Clinical profile and evolution of patients with subarachnoid haemorrhage for 11 years

Perfil clínico y evolución de pacientes con hemorragia subaracnoidea durante 11 años

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Abstract

Introduction. Spontaneous subarachnoid haemorrhage is a rare cause of stroke, but it causes great socioeconomic impact and high morbidity and mortality.

The aim of this study is to describe the clinical profile and evolution of a series of patients with SAH admitted to a tertiary hospital, as well as the diagnostic and therapeutic management.

Material and methods. Retrospective study of 536 patients diagnosed with SAH admitted to the ICU of the Hospital Universitario de A Coruña between 2003 and 2013 (Age: 56.9 ± 14.1 years, female/male ratio: 1.5:1). Demographic characteristics, risk factors, aetiologies and clinical signs, prognostic scales, diagnostic tests and treatment were collected. A comparative analysis was made between the general series and subgroups of patients with aneurysmal (SAH-A) and idiopathic (SAH-I) subarachnoid haemorrhage.

Results. There were 49.0 ± 15.1 patients/year (2013 incidence: 4.3/100,000 inhabitants). 60.3% presented Glasgow Coma Scale (GCS) 14-15, with scarce symptomatology (Hunt-Hess I-II 61.9%, World Federation Neurosurgeons Scale I-II 60.4%). 50.7% presented Fisher IV.

SAH-A was diagnosed in 78.3% (n = 396); perimesencephalic subarachnoid haemorrhage (SAH-PM) in 3.2%; and SAH-I in 17.9%. During the study period there was an increase in the prevalence of aneurysms, causing an increased number of surgeries in recent years. Both SAH-A and SAH-I presented greater severity upon admission. Patients with SAH-A had higher

percentage of complications and mortality, with lesser degree of independence at 6 and 12 months.

Conclusions. The incidence of SAH appears to have decreased in recent years, with SAH-I comprising 17.9% of the cases. Patients with SAH-I have better prognosis and lower risk of complications, highlighting the benignity of SAH-PM.

Resumen

Introducción. La hemorragia subaracnoidea espontánea es una causa poco frecuente de ictus que ocasiona gran impacto socioeconómico y elevada morbimortalidad.

El objetivo de este estudio es describir el perfil clínico y evolución de una serie de pacientes con HSA ingresados en un hospital terciario, así como el manejo diagnóstico-terapéutico.

Material y métodos. Estudio retrospectivo de 536 pacientes diagnosticados de HSA ingresados en la Unidad de Cuidados Intensivos del Hospital Universitario de A Coruña de 2003–2013 (edad: 56,9 ± 14,1 años, ratio mujer/hombre:1,5:1). Se recogieron características demográficas, factores de riesgo, etiología y clínica, escalas pronósticas, pruebas diagnósticas y tratamiento. Se realizó un análisis comparativo entre la serie general y subgrupos de pacientes con HSA aneurismática (HSA-A) e idiopática (HSA-I).

Resultados. Se registraron 49,0 ± 15,1 pacientes/año (incidencia 2013:4,3/100.000 habitantes). 60,3% presentaban *Glasgow Coma Scale* 14-15, con escasa sintomatología (*Hunt-Hess* (H-H) I-II 61,9%; *World Federation Neurosurgeons Scale* (WFNS) I-II 60,4%). 50,7% presentaban Fisher IV. En 78,3%(n = 396) se diagnosticó HSA-A, 3,2% presentaban sangrado perimesencefálico (HSA-PM) y HSA-I 17,9%. Durante el periodo de estudio se registró aumento de la prevalencia de aneurismas, incrementándose en los últimos años la cirugía. Tanto la HSA-A como HSA-I presentaban mayor gravedad al ingreso. Los pacientes con HSA-A presentaron mayor porcentaje de complicaciones y mortalidad, con menor grado de independencia a 6 y 12 meses.

Conclusiones. La incidencia de HSA tiende a descender en los últimos años, representando la HSA-I el 17,9% de los casos. Los pacientes con HSA-I tienen mejor pronóstico y menor riesgo de complicaciones, destacando la benignidad de la HSA-PM.

Keywords

Spontaneous subarachnoid haemorrhage; Intracranial aneurysm; Perimesencephalic haemorrhage; Vasospasm; Clipping; Prognosis

Palabras clave

Hemorragia subaracnoidea espontánea; Aneurisma intracraneal; Hemorragia perimesencefálica; Vasoespasmo; Pinzamiento; Pronóstico

Introduction

Spontaneous subarachnoid haemorrhage (SAH) is a serious disorder which causes major dependence and has a high mortality rate. Although the least common stroke subtype (5%),[1,2,3] in the last 30 years the proportion of SAH has increased with respect to other types of stroke because better control of cardiovascular risk factors has decreased the prevalence of the rest. The overall incidence has remained stable worldwide, with nine cases/100,000 population/year,[3] except for Japan and Finland, where these figures are doubled due to a genetic component.[4] An increased incidence has also been observed with age and in women from the age of 50.[5]

Diagnostic techniques have evolved and, where SAH is suspected, noncontrast cranial computed tomography (CT) is the diagnostic test of choice.[6] This allows us to classify SAH according to the bleeding pattern and assign a score on the Fisher scale, with both these factors affecting prognosis.[7,8,9,10] When establishing the cause of bleeding, angiographic assessment is essential, as 80–90% of SAH are secondary to cerebral aneurysm. However, in around 10–20% of cases no cause is demonstrated and they are classified as idiopathic (SAH-I).[10,11] In fact, in Spain the incidence of SAH-I is higher,[11,12,13,14] but worldwide it has decreased with the improvement in diagnostic techniques.

In recent years, there has been a paradigm shift in the treatment of brain aneurysms with the incorporation of endovascular treatment and the refining of neurosurgical techniques.[15] The above factors, combined with protocolised management in neurocritical care units, contribute to improving the prognosis.[16]

Despite improvements, however, SAH remains a serious condition with a high premature mortality rate (42%).[17] Aneurysmal SAH is the subtype that causes the greatest socio-economic impact (23−51% of deaths)[14]; as it affects young patients, the sequelae lead to a greater social and healthcare burden[1]. Although mortality rates have remained stable for

a long time, in recent years a decrease (20-25%) has been observed without an associated higher dependency rate.[18]

Knowing more about the characteristics of our population would allow us to act on variables that affect the prognosis and plan necessary resources within the health area. In our study, we describe the clinical profile, diagnostic/therapeutic management and outcome in patients with SAH admitted to the Intensive Care Unit (ICU) of a tertiary hospital in recent years.

Material and methods

Population

Retrospective observational follow-up study of all patients ≥15 years of age admitted during the period 2003–2013 to the ICU of Complexo Hospitalario Universitario de A Coruña (CHUAC) [A Coruña University Hospital Complex] with a diagnosis of SAH according to the American Heart Association.[6]

The CHUAC ICU is a multi-purpose medical-surgical unit with 32 beds, which cares for approximately 990 critically ill patients each year. Admissions come from the accident and emergency department, the hospital itself and first/second level hospitals, for which it is the centre for referrals. During part of the study period (until 2009–2010), it was a referral centre for other healthcare areas in which the Radiology Department of each hospital was implementing interventional neuroradiology procedures, referring complex cases to the ICU at CHUAC.

We excluded patients with: *a)* suspected SAH not confirmed by imaging tests (brain CT/magnetic resonance imaging [MRI]) or lumbar puncture (LP); *b)*post-traumatic SAH; and *c)* presence of aneurysm without SAH.

During the study period, 536 patients were admitted who met the established inclusion criteria. This sample size allowed the characteristics of interest to be estimated with 95% confidence and ± 6% precision.

Protocol

The care was provided by a multidisciplinary team (neurosurgeons, neuroradiologists and intensive care specialists). The CHUAC protocol establishes that, after diagnosis, patients are admitted to the ICU for haemodynamic, respiratory and neurological monitoring. All patients are given prophylaxis for vasospasm, gastric stress ulcers and deep vein thrombosis, and individualised sedation and analgesia is applied. Diagnostic angiography is performed within the first 24−48 h (classifying: aneurysmal SAH [SAH-A] vs no lesion). In the SAH where no aneurysm is identified, patients are divided into two groups according to the location of the bleeding on CT: SAH-PM, defined according to the Rinkel et al. criteria[7] as bleeding anterior to the brain stem, with/without extension to the anterior portion of the Ambient or Sylvian cisterns; and SAH-I, consisting of localised bleeding similar to that caused by aneurysmal lesion, with no culprit lesion. If there is clear evidence of aneurysm, and if feasible, endovascular treatment is performed; otherwise, the patient is scheduled for a second embolisation (2 weeks) or surgery. The surgical approach is indicated when the endovascular approach is not possible due to technical difficulties, aneurysms of the middle cerebral artery (MCA) or presence of intracranial haematoma (> 50 ml). Monitoring for possible neurological complications is performed by neurological surveillance/transcranial Doppler/CT. After their stay in the ICU, the patients are transferred to the hospital ward once stable; to Neurosurgery if they were treated surgically, otherwise Neurology.

Parameters

The data for each patient was obtained by reviewing their medical records. We collected sociodemographic variables (age/gender) and previous medical history and comorbidity (Charlson index). We also recorded the delay in reaching hospital from the onset of symptoms and initial clinical manifestations. We assessed severity on admission to the ICU according to neurological scales (Glasgow Coma Scale [GCS], Hunt-Hess Scale [HH], World Federation of Neurological Surgeons scale [WFNS], Fisher Grading Scale) and overall severity scales (Acute Physiology Chronic Health Evaluation II [APACHE II] and Sequential Organ Failure Assessment [SOFA]). We also collected information on diagnostic tests (CT/MRI/arteriogram) and clinical complications, and recorded the type

of therapeutic management, whether embolisation or surgical clipping. Prognosis was assessed using in-hospital mortality rates and functional scales (Glasgow Outcome Scale [GOS]/Rankin).

Statistical analysis

The statistical analysis was carried out with the SPSS 19.0 program for Windows (IBM Software Group, New York, USA). All statistical tests were performed with a bilateral approach, considering values of $p < 0.05$ as significant.

A descriptive analysis was made of all the variables collected, both overall and according to the type of lesion. For the comparison between patients with SAH-A and patients with SAH-I, the quantitative variables were compared using Student's *t*-test or Wilcoxon's signed rank test. Qualitative variables were compared using the Chi-squared test or Fisher's exact test.

We also analysed changes in the characteristics of admitted patients and their diagnostic-therapeutic management over the course of the study period, considering the periods 2003−2005, 2006−2008, 2009−2011 and 2012−2013. For numerical variables, we used the Kruskall-Wallis test, and in the case of qualitative variables, the Chi-squared test.

Ethical considerations

The study was carried out respecting the ethical and legal requirements of the applicable biomedical research regulations in force at all times. The study was approved by the Comité de Ética de Investigación de Galicia (CAEIG) [Independent Ethics Committee of Galicia] (authorisation code 2012/268).

Results

During the study period, a total of 536 patients with a diagnosis of SAH were admitted to the ICU, with an average of 49.0 ± 15.1 patients/year, decreasing from 73 patients in 2003 to 21 patients in 2013 (Fig. 1). The incidence in our population in 2013 was 4.3 cases/100,000 population.

Sociodemographic characteristics, previous medical history and clinical manifestations on admission are shown in Table 1. The mean age was 56.9 ± 14.1 years, with a female/male ratio of 1.5:1. Among the most common types of medical history were hypertension (41.8%) and use of harmful substances (33.3%); 6.5% (n = 35) of the patients had a previous history of SAH, and 10.1% had received anticoagulant therapy (n = 54). There were no significant changes in terms of distribution by age, gender, comorbidity, or signs or symptoms at the time of admission.

After the first symptoms, 44.8% of the patients were taken to hospital within the first 6 h. The most common clinical manifestation of onset was headache (76.5%) (Table 1). The level of consciousness in 60.3% of patients was found to be good (GCS 14–15), with few symptoms, whether assessed by HH (61.9%: grade i-ii) or WFNS (60.4%: grade i-ii). Bleeding classifiable as Fisher IV was found in 50.7% (n = 272) of the cases. The mean APACHE II score was 11.8 ± 6.8 and the mean SOFA was 2.4 ± 2.8 (Table 1).

The initial diagnosis was made by CT scan in 534 patients (99.6%) and by LP in two cases. Some type of diagnostic test was performed to assess for the presence of an aneurysm in 90.7% of the patients, while 21 (3.9%) cases were diagnosed solely by radiological evidence of SAH at admission. Aneurysm was found in 78.3% (n = 396) (16.9% multiple aneurysms), with the most common locations being the MCA (39.9%), anterior communicating artery (31.6%) and posterior communicating artery (12.1%). The right hemisphere was the more commonly affected (56.6%). Of the patients not diagnosed with aneurysms, 16 (3.2%) had a perimesencephalic SAH (SAH-PM) and 90 (17.9%) had an SAH-I (Fig. 2).

Over the study period, a progressive increase in the prevalence of aneurysmal lesions was recorded, exceeding 80% of all cases of SAH in recent years, at the expense of SAH-I. In the patients with SAH-A, the most common treatment of choice was embolisation, although an increase in surgical clipping was found in the last period studied (2012−2013) (Table 2).

Differences were detected in sociodemographic characteristics, comorbidity and previous medical history, clinical manifestations and status at admission according to the type of lesion (Table 3). Patients with SAH-PM were younger at admission, more likely to be female, less likely to have hypertension and had less comorbidity. There were no cases in

this group with a history of previous SAH, polycystic disease or cancer, and none had coma, focal signs or seizure as an initial clinical manifestation.

Comparing patients with SAH-A with those with SAH-I, in the SAH-A group they were mostly female (63.9% vs 46.7%; $p = 0.003$), were more likely to have had a previous SAH (7.8 % vs 1.1%; $p = 0.020$) and reached hospital earlier (<6 h: 46.7% vs 28.9%; $p = 0.009$). The most common first symptom in both groups was headache (76.3% vs 87.8%; $p = 0.017$), although less so in the SAH-A group, in which there was a higher rate of coma (37.6% vs 11.1%; $p < 0.001$) (Table 3).

On admission to the ICU, patients with SAH-I had a better GCS (11.9 vs 13.4; $p \leq 0.001$) and a lower score on the HH scale (2.8 vs 2.1; $p \leq 0.001$) and the WFNS (2.8 vs 2.2; $p \leq 0.001$), with significant differences. The risk of complications measured by the Fisher scale was significantly higher in the patients with SAH-A (3.3 vs 2.9; $p = 0.001$). The overall severity of the patient assessed by APACHE II (11.8 vs 10.0; = 0.015) and total SOFA day 0 (2.4 vs 1.3; $p \leq 0.001$) was significantly higher in the aneurysmal group (Table 3).

The prognosis estimated by the presence of neurological and systemic complications, hospital mortality and GOS-Rankin at 6 and 12 months differed according to the type of lesion (Table 4). Patients with SAH-A had a higher percentage of complications, higher mortality rate and a lower degree of independence (GOS 4−5) at 6−12 months.

Discussion

This study provides data on the clinical profile, management and outcome of patients admitted with SAH to an ICU of a tertiary hospital in recent years. Studies with a sufficient number of patients to enable the different patterns of SAH to be compared are few and far between, so a registry of 536 cases collected over ten years provides a good opportunity to analyse the characteristics of the population, both overall and according to subtype.

The number of admissions remained stable up to the last two years of the registry, during which time there was a gradual decrease, probably related to the setting up of neuroradiological intervention units in health areas that previously referred patients to CHUAC. The incidence in 2013 was 4.3 cases/100,000 population/year, lower than that described globally in the international literature,[3] influenced by geographic areas with

high prevalence.[6] Here in Spain, we have no general epidemiological data, but there are figures relating to particular autonomous regions which point to a slightly higher incidence (5.7–7 cases/100,000 population/year).[19,20]

Description of the population

In line with other national/international publications,[1,6,13,19,20,21] in our series the demographic characteristics remained stable over the years, with a mean age of 56.9 ± 14.1 years and a higher incidence among females (1.5:1). There are studies that question the female predominance,[17,22] which may be attributed to a heterogeneous population base with geographic differences in healthcare.

Being a young population, there is very little previous medical history and comorbidity (Charlson index: mean 2.0) and we did not detect any differences in this variable in the different periods. The most common previous history was hypertension (40%), followed by use of harmful substances (35%); both were considered the main modifiable risk factors.[6,23] The most common first symptom was sudden/severe headache (75%), similar to that described in the literature.[6,13,24]

The delay in time to hospital care remained stable over the years, with 93.7% of patients admitted within the first 24 h. Reaching hospital early can be related to severity and a worse neurological grade at the time of presentation (coma: 37.4%). The action of the out-of-hospital emergency services is also critical, and in our environment these services are widely deployed with short action times. The pre-hospital delay and delay in diagnosis varies in the literature, depending on the geographical area, but the evidence shows that a delay worsens the prognosis.[23]

Prognostic scales on admission

Apart from enabling comparisons of populations, the distribution of severity scales has prognostic implications.[6] The distribution of clinical grades in our study is similar to that published in other series, making it comparable with previous publications.[13,19,20,25,26] The mean GCS score was 12, similar to that described by Takagi et al. (12.5).[27] More than half of the patients had a good neurological grade (HH I-II: 61.9%; WFNS I-II: 60.5%) and a high risk of developing complications (Fisher 3−4: 70.7%). As far as the overall

severity scales are concerned, most of the published studies do not report them. In our series the mean APACHE II was 11.8 ± 6.8 and total SOFA 2.4 ± 2.8, suggesting low morbidity, with the neurological component being the most important (1.5 ± 1.6) followed by the respiratory component (0.6 ± 0.9).

Diagnostic/therapeutic procedures

In our series, the diagnosis was made by CT without contrast in 99.6% of the patients, with LP only required in two patients, as described in the current guidelines.[6,28,29] It should be noted that this result may be influenced by early access to hospital care, as CT in the first 24 h has a sensitivity of 95%.[24,30]

CT and angiographic study provide aetiological diagnosis in 100% of cases,[30] allowing SAH to be classified into different subtypes. Like the other studies, in our series the most common subtype was SAH-A (78.3%), followed by SAH-I (17.9%) and SAH-PM (3.2%).[6,10,11,20,28,29,31,32] In the case of SAH-I, the rate varies, from 19% to 12.2% depending on the study,[11,28,29,31,33] but with a downward trend over the years. Konczalla et al.[33] report a low incidence of SAH-I (12%) but with an increase in the last 15 years globally, associating it with increased use of antiplatelet/anticoagulant medication. A higher proportion is reported at a national level here in Spain than in international series, but this can be attributed to advances in the sensitivity of diagnostic techniques, as the Spanish studies were earlier in time than the international series.[11,13] In our series, the proportion of SAH-I is lower than in the national series, most likely for the same reasons in terms of timing as above, thanks to the improvements in diagnosis, and a progressive decrease in the use of antiplatelet/anticoagulant medication.

Most of the aneurysms were single, located in the anterior circulation of the circle of Willis, similar to that reported in the literature.[13,28,34,35] Endovascular treatment was performed in 85% of the aneurysms, and considered to be the approach of choice in suitable patients, according to the guidelines in force at the time.[2,6,15] There has also been an increase in the surgical technique in recent years as a result of a more proactive neurosurgical team and protocolisation of the interventional treatment.

Characteristics according to bleeding pattern

In our sample, in contrast to that published by most authors,[6,11,31] the patients with SAH-A were predominantly male, and those with SAH-I predominantly female. However, our results were in line with the literature in terms of the mean age (55-58 years),[6] previous medical history[23] and, in the case of SAH-PM, a younger age at presentation (51.9 ± 12 years) and less hypertension (18.8%).[36]

Patients with SAH-I had a better clinical grade on admission and less blood on CT, compared to patients with SAH-A. Coma was the third most common clinical manifestation in SAH-A (37.6% of this group), with a higher rate than most of the published series.[6,34,37] Schwartz and Solomon[38] reported that 100% of their patients with SAH-PM were grade i-ii on the HH scale, similar to the findings in our series and reaffirming the benign course of SAH-PM.[11] The benign nature of SAH-PM found in all series opens the debate on the need for admission to ICU. However, there are still unanswered questions to be addressed, such as the origin of the bleeding (venous/arterial) and determining factors in the good prognosis of SAH-PM.[36,39] It should be noted that, despite its benign presentation, 100% of the patients with SAH-PM were diagnosed in less than 24 h.

Complications and final outcome according to bleeding pattern

The most serious neurological complication was re-bleeding (10.9%) and the most common vasospasm (49.0%), just as reported in the literature.[22,40] We found differences in complications between subtypes; a higher proportion of neurological complications in SAH-A compared to SAH-I, resulting in a better prognosis at discharge in SAH-I, also similar to other studies.[9,10,11,36,41]

The overall mortality rate in our series was 24%, increasing to 28.2% if only SAH-A were considered, as in other series.[3,13,18,20,21,28,29] We noticed a gradual improvement in the prognosis of the overall sample, measured by the GOS, as time passed. At 12 months after the episode, 85.7% of patients who survived SAH-A and 95.4% of those with SAH-I were independent for activities of daily living (GOS 4-5), figures which slightly improve on international results.[2,3,18] We agree with Nieuwkamp et al.,[5] who report better survival data at one year for SAH-A (89.8%); this could be related to a better management

strategy, more involvement of the Rehabilitation department or patients with greater morbidity dying sooner.

Study limitations

The main limitation is due to the fact that the data was obtained from a single hospital retrospectively. However, the large number of patients we studied gave us a sufficiently large sample size in each of the SAH subgroups to be able to draw conclusions. These patients were grouped according to the same diagnostic criteria and received similar treatments, increasing the internal validity of the study. The study was carried out at a referral hospital for SAH, which could have incurred selection bias as it receives more severe patients. The retrospective nature made it vulnerable to information biases, although these were minimised as data collection was performed by a single researcher. In spite of the limitations, however, our study provides an overview of the developments in this area in the Galicia region of Spain.

Last of all, the results show that, in our population, the number of cases of SAH remained stable in the early years of the study, with a downward trend in the more recent years. SAH-A has a more serious clinical presentation, probably related to the amount of bleeding, which leads to a higher rate of complications and mortality, but those who survive have good functional status at one year. SAH-I represents 17.9% of all episodes and has a better prognosis and lower risk of complications. SAH-PM stands out for its benign nature. A multicentre study would be needed to confirm these data.

Funding

This study has received no specific funding from public, private or non-profit organisations.

Conflicts of interest

None.

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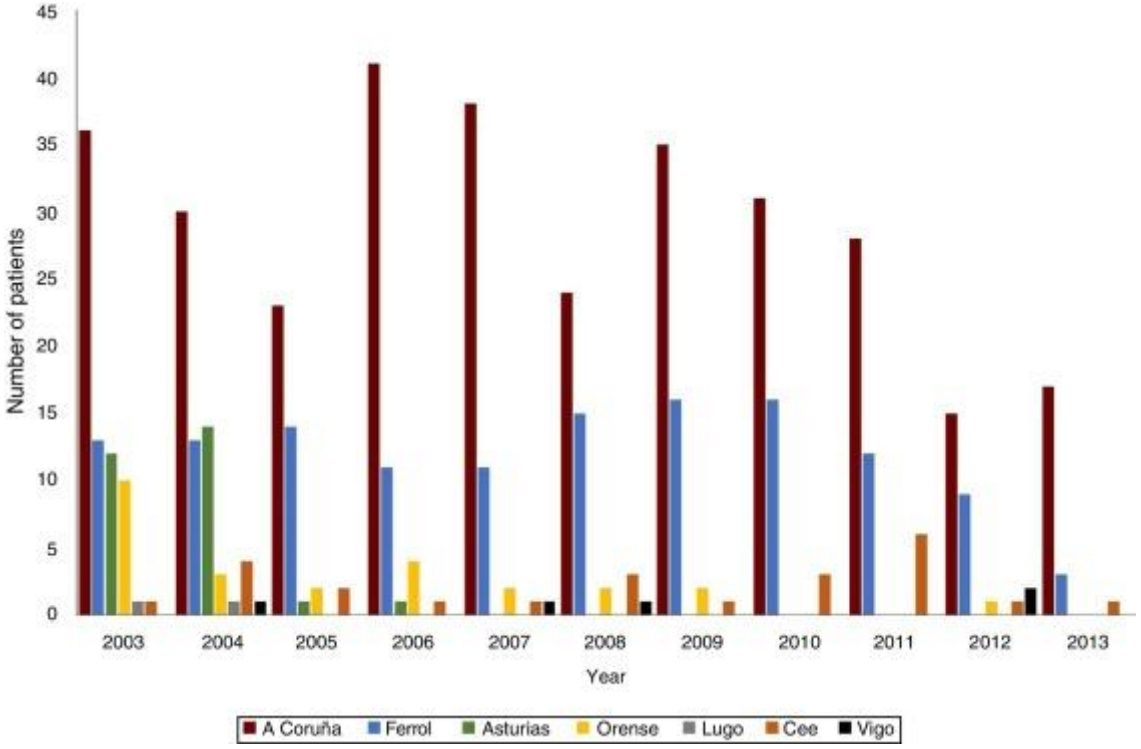

Fig. 1. Distribution according to the reference area of patients with spontaneous subarachnoid haemorrhage admitted to the Intensive Care Unit of Complexo Hospitalario Universitario de A Coruña in the period 2003-2013.

Table 1. Sociodemographic characteristics, previous medical history and clinical manifestations on admission in patients with spontaneous subarachnoid haemorrhage during the study period.

Variable	Total n = 536	2003−2005 n = 181	2006−2008 n = 156	2009−2011 n = 150	2012−2013 n = 49	p[a]
Age (years), mean ± SD (median)	56.9 ± 14.1 (56.5)	56.0 ± 14.5 (55.0)	56.7 ± 15.4 (56.0)	58.5 ± 12.6 (59.0)	56.4 ± 13.0 (54.0)	0.470
Gender, n (%)						0.091
Male	218 (40.7)	87 (48.1)	59 (37.8)	53 (35.3)	19 (38.8)	
Female	318 (59.3)	94 (51.9)	97 (62.2)	97 (62.2)	30 (61.2)	
Previous medical history, n (%)						
Previous SAH	35 (6.5)	18 (9.9)	9 (5.8)	7 (4.7)	1 (2.0)	–
HBP	224 (41.8)	70 (38.7)	71 (45.5)	62 (41.3)	21 (42.9)	0.649
Unhealthy habits	177 (33.0)	68 (37.6)	39 (25.0)	51 (34.0)	19 (38.8)	0.071
Smoking	158 (29.5)	63 (34.8)	35 (22.4)	47 (31.3)	18 (36.7)	
Alcohol	48 (9.0)	21 (11.6)	10 (6.4)	13 (8.7)	4 (8.2)	
Cocaine	7 (1.3)	2 (1.1)	2 (1.3)	2 (1.3)	1 (2.0)	
Migraine	52 (9.7)	19 (10.5)	16 (10.3)	14 (9.3)	3 (6.1)	0.819
Polycystic disease	11 (2.1)	4 (2.2)	3 (1.9)	4 (2.7)	0 (0)	–
Anticoagulants	54 (10.1)	14 (7.7)	16 (10.3)	22 (14.7)	2 (4.1)	0.088
Cancer	42 (7.8)	7 (3.9)	11 (7.1)	18 (12.0)	6 (12.2)	–
Charlson index adjusted for age, mean ± SD (median)	2.0 ± 2.0 (2.0)	1.9 ± 1.6 (2.0)	2.0 ± 1.8 (2.0)	2.2 ± 1.9 (2.0)	2.2 ± 2.3 (2.0)	0.661
Delayed hospital care, n (%)						–
< 6 h	240 (44.8)	90 (49.7)	78 (50)	51 (34.0)	21 (42.9)	
6−12 h	177 (33.0)	53 (29.3)	45 (28.8)	63 (42.0)	16 (32.7)	
12−24 h	85 (15.9)	19 (10.5)	32 (20.5)	28 (18.7)	6 (12.2)	
> 24 h	34 (6.3)	19 (10.5)	1 (0.6)	8 (5.3)	6 (12.2)	

Table 1. Sociodemographic characteristics, previous medical history and clinical manifestations on admission in patients with spontaneous subarachnoid haemorrhage during the study period.

Variable	Total n = 536	2003−2005 n = 181	2006−2008 n = 156	2009−2011 n = 150	2012−2013 n = 49	p[a]
Initial clinical manifestations, n (%)						
Headache	410 (76.5)	148 (81.8)	102 (65.4)	122 (81.3)	38 (77.6)	0.001
Dizziness	290 (54.1)	109 (60.2)	71 (45.5)	86 (57.3)	24 (49.0)	0.037
Focal neurological signs	63 (11.8)	21 (11.6)	19 (12.2)	20 (13.3)	3 (6.1)	0.596
Seizures	69 (12.9)	20 (11.0)	23 (14.7)	18 (12.0)	8 (16.3)	0.649
Coma (GCS < 9)	182 (34.0)	52 (28.7)	65 (41.7)	45 (30.0)	20 (40.8)	0.038
Neurological assessment scales, mean ± SD (median)						
GCS	11.9 ± 4.1 (14.0)	12.2 ± 3.9 (15.0)	11.5 ± 4.4 (14.0)	12.2 ± 4.0 (14.0)	11.4 ± 4.5 (14.0)	0.399
HH	2.7 ± 1.4 (2.0)	2.5 ± 1.3 (2.0)	2.9 ± 1.5 (2.0)	2.7 ± 1.4 (2.0)	2.9 ± 1.4 (2.0)	0.055
Fisher scale	3.2 ± 0.9 (4.0)	3.1 ± 1.0 (3.0)	3.1 ± 1.0 (3.0)	3.3 ± 0.9 (4.0)	3.3 ± 0.9 (4.0)	0.296
WFNS scale	2.7 ± 1.5 (2.0)	2.6 ± 1.4 (2.0)	2.9 ± 1.5 (2.0)	2.6 ± 1.6 (2.0)	2.7 ± 1.7 (2.0)	0.067
Overall assessment scales, mean ± SD (median)						
APACHE II	11.8 ± 6.8 (11.0)	10.6 ± 5.1 (10.0)	15.0 ± 7.4 (13.0)	10.8 ± 6.5 (10.5)	9.1 ± 7.2 (7.0)	< 0.001
SOFA scale	2.4 ± 2.8 (1.0)	1.8 ± 2.4 (1.0)	3.0 ± 3.2 (2.0)	2.3 ± 2.6 (1.0)		

APACHE II: Acute Physiology Chronic Health Evaluation II; SD: standard deviation; GCS: Glasgow Coma Scale; HH: Hunt-Hess; SAH: subarachnoid haemorrhage; HBP: high blood pressure; SOFA: Sequential Organ Failure Assessment; WFNS: World Federation of Neurosurgeons Scale.

[a] Calculated comparing SAH-A to the SAH-I sample. Patients with SAH-PM were excluded as they have a very different prognosis.

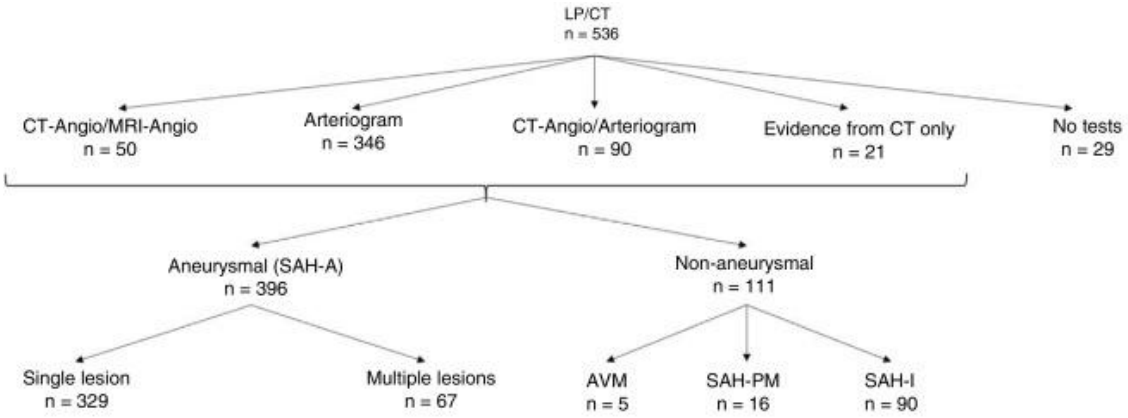

Fig. 2. Distribution of patients after diagnosis of subarachnoid haemorrhage according to the findings of the tests performed. LP: lumbar puncture; CT: computed tomography; SAH-A: spontaneous aneurysmal subarachnoid haemorrhage; AVM: arteriovenous malformation; SAH-PM: spontaneous perimesencephalic subarachnoid haemorrhage; SAH-I: idiopathic spontaneous subarachnoid haemorrhage.

Table 2. Distribution of patients with spontaneous subarachnoid haemorrhage according to the type of lesion during the study period, and therapeutic management of aneurysmal lesions.

Variable	Total	2003−2005	2006−2008	2009−2011	2012−2013	p
Type of lesion, n (%)						
Aneurysmal	396 (78.1)	123 (72.8)	109 (76.8)	122 (82.4)	42 (87.5)	0.008
AV malformation	5 (1.0)	3 (1.8)	1 (0.7)	0 (0)	1 (2.1)	–
Perimesencephalic	16 (3.1)	3 (1.8)	3 (3.5)	7 (4.7)	1 (2.1)	–
Idiopathic	90 (17.8)	40 (23.7)	27 (19)	19 (12.8)	4 (8.3)	0.002
Treatment of the aneurysm, n (%)	322 (81.3)					
Embolisation	306 (95.0)	96 (85.0)	87 (88.8)	94 (87.0)	29 (85.3)	0.866
Total	231 (75.5)					
Partial	59 (19.3)					
Stent	16 (5.2)					
Days from lesion to therapeutic arteriogram, mean ± SD (median)	1.7 ± 3.4 (1.0)	1.7 ± 1.8 (1.0)	1.6 ± 3.8 (1.0)	1.7 ± 2.7 (1.0)	2.8 ± 6.5 (1.0)	0.065
Clipping, n (%)	16 (5.0)	3 (2.5)	3 (2.8)	6 (4.9)	4 (9.5)	–
Days from lesion to surgery, mean ± SD (median)	5.9 ± 12.6 (1.0)	2.3 ± 2.5 (2.0)	11.3 ± 17.9 (1.0)	7.3 ± 17.5 (0)	2.2 ± 2.6 (2.0)	–

SD: standard deviation.

Table 3. Sociodemographic characteristics, previous medical history, clinical manifestations and clinical status on admission according to type of lesion in patients with spontaneous subarachnoid haemorrhage.

Variable	Aneurysmal n = 396	Perimesencephalic n = 16	Idiopathic n = 90	p[a]
Age (years), mean ± SD (median)	56.5 ± 13.6 (56.0)	51.9 ± 12.4 (53.5)	59.7 ± 15.3 (58.0)	0.053
Gender, n (%)				0.003
Male	253 (63.9)	6 (37.5)	42 (46.7)	
Female	143 (36.1)	10 (62.5)	48 (53.3)	
Delayed hospital care, n (%)				0.009
< 6 h	185 (46.7)	9 (56.3)	26 (28.9)	
6−12 h	128 (32.3)	4 (25.0)	34 (37.8)	
12−24 h	58 (14.6)	3 (18.8)	23 (25.6)	
> 24 h	25 (6.3)	0	7 (7.7)	
Previous medical history, n (%)				
Previous SAH	31 (7.8)	0	1 (1.1)	0.020
HBP	168 (42.4)	3 (18.8)	35 (38.9)	0.539
Unhealthy habits	141 (35.6)	6 (37.5)	25 (27.8)	0.157
Migraine	42 (10.6)	3 (18.8)	5 (5.6)	0.143
Polycystic disease	9 (2.3)	0	0	0.221
Anticoagulants	38 (9.6)	2 (12.5)	11 (12.2)	0.455
Cancer	30 (7.6)	0	8 (8.9)	0.675
Charlson index adjusted for age, mean ± SD (median)	2.0 ± 1.9 (2.0)	1.4 ± 1.5 (1.0)	2.4 ± 1.9 (2.0)	0.045
Clinical manifestations on admission, n (%)				
Headache	302 (76.3)	15 (93.8)	79 (87.8)	0.017
Dizziness	215 (54.3)	11 (68.8)	56 (62.2)	0.172
Focal neurological signs	47 (11.9)	0	11 (12.2)	0.926

Table 3. Sociodemographic characteristics, previous medical history, clinical manifestations and clinical status on admission according to type of lesion in patients with spontaneous subarachnoid haemorrhage.

Variable	Aneurysmal n = 396	Perimesencephalic n = 16	Idiopathic n = 90	p[a]
Seizures	58 (14.6)	0	8 (8.9)	0.150
Coma (GCS < 9)	149 (37.6)	0	10 (11.1)	< 0.001
Prognostic scales, mean ± SD (median)				
GCS	11.9 ± 4.0 (14.0)	15.0 ± 0.0 (15.0)	13.4 ± 3.3 (15.0)	< 0.001
Hunt-Hess	2.8 ± 1.4 (2.0)	1.5 ± 0.5 (1.5)	2.1 ± 1.2 (2.0)	< 0.001
Fisher scale	3.3 ± 0.9 (4.0)	2.0 ± 1.0 (2.0)	2.9 ± 1.1 (3.0)	0.001
WFNS	2.8 ± 1.5 (2.0)	1.3 ± 0.4 (1.0)	2.2 ± 1.3 (2.0)	< 0.001
APACHE II	11.8 ± 6.4 (11.0)	8.3 ± 4.7 (8.5)	10.0 ± 5.6 (9.0)	0.015
Total SOFA	2.4 ± 2.6 (1.0)	0.3 ± 0.6 (0.0)	1.3 ± 2.1 (0.0)	< 0.001

APACHE II: Acute Physiology Chronic Health Evaluation II; SD: standard deviation; GCS: Glasgow Coma Scale; HH: Hunt-Hess; SAH: subarachnoid haemorrhage; HBP: high blood pressure; SOFA: Sequential Organ Failure Assessment; WFNS: World Federation of Neurosurgeons Scale.

[a] p value for comparison of the aneurysmal group and the idiopathic SAH patient sample.

Table 4. Complications and prognosis according to the type of lesion.

	Aneurysmal n = 396	Perimesencephalic n = 16	Idiopathic n = 90	p[a]
Complications related to the SAH, n (%)	251 (63.4)	2 (12.5)	29 (32.2)	< 0.001
Re-bleeding	40 (10.1)	0	2 (2.2)	0.012
Vasospasm	176 (44.4)	2 (12.5)	11 (12.2)	< 0.001
Hydrocephalus	122 (30.8)	0	23 (25.6)	0.326
Systemic complications, n (%)	212 (53.5)	1 (6.3)	34 (37.8)	0.007
In-hospital mortality, n (%)	113 (28.5 %)	0	11 (12.2)	0.001
Prognostic scales				
GOS[a] on discharge from ICU, mean ± SD (median)	3.9 ± 1.0 (4.0)	4.9 ± 0.3 (5.0)	4.4 ± 0.8 (5.0)	< 0.001
4−5, n (%)	195 (65.2)	16 (100)	69 (85.2)	0.001
≤3, n (%)	104 (34.8)	0 (0)	12 (14.8)	
GOS[a] at 6 months, mean ± SE (median)	4.2 ± 0.9 (5.0)	4.8 ± 0.4 (5.0)	4.7 ± 0.7 (5.0)	< 0.001
4−5, n (%)	190 (78.8)	15 (100)	64 (92.8)	0.008
≤3, n (%)	51 (21.2)	0 (0)	5 (7.2)	
GOS[a] at 12 months, mean ± SE (median)	4.5 ± 0.8 (5.0)	4.9 ± 0.3 (5.0)	4.8 ± 0.6 (5.0)	0.011
4−5, n (%)	203 (85.7)	15 (100)	62 (95.4)	0.034
≤3, n (%)	34 (14.3)	0 (0)	3 (4.6)	
Rankin at 6 months, mean ± SE (median)	1.7 ± 1.4 (1.0)	0.6 ± 0.7 (1.0)	1.0 ± 1.3 (1.0)	< 0.001
≤ 3, n (%)	167 (70.8)	13 (100)	59 (88.1)	0.004
3−5, n (%)	69 (292)	0 (0)	8 (11.9)	
Rankin at 12 months, mean ± SE (median)	1.1 ± 1.4 (0.0)	0.3 ± 0.6 (0.0)	0.6 ± 1.0 (0.0)	0.016
≤ 3, n (%)	195 (83.3)	13 (100)	58 (93.5)	0.042
3−5, n (%)	39 (16.7)	0 (0)	4 (6.5)	

SD: standard deviation; GOS: Glasgow Outcome Scale; SAH: subarachnoid haemorrhage; ICU: Intensive Care Unit.

[a] p value for comparison of the aneurysmal group and the idiopathic SAH patient sample.