition. In the remaining 188 cases information was obtained from both patients and family members. In about a quarter of these cases either the patient or the family member underestimated or overestimated alcohol intake. Because underestimation is more likely in alcohol intake, the greater amounts reported in these cases were registered.

Alcohol consumption, both recent and long term, was calculated from the amount of alcohol consumed before haemorrhage. Patients with two or more positive answers to the four questions in the CAGE interview were considered to be "CAGE positive," a classification that correlates well with heavy drinking.^{17,18} On admission, blood samples were obtained for measurement of markers of alcohol intake (erythrocyte mean cell volume, γ -glutamyltransferase concentration, and platelet count). Cigarette smoking was categorised as never smoked, former smoker, and current smoker— ≤ 10 , 11-20 >20 cigarettes a day, respectively. Use of

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TABLE 1—Clinical characteristics and outcome in patients with aneurysmal subarachnoid haemorrhage. Values are numbers (percentages)

Characteristic	All patients (n=291)	Patients undergoing surgery (n=204)
Clinical grade (Hunt and Hess ¹⁰):*		
On admission		
I	51 (18)	44 (22)
II	101 (35)	88 (43)
III	77 (26)	56 (27)
IV	32 (11)	13 (6)
V	30 (10)	3 (1)
Before surgery		
I		85 (42)
II		45 (22)
III		63 (31)
IV		6 (3)
V		5 (2)
Clinical grade (Glasgow coma scale ¹⁹) on admission:		
3-6	33 (11)	4 (2)
7-9	15 (5)	4 (2)
10-12	19 (7)	12 (6)
13-14	70 (24)	50 (25)
15	154 (53)	134 (66)
Intracerebral haematoma (≥10 mm diameter):		
No	216 (74)	162 (79)
Yes	75 (26)	42 (21)
Rebleeding		
No	230 (79)	183 (90)
Yes	61 (21)	21 (10)
Delayed cerebral ischaemia†		
No	170 (65)	120 (59)
Reversible deficit	36 (14)	35 (17)
Fixed deficit	54 (21)	47 (23)
Outcome at one year (Glasgow outcome scale ¹⁹):		
Good recovery of minimal disability	150 (52)	136 (67)
Moderate disability	29 (10)	25 (12)
Severe disability	25 (9)	24 (12)
Vegetative state	3 (1)	3 (1)
Dead‡	84 (29)	16 (8)

*Hunt and Hess grades: 1=no symptoms or minimal headache and slight nuchal rigidity; 2=moderate to severe headache, nuchal rigidity, no neurologic deficit except possible cranial nerve palsy; 3=drowsiness, confusion, or mild focal deficit; 4=stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity, and vegetative disturbances; 5=deep coma, decerebrate rigidity, moribund state.

†n=260 in all patients and n=202 in surgical cases; patients who died due to the primary bleed are excluded.

‡Causes of death: 31 died of the primary bleed, 34 of a rebleed, 11 of delayed cerebral ischaemia, 2 of pneumonia, 2 of an operative complication, 2 of trauma, 1 of pulmonary embolus, and 1 of duodenal ulcer.

non-steroidal anti-inflammatory drugs before admission was recorded, and apart from a few exceptions these drugs were not given to patients during the hospital stay. On admission, the patients' urine was also screened qualitatively for salicylates.

Hospital records from other hospitals and general practitioners were reviewed for previous diseases. The body mass index, calculated as weight/(height)² (kg/m²), was used as the index of relative weight. Seventy nine (27%) patients had hypertension (blood pressure readings had repeatedly exceeded 160/95 before haemorrhage or patients were using antihypertensive drugs).

The patient's clinical condition on admission and before operation was graded with the Glasgow coma scale¹⁹ and the Hunt and Hess grading system (see table I).²⁰ Subarachnoid haemorrhage was verified by computed tomography, lumbar puncture, necropsy, or operation, as applicable. Computed tomography was repeated after clinical deterioration, on discharge, and during follow up. In all patients the aneurysmal origin of the haemorrhage was confirmed.

A total of 204 of the 291 patients (70%) were operated on. The median time from haemorrhage (day 0) to surgery was seven days, and 50% of the operations were performed within three to nine days from haemorrhage. Fourteen patients were operated on as an emergency because of a haematoma occupying intracerebral space.

Neurological deterioration was monitored throughout the hospital stay. Causes of a poor clinical condition and outcome were determined by repeated computed tomography scans, a routine postoperative angiogram, necropsy, or laboratory investigations. Outcome at one year was assessed with the Glasgow outcome scale.²¹

The data were analysed by the biomedical data package statistical programs.²² Fisher's exact two tailed test, the χ^2 test, Spearman rank correlation coefficients, the Mann-Whitney U test, Student's *t* test, and two way analysis of variance were used when appropriate. Independent prognostic risk factors for a poor outcome were analysed by unconditional multiple stepwise logistic regression. The simultaneous predictive value of the following variables was tested: sex; age; body mass index; hypertension; clinical grade on admission; presence of blood or intracerebral haematoma on the first computed tomography scan; occurrence of rebleeding or delayed cerebral ischaemia; amount of alcohol consumed before haemorrhage; CAGE positiveness; occurrence of heavy drinking before haemorrhage; source of information on patient's health habits; smoking habit; use of non-steroidal anti-inflammatory drugs; physical exertion during haemorrhage; deterioration due to primary bleed after admission; surgery; and timing of surgery. Adjustments were carried out by using logistic regression models.

Results

Table I shows the baseline clinical characteristics of patients and outcome at one year and table II shows the characteristics and laboratory values by sex. Eight former heavy drinkers had been abstainers for years; including them in the CAGE negative group did not affect the statistical results. Fifty six of the 59 CAGE positive patients had used ≥300 g alcohol weekly during the year before haemorrhage. Three women who were CAGE positive had used 200-300 g alcohol weekly, and one man who was CAGE negative had used more than 300 g weekly.

Specificity of high values of erythrocyte mean cell volume and γ -glutamyltransferase as well as of thrombocytopenia for heavy drinking and CAGE positiveness was high, about 90% (table III). On the other hand, sensitivity was about 60% for high levels of

TABLE II—Baseline characteristics, health habits, and laboratory markers of alcohol consumption in patients with aneurysmal subarachnoid haemorrhage (SAH). Values are numbers (percentages) unless otherwise indicated

	Men (n=149)	Women (n=142)	All patients (n=291)
Median (range) age in years	44.2 (21 to 65)	47.7 (15 to 65)*	45.8 (15 to 65)
Median (range) body mass index (kg/m ²)	24.7 (16.9 to 39.5)	24.0 (16.9 to 39.5)	24.3 (16.9 to 39.5)
Alcohol use before SAH:			
≥80 g/24 h	46 (31)	19 (13)†	65 (22)
≥150 g/72 h	46 (31)	16 (11)†	62 (21)
≥300 g/1 week	46 (31)	14 (10)†	60 (21)
Heavy drinkers/last year	42 (28)	15 (11)†	57 (20)
CAGE positive (interview score ≥2)	42 (28)	17 (12)†	59 (20)
Cigarette smoking:‡			
Never smoked	19 (13)	69 (49)†	88 (30)
Former smoker	10 (7)	5 (4)†	15 (5)
1-10 cigarettes/day	6 (4)	13 (9)†	19 (7)
11-20 cigarettes/day	12 (8)	16 (11)†	28 (10)
>20 cigarettes/day	102 (68)	39 (27)†	141 (48)
Use of non-steroidal anti-inflammatory drugs:			
None	75 (50)	69 (49)	144 (49)
Only before SAH	28 (19)	34 (24)	62 (21)
Between SAH and admission	34 (23)	25 (18)	59 (20)
Before SAH and before admission	12 (8)	14 (10)	26 (9)
Salicylates in urine on admission:			
No of samples	119	104	223
Positive result	25 (21)	23 (22)	48 (22)
Erythrocyte mean cell volume (fl):			
No of samples	138	130	268
Median (range)	95.0 (85 to 108)	93.0 (60 to 110)†	94.0 (60 to 110)
≥97	51 (37)	32 (25)†	83 (31)
≥100	30 (22)	19 (15)†	49 (18)
γ -Glutamyltransferase (U/l):			
No of samples	140	124	264
Median (range)	25.5 (8 to 586)	15.5 (6 to 246)†	21.0 (6 to 586)
≥45 (%)	41 (29)	19 (15)†	60 (23)
Platelet count (10 ⁹ /l):			
No of samples	141	127	268
Median (range)	233 (67 to 409)	243 (134 to 401)	237 (67 to 409)
≤149	14 (10)	7 (6)	21 (8)

*p=0.0169.

†p<0.001.

the two first variables, but only 10-15% for thrombocytopenia.

Non-parametric correlations of continuous variables in their original form are shown in table IV. Two way analysis of variance showed that values of mean erythrocyte volume were significantly raised in heavy drinkers ($p<0.01$) and cigarette smokers ($p<0.05$), without interaction, but only heavy drinking increased γ -glutamyltransferase values ($p<0.01$).

Table V shows many univariate associations between poor outcome and other variables. Surgery

TABLE III—Heavy drinking related to laboratory markers

	Heavy drinking*		CAGE score	
	No	Yes	0-1	2-4
Erythrocyte mean cell volume (fl) (n=268)				
≤96	177	8	176	9
97-99	20	14	20	14
≥100	15	34†	14	35†
γ -Glutamyltransferase (U/l) (n=264)				
<45	183	21	180	24
≥45	25	35†	26	34†
Platelet count (10 ⁹ /l) (n=268)				
<150	13	8	14	7
≥150	199	48‡	196	51

*Heavy drinking=average alcohol consumption of at least 300 g/week during the year before subarachnoid haemorrhage.
† $p<0.0001$. ‡ $p<0.05$.

was associated with outcome because surgery was performed almost entirely in good grade patients to prevent rebleeding. Only 14 of the 204 operations (7%) were performed to improve the clinical state and outcome of the patient by evacuation of a haematoma occupying intracerebral space. Twenty one of the 61 patients with rebleeding (34%) recovered from the bleed and underwent surgery.

When stepwise logistic regression was used, the variables that had simultaneous significant predictive value for poor outcome were (in order of entrance in the model): Glasgow coma score on admission; occurrence of rebleeding or delayed cerebral ischaemia; surgery (inversely); and being positive on the CAGE questionnaire ($p<0.01$ for each variable). Between each step the χ^2 value ($p<0.01$) improved significantly, and during the stepping procedure the p value for goodness of fit increased from 0.57 to 0.83. The significant predictors were the same for men and women. Predictive variables were adjusted for sex, age, and the interaction of sex and age because the men had consumed more alcohol and were younger than the women. The adjusted results are presented in table VI. The logistic model fitted well with the observed data (tests of goodness of fit, $p>0.76$).

After the CAGE variable had been excluded from

TABLE IV—Spearman rank-order correlation coefficients for continuous baseline characteristics, laboratory variables, and outcome at one year in 291 patients with aneurysmal subarachnoid haemorrhage

	Age	Body mass index (kg/m ²)	Alcohol consumption before haemorrhage		CAGE score	No of cigarettes/day	Erythrocyte mean cell volume	γ -Glutamyltransferase	Platelet count	Score on admission	
			g/24 h	g/wk						Hunt and Hess	Glasgow coma scale
Body mass index	0.32**										
Alcohol consumption before haemorrhage:											
g/24 h	0.02	0.05									
g/wk	-0.07	0.04	0.71**								
CAGE score	0.03	0.07	0.57**	0.71**							
No of cigarettes/day	-0.10	0.04	0.29**	0.47**	0.45**						
Erythrocyte mean cell volume	-0.08	-0.02	0.41**	0.52**	0.61**	0.42**					
γ -Glutamyltransferase	0.06	0.22**	0.32**	0.45**	0.54**	0.37**	0.39**				
Platelet count	0.05	0.07	-0.03	-0.05	0.00	0.01	0.01	0.00			
Score on admission:											
Hunt and Hess	0.14*	0.00	0.11	0.11	0.14*	-0.02	0.11	0.13*	-0.01		
Glasgow coma scale	-0.09	0.06	-0.07	-0.10	-0.15*	-0.01	-0.08	-0.13*	0.02	-0.93**	
Glasgow outcome scale	0.16**	0.08	0.09	0.12*	0.16**	0.11	0.13*	0.15*	0.03	0.52**	-0.55**

* $p<0.05$. ** $p<0.01$.

TABLE V—Outcome of aneurysmal subarachnoid haemorrhage related to baseline characteristics and health habits. Values are numbers (percentages) of patients unless otherwise indicated

	Independent* (n=179)	Dependent* or dead (n=112)	p Value
Sex ratio (male:female)	92:87	57:55	NS
Median (range) age (years)	44.6 (15 to 65)	48.5 (21 to 65)	0.0066
Median (range) body mass index (kg/m ²)	24.7 (16.9 to 39.1)	25.8 (17.8 to 39.5)	0.084
Hypertension	36 (20)	43 (38)	0.0006
Current smoker	113 (63)	75 (67)	NS
Alcohol consumption before haemorrhage			
≥80 g/24 h	36 (20)	29 (26)	NS
≥300 g/week	30 (17)	30 (27)	0.039
Heavy drinking†	25 (14)	32 (29)	0.0023
CAGE score ≥2	25 (14)	34 (30)	0.0007
Blood on CT scan (n=282)	161/176 (91)	105/106 (99)	0.0077
Intracerebral haematoma	29 (16)	46 (41)	<0.0001
Clinical grade on admission:			
Hunt and Hess ²⁰			<0.0001
1-2	121 (68)	31 (28)	
3	52 (29)	25 (22)	
4-5	6 (3)	56 (50)	
Median (range) Glasgow coma score	15 (8-15)	12 (3-15)	<0.0001
Deterioration due to primary bleed	22 (12)	39 (35)	<0.0001
Rebleeding	19 (11)	42 (38)	<0.0001
Delayed cerebral ischaemia:			
No of patients‡	179	81	
No ischaemia	125 (70)	45 (56)	
Reversible deficit	36 (20)		
Fixed deficit	18 (10)	36 (44)	
Surgery	161 (90)	43 (38)	<0.0001

*Independent=good recovery or moderate disability, dependent=severe disability or vegetative state, according to Glasgow outcome scale.²¹

†Heavy drinking=average alcohol consumption of at least 300 g/week during the year before haemorrhage.

‡Patients who died due to the primary bleed are excluded.

the model heavy drinking during the year before haemorrhage became a significant prognostic factor for poor outcome (adjusted relative risk 3.0, 95% confidence interval 1.2 to 7.3, $p=0.017$). When the analysis was performed without the heavy drinkers the amount of alcohol consumed shortly before haemorrhage did not affect the outcome.

When the laboratory markers were tested with clinical variables the mean erythrocyte volume was directly associated with a poor outcome after adjustment for the significant and non-significant prognostic variables mentioned above and for smoking status ($p=0.021$). γ -Glutamyltransferase was not significantly associated with outcome, probably because the values correlated significantly with Glasgow coma score (table IV).

Poor outcome after subarachnoid haemorrhage in heavy drinkers was due to an increase in the occurrence of severe disability and mortality. Twenty three of 59 patients positive on the CAGE questions (39%) died, and 11 (19%) were severely disabled or in a vegetative state at one year. The causes of death did not differ significantly according to alcohol consumption, but death due to rebleeding was higher than expected in patients positive on the CAGE questions. Causes of death in the CAGE positive patients were: primary bleed, seven (30%); due to rebleeding, 11 (48%); delayed cerebral ischaemia, two (9%); and other

TABLE VI—Logistic regression model for predicting poor outcome after aneurysmal subarachnoid haemorrhage

Variable	Numerical value	Coefficient*	Standard error	Relative risk*	95% Confidence interval	p Value
Glasgow coma score	3-15	C ₁ = -0.561	0.094			<0.0001
Rebleeding	0 = Absent, 1 = present	C ₂ = 1.954	0.478	7.06	2.77 to 18.01	<0.0001
Delayed cerebral ischaemia	0 = Absent, 1 = present	C ₃ = 2.333	0.459	10.31	4.19 to 25.35	<0.0001
Surgery	0 = No, 1 = yes	C ₄ = -2.067	0.522	0.13	0.05 to 0.35	<0.0001
CAGE	0 = Negative, 1 = positive†	C ₅ = 1.495	0.462	4.46	1.80 to 11.03	0.0014
Sex	0 = Woman, 1 = man	C ₆ = 0.735	1.748	2.09	0.07 to 64.14	NS
Age	No of years	C ₇ = 0.005	0.028			NS
Sex × age	Product of sex and age	C ₈ = -0.027	0.038			NS
Constant		C ₀ = 6.596	1.838			

$$P(\text{poor outcome}) = \frac{e^x}{1 + e^x} \text{ where}$$

$$x = C_0 + C_1 \times (\text{Glasgow coma score}) + C_2 \times (\text{rebleeding}) + C_3 \times (\text{delayed cerebral ischaemia}) + C_4 \times (\text{surgery}) + C_5 \times (\text{CAGE}) + C_6 \times (\text{sex}) + C_7 \times (\text{age}) + C_8 \times (\text{sex} \times \text{age})$$

(Poor outcome) = death, vegetative state or severe disability after subarachnoid haemorrhage.

*Coefficient and relative risk for each variable were adjusted for other variables listed in table.

†Two or more positive responses to four questions in CAGE interview.

reasons, three (13%). The causes of death in the 61 CAGE negative patients were: primary bleed, 24 (39%); rebleeding, 23 (38%); delayed ischaemia, nine (15%); and other reasons, five (8%).

CAGE positive patients were in a poorer clinical condition on admission (tables IV and VII); therefore they were operated on less often than others (36/59, 61% v 168/232, 72%; $p=0.088$). Heavy drinkers did not have episodes of rebleeding or delayed ischaemia more often than others, but these causes of deterioration were more disastrous in heavy drinkers (table VII). Heavy drinkers also had hypodense lesions on the follow up computed tomography scan consistent with cerebral infarction in areas other than previous intracerebral haematoma as often as others (17/39, 44% v 68/156, 44%).

Patients who were positive on the CAGE questionnaire had not used anti-inflammatory drugs more often nor did they have salicylates in their urine on admission more often than others (27/59, 46% v 120/232, 52%). Neither did they undergo physical exertion during haemorrhage (13/56, 23% v 75/225, 33%), nor show blood on the first scan more often than others (56/58, 97% v 210/224, 94%). However, CAGE positiveness was associated with hypertension (23/59, 39% v 56/232, 24%; $p=0.022$) and the presence of an intracerebral haematoma (21/59, 36% v 54/232, 23%; $p=0.053$). After additional adjustment for hypertension, presence of intracerebral haematoma, body mass index, and smoking habit, CAGE positiveness remained a significant predictor of poor outcome

(relative risk 3.9, 1.5 to 9.9, $p=0.0056$) as did heavy drinking (2.6, 1.1 to 6.4, $p=0.032$) and mean erythrocyte volume ($p=0.035$).

In surgically treated patients the independent factors predicting poor outcome were Glasgow coma score on admission ($p<0.0001$); delayed cerebral ischaemia (relative risk 9.9, 3.7 to 26.6, $p<0.0001$); CAGE positiveness (5.3, 1.9 to 14.7, $p<0.01$); and increase in body mass index ($p<0.05$).

Smoking affected neither outcome nor incidence or severity of rebleeding or delayed ischaemia. Use of non-steroidal anti-inflammatory drugs before admission did not affect the presence of rebleeding or delayed ischaemia, but those patients who had salicylates in their urine on admission had delayed ischaemia with fixed neurological deficit more rarely than those without salicylates in the urine (5/45, 11% v 38/156, 24%; $p=0.056$).

Discussion

The outcome after aneurysmal subarachnoid haemorrhage is determined by the severity of bleeding assessed by the clinical condition and amount of subarachnoid, intracerebral, and intraventricular blood shown on computed tomography, as well as by the occurrence of rebleeding or delayed cerebral ischaemia.¹⁻⁶ The independent role of previous health habits and hypertension in the outcome has been unknown. The patient population in this study was unselected, as seen by the number of patients who died as a result of the initial haemorrhage and early rebleeding. However, 10-15% of patients do not reach medical attention after subarachnoid haemorrhage.¹⁻³

It is well known that heavy drinkers tend to deny their problems. This may cause bias due to underestimation of alcohol intake. Therefore, three separate means were used to identify alcohol consumption in this study. Two methods were based on interview: calculation of the amount of alcohol consumed within the year before the subarachnoid haemorrhage, and the CAGE interview, which relates to abnormal drinking behaviour (for example, drinking on waking) and alcohol induced problems, rather than merely the amount of alcohol consumed.^{17,18} CAGE positiveness is sensitive for detection of heavy drinking and alcoholism (90%), and its specificity is 75-80%.¹⁷⁻¹⁸ The third method used was determination of laboratory markers— γ -glutamyltransferase concentration and erythrocyte mean cell volume—to detect excessive drinkers. The reported sensitivity of high values of these markers for heavy drinking has ranged from 30% to 90%, but specificity has usually been high (80-99%).^{18,23-26}

When interviewed, patients in good clinical condition might possibly underestimate alcohol intake more than would family members of patients in poor condition. This could lead to a biased increase in risk

TABLE VII—Clinical grade on admission and outcome after rebleeding and delayed cerebral ischaemia according to heavy drinking. Values are number (percentage) of patients

	Heavy drinking		CAGE score	
	No (n=234)	Yes (n=57)	0-1 (n=232)	2-4 (n=59)
Hunt and Hess ²⁰ grade on admission*:				
I	45 (19)	6 (11)	44 (19)	7 (12)
II	87 (37)	14 (25)	87 (37)	14 (24)
III	58 (25)	19 (33)	57 (25)	20 (34)
IV	21 (9)	11 (19)	21 (9)	11 (19)
V	23 (10)	7 (12)	23 (10)	7 (12)
Glasgow coma score on admission*:				
3-6	23 (10)	10 (17)	23 (10)	10 (17)
7-9	12 (5)	3 (5)	12 (5)	3 (5)
10-12	14 (6)	5 (9)	14 (6)	5 (9)
13-14	52 (22)	18 (32)	51 (22)	19 (32)
15	133 (57)	21 (37)	132 (57)	22 (37)
Rebleeding	48 (21)	13 (23)	48 (21)	13 (22)
Outcome				
Independent	18	1*	18	1*
Dependent or dead	30	12*	30	12*
Delayed cerebral ischaemia†	74/210	16/50	74/208	16/52
Outcome				
Independent	47	7	47	7
Dependent or dead	27	9*	27	9

Heavy drinking = average alcohol consumption ≥ 300 g/week during year before haemorrhage.

* $p<0.05$ No v Yes and 0-1 v 2-4.

†Excluding patients who died of primary bleed.

for poor outcome in heavy drinkers. However, CAGE positiveness and results of laboratory markers accorded with the estimated alcohol intake. Heavy drinkers seem to be in a poorer condition after haemorrhage than others. To reduce underestimation I recorded the greater reported values obtained from either the patient or family member even though I did not observe any decisive differences between the reported values during a careful interview.

Poor outcome in heavy drinkers was caused mainly by an increase in mortality and morbidity due to rebleeding and delayed ischaemia, although occurrence and time of onset of rebleeding and delayed ischaemia were not affected by drinking habits. Hypodense lesions on the follow up computed tomography scan in areas other than the previous intracerebral haematoma were as common in heavy drinkers as in others. These lesions can be symptomatic or symptomless depending on the location and size of the lesion.^{6 27} Besides causing delayed cerebral ischaemia and intracerebral haematoma, surgery can cause hypodense lesions that have been attributed to spatula pressure or injury to penetrating arteries during operation.^{6 27}

Heavy drinking and ethanol withdrawal can predispose to poor outcome after subarachnoid haemorrhage through various mechanisms. These include the effects of blood pressure,²⁸⁻³⁰ platelet function,^{31 32} clotting factors,³³ alcohol induced cardiac arrhythmias,³⁴ and changes in cerebral blood flow.³⁵ Alcohol consumption, independently of other factors, raises blood pressure, as does alcohol withdrawal transiently.²⁸⁻³⁰

Long term severe heavy drinking can cause thrombocytopenia, reduced platelet aggregability and thromboxane formation capacity, increased prostacyclin production in the endothelium, and defects of clotting factors.³¹⁻³³ These, possibly together with hypertension, could explain the severity of rebleeding and presence of intracerebral haematoma in heavy drinkers. Stopping alcohol abuse results in rebound thrombocytosis^{31 32} and increased thromboxane formation by platelets³² within two weeks, thus favouring thrombosis formation.³² In this study heavy drinking and the occurrence and severity of rebleeding or delayed ischaemia were not associated with platelet count on admission. Increased platelet function and thromboxane formation capacity have recently been associated with delayed cerebral ischaemia after subarachnoid haemorrhage.^{27 36 37}

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ONE HUNDRED YEARS AGO

MR. GLADSTONE.

Dr. Grainger, of Chester, reports to us that the bandages were removed from Mr. Gladstone's eye on Tuesday night. The wound of the cornea was healed. Dr. Grainger, who travelled with the right hon. gentleman to Lancaster on Wednesday, states that he was in very good health and spirits, and bore the journey well. As to the precise nature

of the injury, Dr. Grainger informs us that when seen an hour after his accident Mr. Gladstone was suffering a good deal of pain from his left eye, the lower lid was bruised, and there was a small wound on the side of the nose. There was an irregular jagged cut or scratch on the outer side of the cornea, about a quarter of an inch in length; the epithelium was stripped from the surface of the cornea to a little beyond the edge of the pupil. (*BMJ* 1892;ii:33)