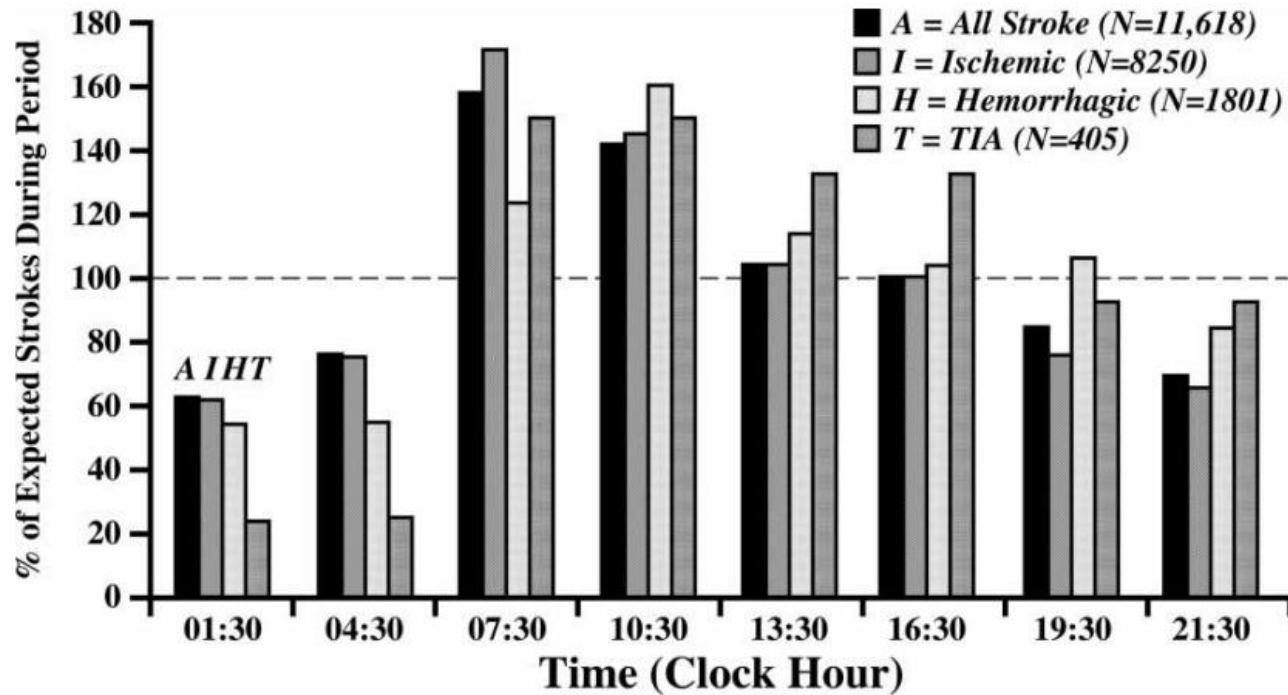# Circadian variation in clinical outcomes of intracerebral haemorrhage: the relevance of location. A retrospective study.

Llorente Iniesta, María Esther[1]; Martínez García, Francisco[1]; Albert Lacal, Laura[1]; García Molina, Estefanía[1]; Sanz Monllor, Ainara[1]; Morales Ortiz, Ana[1]

[1]Hospital Virgen de la Arrixaca (Murcia).

Background

FIGURE 1 24 h pattern in TIA and ischemic and hemorrhagic stroke. The values depict the incidence of each event per 3 h time interval as a percentage of the 24 h mean number set equal to 100% for each type of stroke and for TIA. The figure clearly shows the occurrence of stroke and TIA is greatest in the morning at 07:30 and 10:30 h and lowest over night (modified from Elliott, 1998).

Manfredini R, Boari B, Smolensky MH, Salmi R, la Cecilia O, Maria Malagoni A, Haus E, Manfredini F. Circadian variation in stroke onset: identical temporal pattern in ischemic and hemorrhagic events. Chronobiol Int. 2005;22(3):417-53.

Circadian variation in stroke onset: identical temporal pattern in ischemic and hemorrhagic events

Roberto Manfredini [1], Benedetta Boari, Michael H Smolensky, Raffaella Salmi, Olga la Cecilia, Anna Maria Malagoni, Erhard Haus, Fabio Manfredini

Affiliations + expand
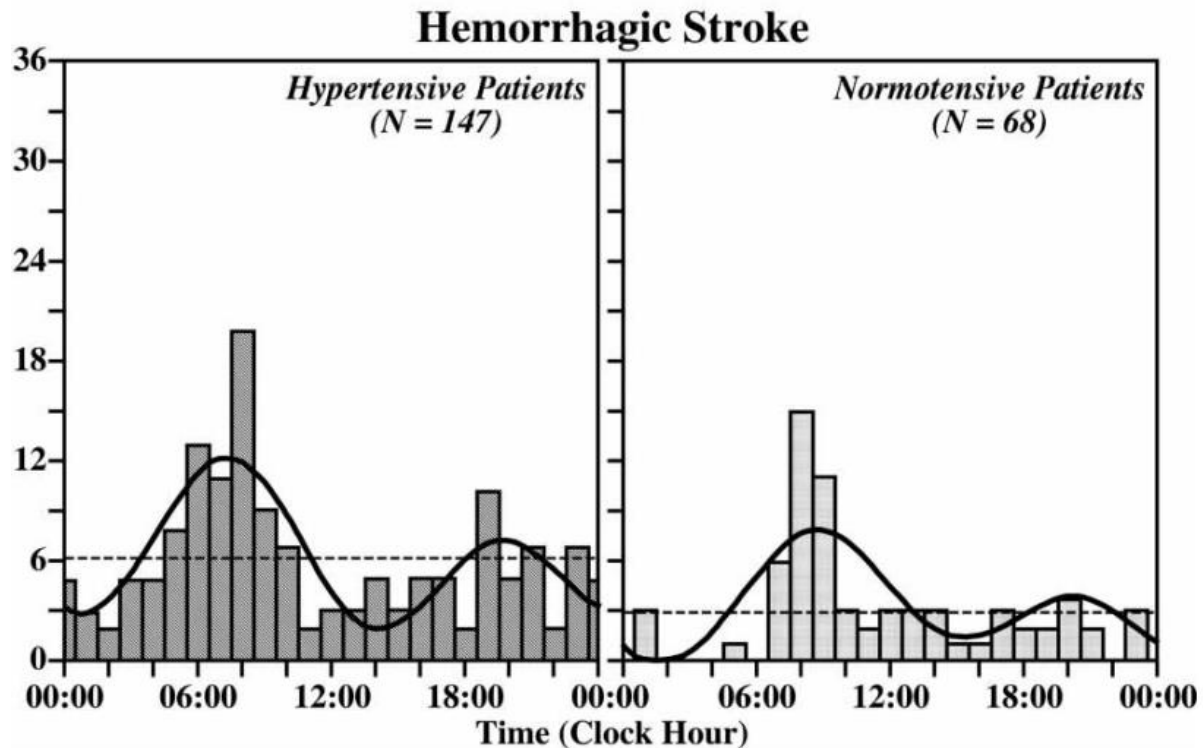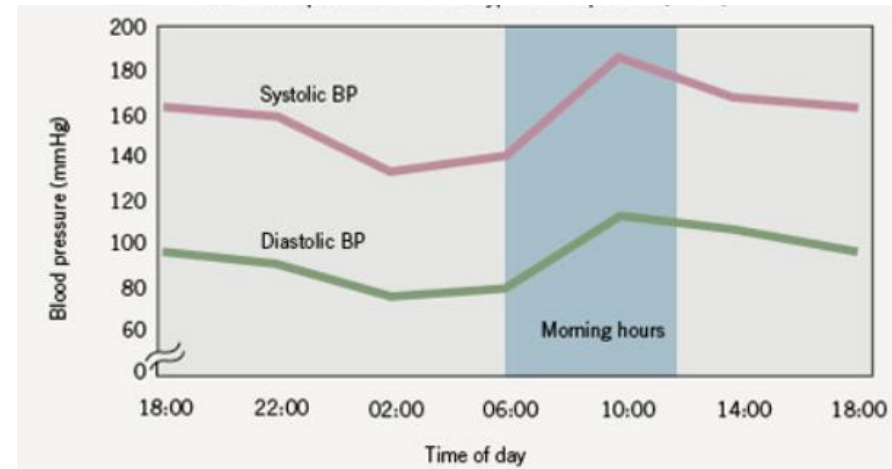
Mechanisms underlying the morning increase in platelet aggregation: a flow cytometry study

N P Andrews [1], H R Gralnick, P Merryman, M Vail, A A Quyyumi

Affiliations + expand
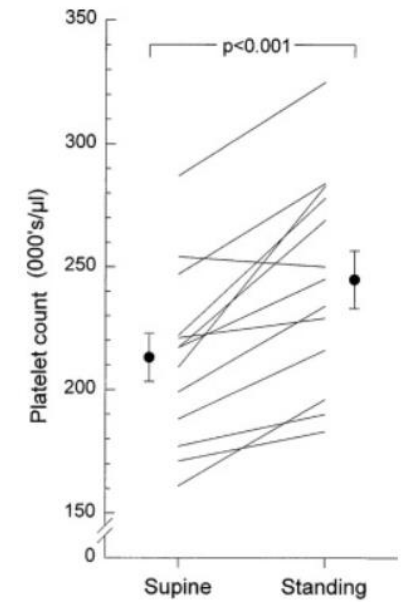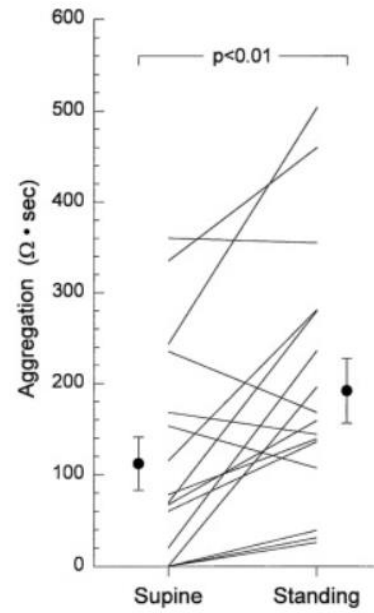
Table 1. Catecholamines and Fibrinolytic and Procoagulant Factors

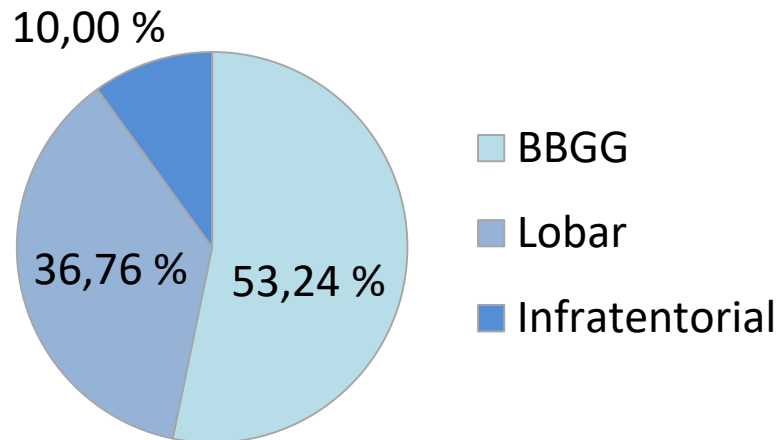|	Supine (mean±SEM)	Standing(mean±SEM)	p Value
Catecholamines			
Epinephrine (pg/ml)	14±2	33±6	< 0.01
Norepinephrine (pg/ml)	177±17	512±50	< 0.001
Fibrinolytic factors			
PAI-1 antigen (ng/ml)	11.4±3.4	13.8±4.8	0.03
t-PA antigen (ng/ml)	6.0±0.9	7.7±1.1	< 0.01
Procoagulant factors			
Fibrinogen (mg/dl)	203±14	241±30	< 0.03
Fibrinogen (whole blood)*	117±7	133±16	0.02
PT fragment 1.2 (nmol/liter)	0.69±0.11	0.86±0.12	0.01
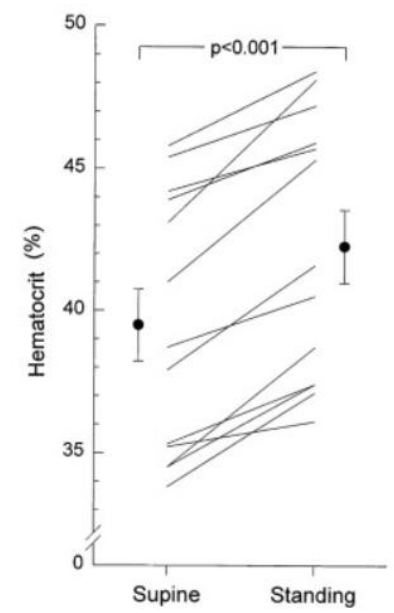
Hypothesis and objectives

- Determine possible associations between ICH onset time and early clinical outcomes (admission severity, in-hospital mortality and neurological sequelae at discharge) taking into account the location of the hemorrhage.

- It is hypothesized that morning bleeding will be more frequent and possibly have a worse prognosis regardless of location.

Results

- 340 patients admitted between 2019-2022.

- Grade of disability:
  - Good functionality: mRS ≤2.
  - Excellent functionality: mRS ≤ 1.

Morning
8:00-15.59 h

Night
00:00-07:59 h

Evening
16:00-23:59 h

10,00 %

36,76 %   53,24 %

- BBGG
- Lobar
- Infratentorial
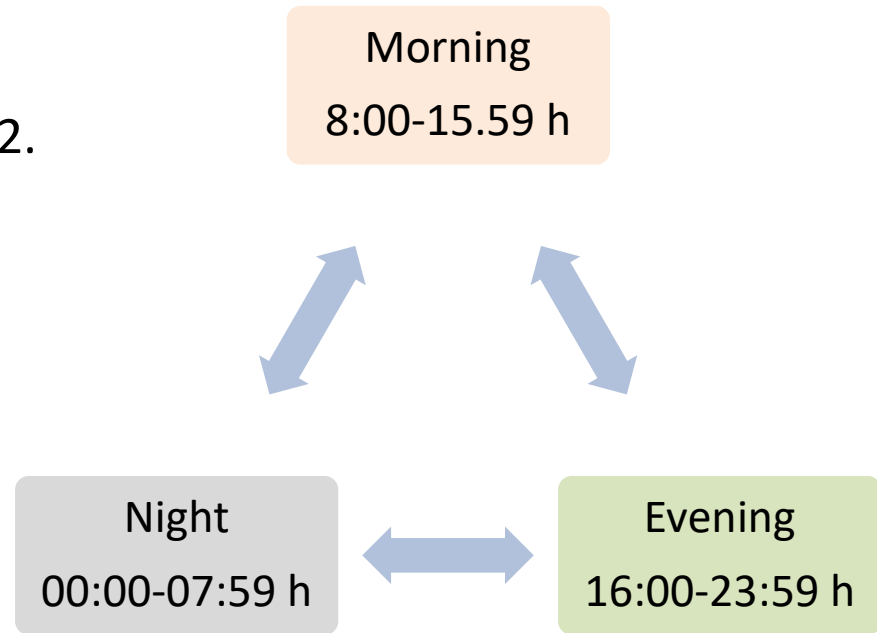
Basal Ganglia ICH

- 181 patients.
- Bleeding was more frequent in the morning.
- No differences in baseline characteristics.
- Greater clinical severity at hospital arrival (NIHSS) was associated with morning bleeding.
- Statistically significant differences were found in the mRs at discharge:
  - Patients with morning onset ICH were less likely to have a good functionality.
  - Patients with night onset were more expected to have an excellent one.
- No statistically differences were found in days of hospitalization, in-hospital mortality or NIHSS at discharge.

23,81 %	40,82 %
35,37 %	

☐ Morning
☐ Evening
☐ Night
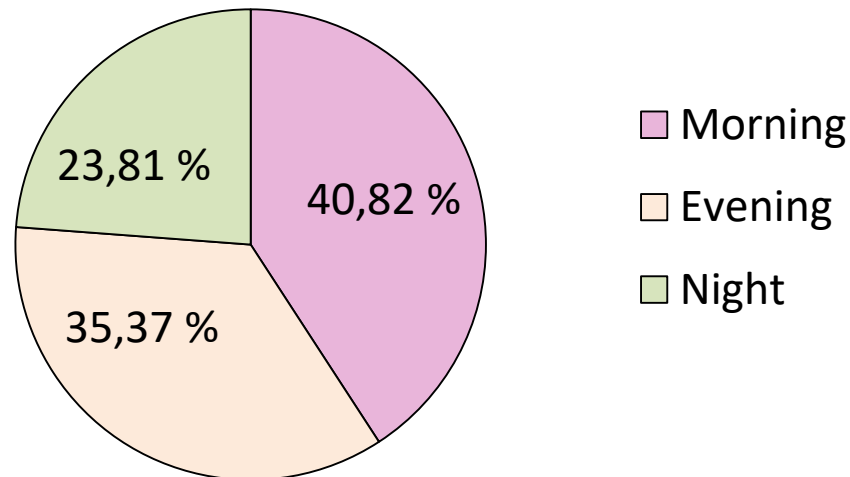
- Basal ganglia ICH

		Sum of Squares	Degrees of Freedom	Mean Squares (MS)	F	p
Age	Between Groups	511,644	2	255,822	1,406	0,248
	Within Groups	26197,676	144	181,928		
SBP (arrival)	Between Groups	491,062	2	245,531	0,339	0,713
	Within Groups	103553,273	143	724,149		
DBP (arrival)	Between Groups	1093,566	2	546,783	1,844	0,162
	Within Groups	42412,544	143	296,591		
Hb (arrival)	Between Groups	0,244	2	0,122	0,042	0,958
	Within Groups	384,871	134	2,872		
Hto (arrival)	Between Groups	0,365	2	0,183	0,008	0,992
	Within Groups	3135,721	133	23,577		
Platelets (arrival)	Between Groups	4448,886	2	2224,443	0,587	0,557
	Within Groups	507488,895	134	3787,231		
NIHSS (arrival)	Between Groups	582,627	2	291,314	5,232	0,006
	Within Groups	7907,138	142	55,684		
Days of hospitalization	Between Groups	150,126	2	75,063	0,691	0,503
	Within Groups	14980,725	138	108,556		
NIHSS (discharge)	Between Groups	242,096	2	121,048	2,566	0,081
	Within Groups	5660,555	120	47,171		

- Basal ganglia ICH

|		Time of symptoms onset (N)			p
		Morning (Z)	Evening (Z)	Night (Z)	
Sex	Women	22	11	7	0,101
	Men	38	41	28	
Hight Blood Pressure	No	20	16	7	0,385
	Yes	39	35	27	
Antiaggregants	No	52	43	29	0,814
	Yes	8	9	6	
Anticoagulants	No	51	45	25	0,151
	Yes	9	7	10	
Good functionality at admission	No	9	5	2	0,350
	Yes	51	47	33	
Excellent functionality at admission	No	13	11	10	0,681
	Yes	47	41	25	
In-hospital mortality	No	42	42	29	0,294
	Yes	14	7	5	
Good functionality at discharge	No	35 (2,4)	27 (-0,8)	15 (-1,8)	0,036
	Yes	9 (-2,4)	17 (0,8)	14 (1,8)	
Excellent functionality at discharge	No	38 (1,9)	35 (0,5)	17 (-2,7)	0,020
	Yes	6 (-1,9)	9 (-,05)	12 (2,7)	

Lobar ICH

- 125 patients.
- Lobar hemorrhages were more frequent at night.
- No differences in baseline characteristics.
- No statistically significant differences were found in clinical outcomes.
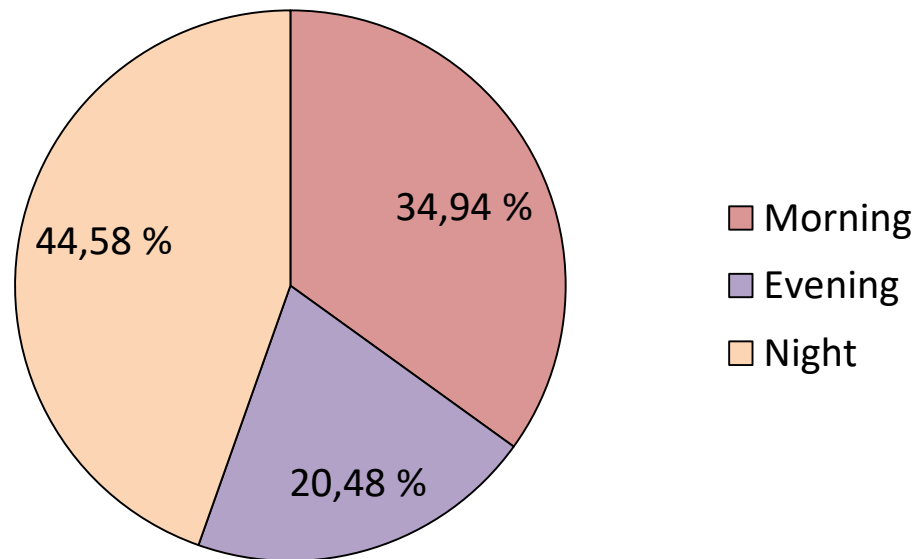
Infratentorial ICH

- 34 patients.
- More frecuent in the morning
- No differences in baseline characteristics.
- No statistically significant differences were found in clinical outcomes.

Pie chart:
- Morning: 42,86 %
- Evening: 19,05 %
- Night: 38,1 %
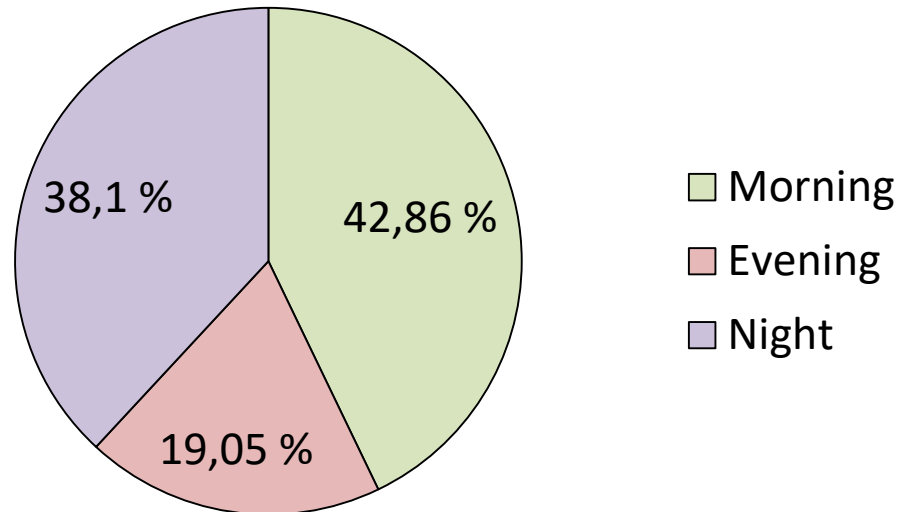
Conclusions

- Basal ganglia haemorrhages that happened in the morning exhibited a greater clinical severity at hospital arrival and a worse functional outcome at discharge compared with those occurred in the evening or at night.

- These circadian patterns were not seen in lobar or infratentorial haemorrhages.