Research Article

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Epidemiology, clinical presentation, treatment and prognostic factors of subaracnoid aneurysmatic hemorrhage. descriptive and analytical study between the years 2010 and 2020

Abstract

Aneurysmal subarachnoid haemorrhage (SAH) is a very serious neurosurgical problem, associated with high rates of morbidity and mortality. After the initial haemorrhage, up to 50% of the patients die, and 30-40% of the patients suffer a new bleeding during the first month. The percentage of deaths due to a new bleeding is between 60% and 75%. Both endovascular embolization and surgery treatments reduce the mortality rate and improve the quality of life of the survivors. In recent years, endovascular embolization has become the method of choice to prevent new bleeding, especially in Europe, widely replacing surgery. The aim of this study was to describe a series of patients with spontaneous subarachnoid haemorrhage, secondary to aneurysmal rupture, treated at the University Hospital of Getafe between 2010 and 2020, to study the different diagnostic and treatment options, and to define the most important prognostic factors. In addition, compare the results of both treatments (surgical and endovascular).

We studied 110 patients, 58 men and 52 women, with an average age of 40.8 years. A retrospective study has been carried out, reviewing clinical histories and collecting epidemiology. Of the total, 25 patients have been treated surgically and 85 by endovascular embolization. It has been established that the best management in this type of patients is the performance of Computed Tomography (CT) of the skull and cerebral arteriography, as well as admission for surveillance in the ICU. In this study, the neurological clinical situation at admission, the volume and distribution of blood in the CT and the age of the patient, seem to be the most influential variables in the final result.

Keywords: subarachnoid aneurysmal hemorrhage, surgical treatment, endovascular embolization

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Introduction

Concept of subarachnoid haemorrhage (SAH)

The SAH is an extravasation of blood in the subarachnoid or leptomeningeal space. Head injury is the most common cause of subarachnoid hemorrhage. Primary spontaneous subarachnoid hemorrhage is most often caused by the rupture of a cerebral aneurysm, although there are other causes such as vascular malformations, brain tumors, alterations in the vascular wall and alterations in coagulation. From 15% to 25% of cases there is no cause of bleeding, this group being idiopathic subarachnoid hemorrhage whose prognosis is much more benign.[1] Several risk factors for SAH have been implicated, including high blood pressure, smoking, alcohol and sympathomimetic drug use.[2] Some studies have described a greater frequency of cases in relation to meteorological stations, when a greater frequency appears in winter and spring, or in relation to pressure changes. However, these data have not been corroborated in national studies.[3] It seems that there is a familial predisposition to the formation of aneurysms and therefore to suffer from SAH. There are genetic syndromes with a greater predisposition to presenting aneurysms such as autosomal dominant polycystic kidney disease or Ehlers-Danlos type IV[4] disease. These syndromes support the possible existence of a family aggregation in the presence of aneurysms. The best prevention of SAH would be to detect those patients with cerebral aneurysms and treat them before they rupture. In autopsy and radiological studies it has been estimated that the prevalence of incidental aneurysms (IA) in the general population is around 2%, although other studies have observed a constant increase in the frequency of aneurysms with age ranging from 1% to 30 years, and from 3 to 8% between 40-70 years. With the increase in modern neuroimaging techniques, it is increasingly common to make a decision before a patient with an incidental aneurysm.[5] The ideal treatment in these cases is still the subject of discussion due to the selection of the populations included in the different studies. King in 1994 carried out a systematic study and a meta-analysis of the most important series published up to that date. In this study, a morbidity of 4.1% and a mortality rate of 1% was observed in the selectively treated patients. However, the risk factors to be taken into account to indicate the surgical treatment could not be identified. In 2014, the results obtained in the International Study of Incidental Intracranial Aneurysms were published. This work consists of a group of 1449 patients in whom the natural history is retrospectively analyzed and a second group of 1172 patients in whom the morbidity and mortality of the treatment is analyzed prospectively. The average incidence of bleeding is 0.5% / year. This figure varies depending on the size of the aneurysm, with an incidence of rupture of 0.05% / year in aneurysms smaller than 5 mm and without a history of previous SAH; about 1% / year in patients with aneurysms greater than 10 mm and 6% / year in giant aneurysms. In this analysis, aneurysmal size (> 10 mm) and location (vertebrobasilar) are independent predictors of rupture. The morbidity and mortality found in the prospective study was much higher than that reported to date (13-15% per year), with age being the main predictive factor.[6] Therefore, they concluded that the risk of rupture in small aneurysms was very low, exceeding the surgical treatment the risk of rupture in these cases. However, several editorial notes have been published refuting these conclusions due to the bias introduced when comparing both populations. Other authors have identified factors dependent on the individual and the aneurysm as predictors of rupture of an AI, among which are the age over 60 years, the female sex, the location in the posterior circulation, the size greater than 5 mm and if it is a symptomatic aneurysm. The decision to treat an AI should be individualized in each case taking into account the age, size and location of the aneurysm, base pathology and experience of the surgical and endovascular team.

Incidence and prevalence

SAH accounts for 6 to 8% of all acute cerebral vascular diseases, although its importance is that it affects younger patients in general than ischemic stroke and has a high morbidity and mortality. Its incidence has not changed significantly in recent years. New therapeutic methods have been introduced and increasingly protocols are used that seem to have improved the overall mortality of this disease in recent decades. Aneurysmal subarachnoid hemorrhage (SAH) is a frequent and potentially curable disease, although morbidity and mortality, considered globally, is high. Up to 12% of patients who suffer from it are not properly diagnosed or die before reaching the hospital, and about 30% of patients who arrive alive to the hospital die in the first days. In addition, morbidity is significant in 50% of survivors.[7] Hospital mortality in our country is similar to that described in international studies, being 26%. The incidence of SAH has remained practically stable over the past 30 years, unlike other types of strokes. The age of presentation most frequent in the SAH is around 55 years, increasing the incidence with increasing age. In the epidemiological studies analyzed, a higher incidence is observed (between 1.6 and 4.5 times) in women, especially after 55 years of age. In our setting, since there is no centralized registry, it is impossible to know the exact data on the incidence and prevalence of SAH.[9]

Clinical presentation and diagnosis

Although the early treatment of aneurysms is increasingly widespread, rebleeding continues to be an important cause of mortality and morbidity. The risk of rebleeding with conservative treatment of aneurysms is up to 30% in the first month, subsequently stabilizing at 3% per year. The risk of rebleeding increases in patients with high blood pressure, poor clinical grade and in those in whom the period between diagnosis and treatment is higher. Rebleeding is the leading cause of treatable mortality and should be avoided. Before the "greater" rupture of an aneurysm, premonitory symptoms ("sentinel headache") can occur in up to 45% of cases.[10] The most frequent symptom is a sudden headache. Although there is no perfect scale, today the most validated are Hunt and Hess and the one proposed by the World Federation of Neurosurgical Societies, WFNS (I GCS 15 No Focal, II GCS 14-13 No Focal, III GCS 14-13 Yes Focal; IV GCS 12-7 Yes / No Focal; V GCS 6-3 Yes / No Focal) based on the Glasgow comma scale whose disaggregated score should also be recorded.

Computed tomography (CT) is the most sensitive test in the diagnosis of SAH and should always be practiced as soon as possible after the clinical suspicion of SAH. The quantification of the blood supply in the subarachnoid space is very difficult to determine. The scale most used today is Fisher's, although others have been proposed that take into account the volume of intraventricular bleeding. Clinically, the Hunt and Hess Scale is also used. However, the standard test for the diagnosis of aneurysms responsible for SAH is still cerebral angiography (Figure 1) to rule out the presence of underlying vascular pathology.

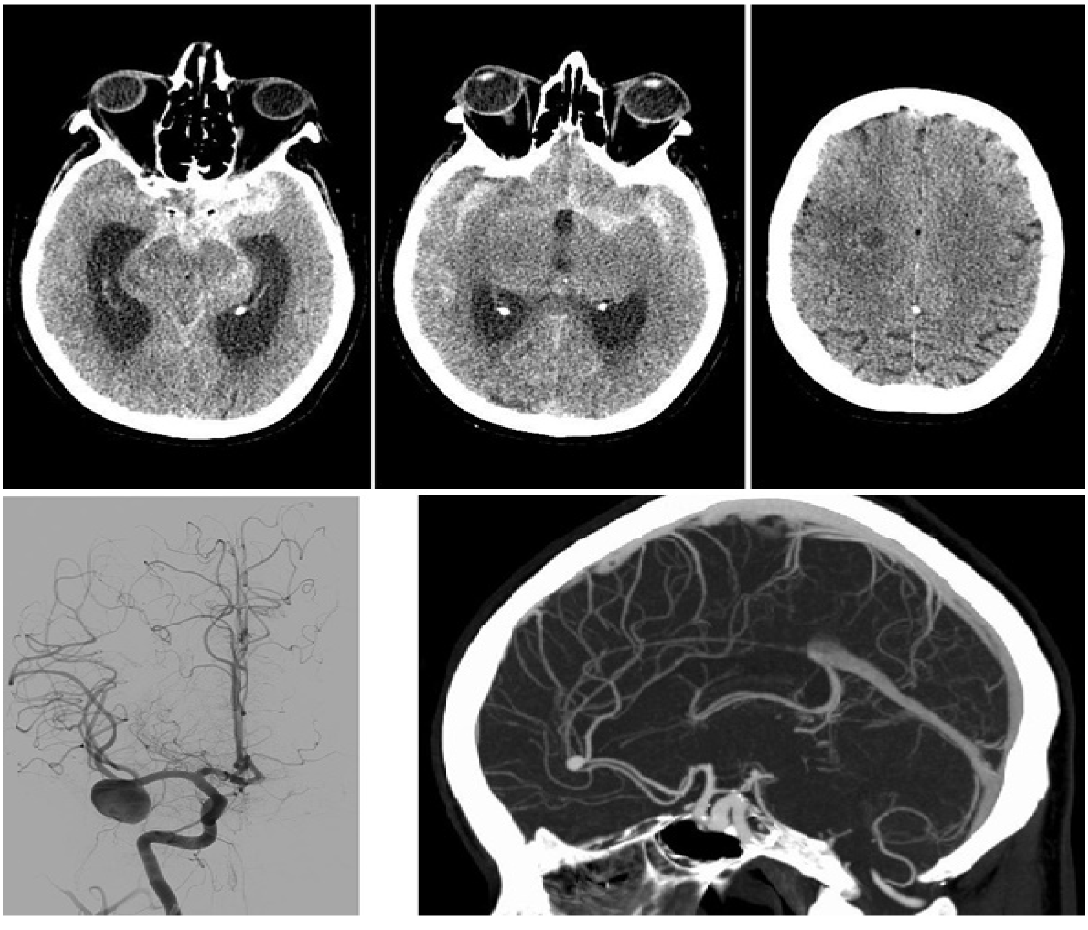

Figure 1 Images of SAH in CT (Above) and cerebral Arteriography with aneurysm of middle cerebral artery (Down).

Treatment

There is not yet a general consensus among different authors to treat the different aspects of this disease and the management protocols have changed considerably over time, varying between different centers and countries. Recently, most of the centers tend to adopt a more uniform management protocol, specially designed to improve the overall evolution of the disease and not only of the cases selected for surgery.[11] To fit these protocols successfully, close collaboration between neurologists, neurosurgeons, intensivists and interventional neuroradiologist is necessary. The fundamental objectives for a correct treatment of this disease are:

i. Early diagnosis: in 20% of cases the first hemorrhage is not diagnosed adequately. Immediate transfer to a hospital center with Neurosurgery, ICU, and Neuroradiology services is essential. The neurosurgeon would be responsible for coordinating the different specialists integrated in the management of the SAH.
ii. Prevention of rebleeding: by surgery and / or embolization.
iii. Stabilization of the critical patient in the ICU, in order to try that the majority of cases are potentially treatable, through surgery and / or embolization.
iv. Prevention and aggressive treatment of cerebral ischemia, especially in cases in which the aneurysm has already been occluded.

Surgical treatment

The primary purpose of surgical treatment is to avoid rebleeding, with the appropriate placement of a clip in the aneurysmal neck. Coating ("coating") or bagging ("wrapping") of the bag is not recommended, as it does not significantly reduce the risk of rebleeding. The "trapping" of the aneurysm or the carotid ligature may be indicated in certain occasions.[12]

Endovascular treatment

In the early 90's, endovascular embolization with coils ("coil") of platinum was introduced.

The main indications of embolization, although these are in continuous evolution and change are fundamentally:

i. Failure of the surgical exploration.
ii. Poor initial clinical grade.
iii. Bad medical condition.
iv. Complex aneurysms with high surgical risk.
v. Aneurysms of posterior circulation.
vi. No surgical indication due to anatomical considerations.

Embolization is not clearly indicated or its results will be lower in aneurysms with wide necks, intraparenchymal hematomas that require urgent evacuation, giant and large aneurysms of easy neurosurgical access (in anterior circulation), middle cerebral aneurysms and very small aneurysms (< 2 mm). In the case of multiple aneurysms, the aneurysm with more chances of rupture will begin, for which the following signs will be assessed:

i. Blood distribution in initial CT.
ii. Larger aneurysms.
iii. Lobulated or irregular edges of the aneurysm.
iv. The most proximal aneurysm.

The main complications and their most appropriate treatment after SAH are rebleeding, vasospasm / ischemia, hydrocephalus or seizures.

Prognostic factors

In many studies Glasgow scales have been used, both the scale for Coma and the Evolutionary or Prognostic scale, as indices of clinical outcome of the treatment of aneurysmal SAH. However, both scales have a high interpersonal variability and are dependent on the residual clinical status pre-treatment, so they are not universally accepted, with some questions. The ultimate goal, both surgery and embolization, is to avoid rebleeding, maintaining the best possible neurological situation. The final result of the SAH treatment also depends on the patient's medical care, such as the anti-vaso-spasm measures, the prophylaxis of seizures and the treatment of associated complications, procedures well described in a large number of protocols. The relative merits of both conventional surgical treatment and endovascular embolization depend both on their safety (risk of associated medical complications, hospital stay or neurological integrity, among others) and on their ability to prevent re-bleeding.[1]

Approach and objectives

Spontaneous subarachnoid hemorrhage (SAH) is a neurological emergency characterized by the extravasation of blood within the spaces that cover the central nervous system and that are normally occupied by cerebrospinal fluid (CSF). The main cause of non-traumatic SAH is the rupture of an intracranial aneurysm, which accounts for around 80-85% of cases and has a high mortality rate and complications. Non-aneurysmal SAH includes isolated perimesencephalic SAH (10-15% of cases), which has a good prognosis with few neurological complications and a large number of very infrequent causes that explain the rest of the cases. Saccular aneurysms develop at the points of arterial division, usually in the polygon of Willis or in the next branch. Most intracranial aneurysms never break. The risk of rupture depends directly on the size and location of the aneurysm. The major modifiable risk factors for SAH are hypertension, smoking and excessive alcohol intake; they all more or less double the risk. The factors that precipitate the rupture of an aneurysm are complex; in 20% of the cases the SAH is preceded by some type of effort that implies an increase in blood pressure, but they are not necessary factors. The diagnosis and acute phase management of SAH represent a challenge for neurologists, neurosurgeons, anesthesiologists, interventional radiologists and intensivists. Angiographic studies serve to identify the existence of one or more aneurysms as potential causes of bleeding and study the anatomical configuration of the aneurysm in relation to the adjacent arteries, which allows an optimal treatment selection (surgical clipping or embolization).

Considering all of the above, this work tries to fulfill the following objectives:

A. Collect a wide range of patients who have suffered SAH, and study their epidemiological profile and their most common clinical presentation.
B. Design a practical scheme of clinical performance in these patients, as well as describe the risk factors that determine the probability of developing complications in the group of patients suffering from SAH, studying the main factors that influence the clinical evolution. Determine the best possible medical treatment. Bibliographic review.
C. Compare, in a simple way, the conventional surgical treatment ("clip") with the endovascular embolization therapy ("coil"). Advantages and disadvantages. Results
D. Analyze the different clinical variables that can act on the "good" or "bad" result, and the final prognosis of the patient suffering subarachnoid hemorrhage.

Material and methods

A retrospective study of the review of clinical histories of patients presenting with aneurysmal SAH treated at the University Hospital of Getafe, Madrid, Spainm, from 2010 to 2020 has been carried out.

The inclusion criteria (110 patients) were: spontaneous SAH. Cerebral arterial aneurysm. Treatment of the aneurysm either by classic surgical clipping or by endovascular embolization.

Exclusion criteria (56 patients) were: traumatic or "unfiliated" (non-aneurysmal) SAH. Patients admitted for treatment of asymptomatic cerebral arterial aneurysms ("not broken" or incidental aneurysms). Patients treated in other centers. Patients in whom it was decided not to carry out treatment. History and / or incomplete data.

With the revision of the Clinical Histories the following variables have been collected:

i. Age
ii. Sex.
iii. Date Of Entry.
iv. Clinical Situation To The Income According To The Wfns Scale.
v. Medical Background.
vi. Fisher Scale
vii. Scale Of Hunt And Hess.
viii. Number Of Aneurisms Found In The Arteriography.
ix. Anatomical Localization Of The Aneurism Responsible For Bleeding.
x. Type Of Treatment Carried Out (Classic Surgical Clipping *Versus* Endovascular Embolization), Date Of The Same
xi. If A New Re-Treatment Has Been Required.
xii. Number Of Days Of Stay In Icu.
xiii. Complications.
xiv. Morbidity.
xv. Re-Bleeding Development.
xvi. Final Evolution To The Hospital Alarm, According To The Glasgow Scale.
xvii. Evolution Through Interview After High.

With the data obtained in the work, the incidence of SAH has been calculated in relation to the sanitary area dependent on the University Hospital of Getafe, the overall hospital stay, the stay in the ICU, the number of hospital admissions per patient in the Neurosurgery Service, the number of readmissions required in the plant, the number of readmissions in the ICU, the delay between the SAH and the treatment and the post-treatment hospital stay. The aneurysmal locations have been grouped into Anterior Communicating Artery, Posterior Communicator, Internal Carotid, Middle Cerebral, Posterior Cerebral Circulation or others. Both treatments have been compared according to the average global hospital stay, the number of patients with average hospital admissions, the number of patients who have re-admitted, the average stay in the ICU, the time delay between the SAH and the treatment, the number of patients with post-treatment morbidity, the number of patients who have required re-treatment, the number of patients who have developed re-bleeding and the final outcome, as a result of "good" (good recovery or moderate disability) or "bad" (severe disability) , persistent vegetative state or exitus).

The final evolution of the patient with subarachnoid hemorrhage was determined at the time of hospital discharge. Within the chapter on analytical statistics, the Chi-square test has been used for the bivariate study. The limit of statistical significance has been established in a confidence interval of 95% ($p < 0.05$). The IBM SPSS 22.0 statistical package (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY: IBM Corp.) has been used. In the future, the Neurosurgery Service of the Hospital de Getafe, collecting patient data between 1995 and 2020, will assess the influence of various variables on a previously established model, generally good or bad evolution, enabling the realization of a scale of prognostic factors, and through various mathematical models, an index of prognostic reliability.

Results

Descriptive study

166 Clinical Histories have been reviewed, 56 patients were excluded due to the fact that they did not meet inclusion criteria or fulfilled exclusion criteria, so finally in this study we analyzed the data of 110 patients with aneurysmal SAH. Of these, 25 have been treated by surgery and 85 with endovascular embolization. The presence of multiple aneurysms has been demonstrated in 15.73% of patients (clipping = 12.94% versus embolization = 21.79%). Of the total of 110 patients, 52 were women (47.28%) and 58 men (52.72%). The age range ranges from 14 to 82 years with an average age of 40.8 +/- 13 years. The average annual incidence estimated in the study was 1.85 +/- 0.64 per 100,000 inhabitants, per year (considering the health area dependent on our center as of 863,000 inhabitants).

No statistically significant differences were found in the two groups in relation to the mean age at admission ($p = 0.13$), sex ($p = 0.12$) and the presence of multiple aneurysms ($p = 0.08$). . On the other hand, statistically significant differences ($p < 0.04$) were found in the aneurysmal location, according to the groups described above.

When comparing both types of treatment (Figure 2), no statistically significant differences were found in the mean global hospital stay (clipados = 32 days, embolized = 28 days, $p = 0.29$); the number of admissions made by each patient; the number of patients who needed new admission (clipping = 59.41%; embolized = 65.38%, $p = 0.37$); the average stay in ICU (clipados = 8 days; embolized = 9 days, $p = 0.47$); the time elapsed since the SAH and the treatment applied (clipping = 6 days; embolized = 4 days, $p = 0.13$); the average postoperative stay (clipping = 23 days, embolization = 23 days, $p = 0.98$) and morbidity that developed after both surgical or vascular procedures (clipping = 5.76%; embolization = 1.13%, p = 0, 62).

A total of 15 patients have required new treatment. Of these, 10 have been due to the presence of multiple aneurysms. But only 5 of them have required "true" re-treatment in the initial aneurysm. Statistically significant differences have been found in relation to the number of patients who required re-treatment (both for multiple aneurysms and for "true" re-treatment), the endovascular group being the one that most patients required re-treatment (clipping = 8.24% *versus* embolized = 20.51%, $p < 0.007$). By excluding re-treatments due to multiple (incidental) aneurysms, the significant differences remain, showing a higher percentage of patients who have required a "true" re-treatment among previously embolized patients (clipping = 1.18% *versus* embolized = 10.26%, $p < 0.003$). Nevertheless, it should not be forgotten that the "n" compared in this case is quite small and that the size of the sample may not have enough statistical power. A total of 10 patients have developed re-bleeding. Of these, 4 patients presented re-bleeding pretreatment and 6 post-treatment. All of them were secondary to re-bleeding of the initial aneurysms, although in 4 of them multiple incidental aneurysms coexisted at a distance.

Analyzing the total of rebleeds, although no significant differences were reached between the two procedures, the results show a greater tendency to re-bleeding in the embolized group (clipping = 5.88% *versus* embolized = 12.82%, p = 0.06). This trend reached statistical significance by excluding patients who had bled before treatment and analyzing those who truly re-bled post-treatment (clipping = 2.35% *versus* embolized = 11.54%, p <0.006), although it is true that the sample is small, so this feature remains pending confirmation.

No statistically significant differences were found in relation to the percentage of hospital deaths among patients treated in our center, although there is a trend towards a higher percentage of deaths among surgically treated patients (clipping = 8.97% *versus* embolized = 2.94 %, p = 0.055).

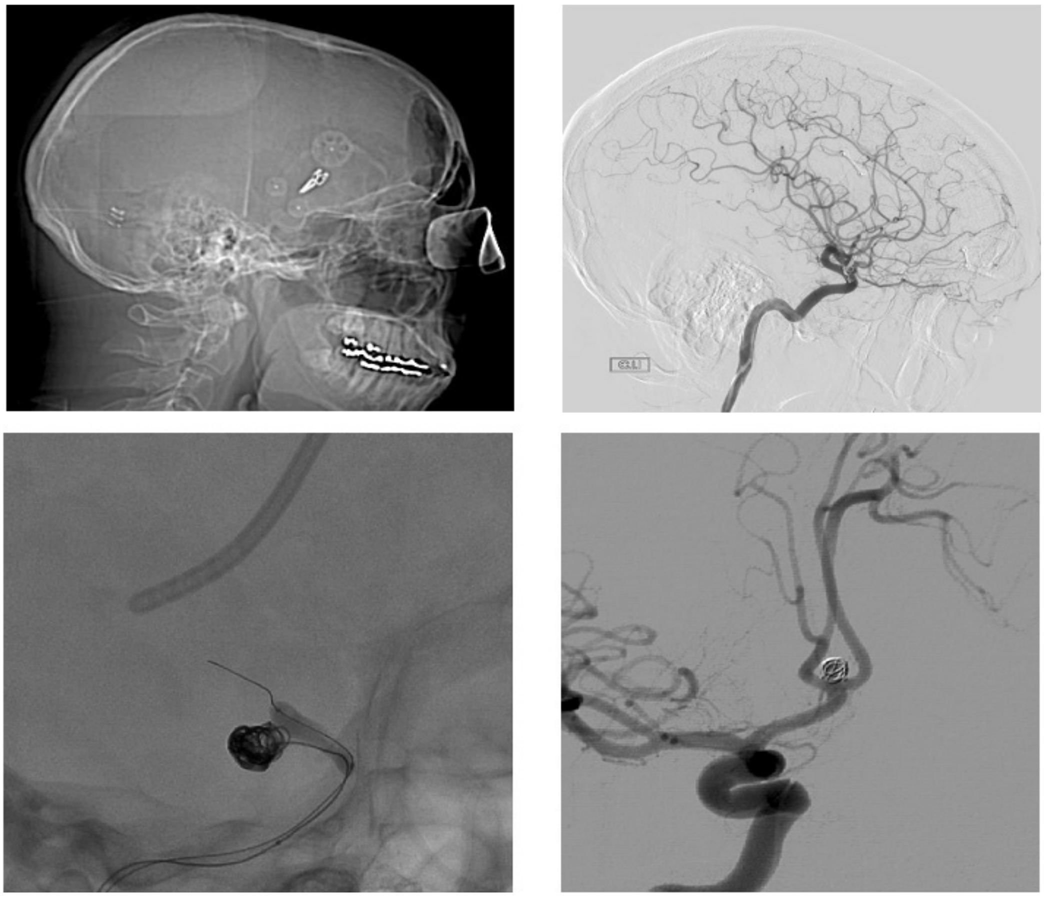

Figure 2 Surgical treatment in upper images and endovascular embolization in lower images.

Results

Main forecast variables

The variables that showed statistical significance (p <0.05) in the final result were:

a. Clinical and neurological situation at admission, according to the Glasgow scale for coma (WFNS).

b. Fisher's scale, according to the CT findings.

c. Age of the patient (Worse prognosis in people over 55 years of age) (Table 1).

Table 1 Global results according to the Glasgow Outcome Scale (GOS)

General outcome results:	
Good recovery	44
Moderate disability	36
Severe disability	10
Persistent vegetative state	8
Exitus	12

Discussion

The incidence of stroke in general has decreased in the last decade mainly due to the decrease in smoking and the better control of arterial hypertension.[1,9] Given that both factors are also risk factors for SAH, we would expect to find a similar decrease in the risk of SAH. However, the decrease found in a recent meta-analysis of different epidemiological studies has been only 0.6% in the last two decades.[2] A detailed analysis of the epidemiological studies published to date shows that the incidence of SAH is around 9 / 100,000 inhabitants / year.[3,4] In Finland or Japan for unknown reasons, figures have been reported that triple this incidence.[5] There are no general epidemiological data in our country on the incidence of this disease, although there is some partial data referring to some autonomous community, with the estimated incidence of SAH being lower than in other countries, since in these studies it does not exceed 5 cases annual per 100,000 inhabitants.

Many studies find a predominance of women between 55 and 85 years, but instead recognize that there were more cases of male sex in adults aged between 25 and 45 years, which corresponds to what was reflected in our research. With regard to age, there was a predominance of the group of ages between 44 and 56 years, which coincides with many publications by different authors[7-9]. Several studies found a predominance in the age group of 45 to 65 years with a higher number of women than men, and in other series a predominance of individuals with average ages of 55 years was published.

The SAH prevailed the less severe clinical group (Hunt and Hess grade I and II), which corresponds to several authors. The initial clinical condition had a statistically significant association with the state at hospital discharge. However, although there was a predominance of low clinical grades, when applying the multivariate analysis, the clinical grade variable III-IV-V of Hunt and Hess was significant, implying an unfavorable evolution risk 14.3 times higher than the patients with Initial clinical grades I and II. Several authors publish that grades III and IV of the Hunt and Hess scale behave as predictors of mortality and severe disability after hemorrhage, also relating it to neurological deterioration early in the hours after subarachnoid bleeding. Another study shows a predominance of patients with less severe degrees (I and II), finding no significant association between this variable and the state at discharge.[5]

The use of the Fisher scale to estimate the intensity of bleeding in the subarachnoid space is a standard step for several decades. It has been seen that increasing its score is more frequent the appearance of significant intracranial complications such as cerebral vasospasm and hydrocephalus. However, other studies did not find significant differences between the pattern in the CT of the hemorrhage and the long-term prognosis of the patients. This does not coincide with the present study where there was a statistically significant association between the initial status and the clinical condition at discharge.Other authors associate grades III and IV (Fisher's scale) with an unfavorable evolution, being predictive of poor prognosis. Several authors agree that complications during hospitalization are frequent, assuming in many of them a predominance of non-neurological complications. Regarding neurological complications, there was a predominance of rebleeding and symptomatic cerebral vasospasm (28.6% each), however, rebleeding was demonstrated as an independent predictor of poor evolution, with similar publications in other articles.[3,7,12] Risk factors for rebleeding are essentially, the delay in admission and in the beginning of treatment, high blood pressure, although it is more related to changes in blood pressure, than to a certain number, and the poor neurological situation on admission. . In the research carried out in several studies, this variable turned out to be an unfavorable factor of evolution as demonstrated in the logistic regression analysis, with a predictive estimate of poor prognosis that was 9.7 times higher than that of patients without rebleeding.

Another of the neurological complications present in our study was symptomatic cerebral vasospasm. This complication usually appears between days 4 and 12, with cases of vasospasm occurring up to several weeks after the initial bleeding or earlier onset from the first 48 h. The presence of angiographic vasospasm occurs in up to 66% of patients, but symptomatic vasospasm (late cerebral ischemia) is only 30%. Its intensity is directly related to the amount of blood extravasated initially.

In one study, they reported high mortality in patients with symptomatic vasospasm (42%) after subarachnoid bleeding, 5 with cognitive and behavioral changes being the most common manifestations. There was a statistically significant relationship between the symptomatic vasospasm and the state at hospital admission, although this variable was not included in our statistical model. The finding may be due to the close relationship that this variable has with the state at hospital admission and the assessment of the amount of bleeding by means of the Fisher scale. As reflected by different authors, the rupture of the intracranial aneurysm as the main cause of subarachnoid bleeding (60%) also predominated in our study. The main location of the aneurysms was at the level of the anterior cerebral artery (42.9%), which corresponds to that published in different studies. Although a statistically significant association was found between the causes of SAH and the state at hospital discharge, there was no statistical significance between the aneurysmal cause and the unfavorable outcome when performing the multivariate analysis in various publications[2,4,10]. This can be explained by the predominance of patients with aneurysmal SAH in these studies and the close relationship of this cause and the main neurological complications presented by patients, one of them being a predictor of poor outcome (rebleeding). There was a discrete predominance of patients with clinical evolution favorable to discharge, which has been previously collected in several studies. Because of the progress of diagnostic means and medical care, the prognosis for these patients has improved significantly in recent decades. However, the current epidemiological data still indicate a high percentage of disability (33%) and death (44%) among patients with SAH.

In relation to the factors of poor prognosis determined in our work, highlights among others already referred in the results and concordant with the published on the subject, the combination of the deepening of the clinical grade of patients (III-IV-V according to Hunt and Hess) and rebleeding, aspects also expressed in other investigations. Within the limitations of this work, in addition to the fact that the prognosis has a multifactorial relationship, which indisputably not only groups the variables we address, it is a retrospective study. It is also valid to mention the possible introduction of biases during multivariable analysis models. The tools of clinical prediction in patients with subarachnoid hemorrhage constitute a topic of current interest. These allow to quantify the relative contribution of certain variables (for example: WFNS degree at admission, age, large aneurysm size, multiple aneurysms, clinical vasospasm, previous hypertension) and condensed information that identifies important indicators or predictors. However, its determination is limited due to the heterogeneity of the patients studied, regional variations in the treatment, and different points of view on the scales of assessment and prognosis. In the present study, they were predictive factors of poor prognosis at discharge: the clinical status at admission grade III-IV-V according to the Hunt and Hess scale and the rebleed neurological complication. Mortality in SAH is reported internationally in up to 50% of cases; this figure does not agree with what was collected in our study. One of the main predictive variables in our patients was the time of surgical delay. It is possible that acute complications such as vasospasm, cerebral infarction, rebleeding, edema or intracranial hypertension are responsible for such high mortality at this early stage and that aggressive medical, surgical or endovascular management can improve the final prognosis of these patients. Vasospasm is considered the main cause of death or disability and refers to intracranial vasoconstriction that occurs between days 3-15 after hemorrhage. The cause of vasospasm is unknown and even with aggressive therapy it is capable of developing ischemia, infarction and death. Although the acute complications presented by our patients were not evaluated as part of this work, it is possible that some of the causes mentioned are responsible for the deaths.

Hyperglycemia has been shown to be a powerful predictor of poor prognosis in many forms of acute brain injury. Specifically, in patients with SAH, elevated glucose levels at admission have been shown to be a marker of disease severity and are associated with poor functional prognosis and death at 6 months. This reinforces the possibility that hyperglycemia, on admission, is a marker of the severity of the disease and that it is probably a consequence of the exaggerated release of catecholamines during the acute hemorrhagic event. One of the independent factors that was observed with greater prevalence in the patients who died was a history of systemic arterial hypertension, being found in 50% of the fatal cases. Undoubtedly, the treatment of patients with SAH is a challenge. However, during the last decade there has been a decrease in mortality, attributed in part to an increasingly precocious treatment and to the increase of new technologies in the field of diagnostic imaging, as well as surgical procedures. However, it is estimated that the partial or total dependence of patients who survive an SAH reaches up to 20% when patients are evaluated at 12 months, which is in the range of what is published in this series.

Several factors have been associated with a poor evolution, among them: advanced age, female sex, race and previous medical history, among many others. Different factors related to adverse evolution demonstrated in other studies were hyperglycemia, systolic arterial hypertension and clinical status at admission, according to the WFNS[7] scale. Not only the hyperglycemia as a metabolic disorder has been related to an unfavorable prognosis, but also the own variations of the glycaemia, as demonstrated in a recent study, where the variability was associated to a greater cerebral suffering and high mortality. The figures of systolic blood pressure above 160 mmHg were an independent factor of poor prognosis, but it was not analyzed if this is due to its relationship with rebleeding.[8]

Similar situation we present for clinical status at admission and with the highest degrees in the Fisher scale and vasospasm. In the opinion of the authors, it is probably more due to a multifactorial contribution, than a single factor, if we take into account that patients with greater bleeding usually have a worse clinical condition and are more prone to present rebleeding, hydrocephalus and vasospasm, as well as major surgical complications. The complications that were demonstrated as independent predictors of poor outcome were respiratory sepsis, hydroelectrolytic disorders, hydrocephalus, rebleeding, symptomatic vasospasm, cerebral infarction and multiple rebleeding, with very similar publications in other studies. Rebleeding is recognized as one of the complications of worse prognosis and higher mortality. This is reflected in various investigations, which is why it is recommended that surgical treatment be performed as soon as possible. Although there are many difficulties that must be faced to achieve this goal. It should be noted that in other studies there was no relationship between sepsis and the prognosis of patients, as opposed to what is reported in other studies, and in the authors' opinion it is due to the grouping of several conditions that are not similar in as for gravity, as is the case of sepsis of the central nervous system and phlebitis, which could have constituted a source of bias. Undoubtedly, complications are one of the most important factors in the evolution of patients, which is demonstrated in the analysis of the number of complications of the present work, which was most influenced by the absence of complications in the favorable evolution. It is also necessary to point out that, according to the authors, the poor evolution of patients undergoing mechanical ventilation and treatment in an Intensive Care Unit is due to the greater severity of the course of their disease, not to poor attention in these units. Within the limitations of this work are those that are derived from the design (retrospective observational), in addition to the prognosis has a multi-causal relationship, which undeniably not only groups the variables we address.

In our study, we collected two groups of patients, homogeneous, uniform and comparable, that could be grouped into those operated surgically and in patients with embolized aneurysms. Significant differences can be observed in the aneurysmal location. For the treatment of the patients attended in the University Hospital of Getafe, the clinical guidelines universally accepted at each moment were followed. We hypothesize that the neurological status at admission is comparable in the two groups, having been determined by the Glasgow scale and the Hunt and Hess classification. Several publications have found a higher frequency of aneurysms in twins of patients with cerebral aneurysms or in relatives of patients affected of SAH, especially when there is more than one affected in the family. Thus, it has been calculated that having 3 or more family members with aneurysms in a family triples the probability of finding another affected individual in the same family. Some detection protocols for relatives of patients affected with Magnetic Resonance have been proposed, and there is an important diagnostic yield when there is more than one case affected by subarachnoid hemorrhage, and it is also necessary to repeat the study over time. The best studies of the natural history of the SAH are those made in the 60s and 70s, since at that time the proportion of untreated ruptured aneurysms was much higher than today. In these studies a high mortality was evidenced, of around 60% in the first 6 months. When comparing more recent studies with previous ones, it has been proven that there is a slight decrease in mortality and an increase in the percentage of patients with good final evolution after SAH.

This improvement could be related to a better knowledge of the pathophysiology of the disease, and consequently a more adequate treatment of it, although the reason for this improvement is uncertain. However, there are still large differences (up to 20-35%) between the survival described in hospital series and in population series. These high morbidity and mortality figures support the adoption of urgent and effective treatment protocols, based on a systematic analysis of the literature, in order to include the largest possible number of patients with SAH. Several factors influence the evolution of patients with SAH. Among them, the severity of the initial bleeding stands out due to the important repercussion it has on the final evolution of the disease. The hemorrhage produces important and deep reductions in cerebral blood flow associated with an acute increase in intracranial pressure that trigger ischemic damage that can be maintained beyond the first moments of bleeding. These processes, although increasingly recognized, have not yet found an effective treatment. Of course, the existence of comorbidity as in other serious conditions will hinder treatment and worsen the patient's final result. On the other hand there are factors related to the location and morphology of the aneurysm responsible for bleeding that also influence prognosis such as the size of the aneurysm, its location in the posterior circulation and possibly its morphology. On the other hand, it seems increasingly evident that there are factors related to the hospital institution that performs the treatment, such as the availability of endovascular treatment as well as the volume of patients treated.

On the other hand, we must bear in mind that young patients treated for cerebral aneurysms are more predisposed to develop new aneurysms over time. It has been calculated that these patients have a frequency of formation of new aneurysms of 1-2% per year. This data is important to establish the monitoring of these patients, although no specific method can be proposed at the moment. The incidence of SAH collected in our work is lower than that expected with respect to the studies published both in the national and international literature[1]. It is suspected that the cause of this difference could be related to a possible bias of the selection, since one of the exclusion criteria has been not to receive surgical treatment or endovascular therapy, or to exclude patients who have been referred to other centers, due to the dispersion of the sanitary area corresponding to the University Hospital of Getafe. The distribution of the aneurysmal locations collected in the literature is 31-36% of the anterior cerebral artery, 21-36% of the internal carotid artery, 21% of the middle cerebral artery and 6-10% of the posterior circulation. The cases treated in the University Hospital of Getafe show a tendency to have more patients surgically intervened in the territory of the anterior cerebral artery and middle cerebral artery, and more patients submitted to embolization in the territory of the posterior circulation. This trend is similar to that previously published in the literature, both nationally and in international studies.[4]

Despite the fact that ischemic stroke has received attention from the health authorities regarding its acute treatment and its transfer to centers with Stroke Units, the SAH has not received as much attention. However, a good number of patients with SAH may benefit from receiving treatment and transfer initially in a similar way. It is evident that it would be desirable to establish some mechanism to detect those patients with high suspicion of SAH and that these were referred to centers where they could be treated, avoiding secondary transfers. The initial management of a patient with ischemic stroke or hemorrhagic event should be similar. Its neurological situation must be taken into account, giving special importance to the level of consciousness. Therefore, as already mentioned, the initial assessment and monitoring of the patient's neurological situation must be carried out by obtaining the score on the Glasgow coma scale and the WFNS of the patient. It is fundamental, as in any other serious condition, to ensure adequate ventilation through the maintenance of the airway, adequate oxygenation and good perfusion. There is a potential for neurological deterioration and therefore inability to maintain adequate ventilation and therefore patients with altered level of consciousness should be intubated if necessary. For all this, and due to the need for close monitoring of the patients, their neurological exploration and constant, we consider that all patients suffering from SAH should be managed in an Intensive Care Unit. The average hospital stay of all the patients treated in this study (both in the global hospital and in the ICU) exceeds by far the one published by the Vascular Pathology Group of the Spanish Society of Neurosurgery, as well as the series collected internationally.[5] However, it is interesting to note that it has been reported that clearly longer hospital stays are shown in certain centers with a high volume of patients with SAH treatment.[4] The authors argue that this phenomenon could be due to the fact that they group more complex patients or that they are less "efficient" centers.

The average hospital stay previously collected in various publications is 15 to 20 days and 14 to 17 days for patients who underwent surgery or who underwent endovascular embolization, respectively. The vast majority of the series find statistically significant differences in the different hospital stays, tending to show shorter stays for patients with endovascular treatment, although there are some series in which this is not clearly demonstrated. Until today, surgery has been considered the treatment of choice in the aneurysms that cause SAH, although in the best case scenario (immediate referral, early surgery), only about 60% of the patients could be operated on. However, it is difficult to compare the results of the different series published previously in the literature, since they include very diverse populations, and therefore, the mortality figures will be very different according to the criteria used in the study. There is controversy about what is the best time ("timing") to intervene a patient with SAH. To date there are only two prospective, randomized studies that demonstrate the benefit of early surgery (0-3 days) compared to late (> 7-10 days). Although today it is recommended early surgery (0-3 days) in those patients in good clinical grade (I-III of the WFNS) and uncomplicated aneurysms, the date of surgery by itself, has no predictive value. The decision is also influenced by many other factors such as age, concomitant diseases, location, size and complexity of the aneurysm and availability of the necessary means. A decisive factor to take into account at the time of the decision of early or delayed intervention, is the initial clinical bad grade (Grades IV-V of the WFNS). Formerly these patients were managed conservatively or late surgery was practiced on those who survived. Several authors have currently advocated aggressive medical and surgical treatment in these cases, demonstrating a better final evolution, even in patients in grade V, and obtaining a good recovery or mild disability between 20-40% of the total treated patients.

During the procedure, hypotension should be avoided (systolic BP <60 mmHg). During the arterial dissection, temporary "clipping" of one of the aneurysm vessels may be necessary. The maximum safe occlusion time is not yet determined, but it is not advisable to exceed 20 minutes. Intermittent temporary occlusion seems to offer less risk of ischemia, although occlusion times are still not well defined. In some proximal para-clinoid aneurysms, temporary occlusion of the internal cervical carotid can be used, transient clipping distal to the aneurysm, and even retrograde carotid emptying to facilitate definitive dissection and clipping of the aneurysmal neck. As previously mentioned, aneurysms can be treated by occlusion of the carrier artery, although this occlusion carries a risk of ischemia. This procedure is reserved for aneurysms not treatable by other techniques and is a treatment of choice in the case of dissecting aneurysms and ampoules or blebs or aneurysms that cannot be treated by any other available technique. The presence or absence of ischemia after occlusion can be predicted by an occlusion test. Said test is performed by inflating during the angiography of a balloon that occludes the vessel. During this occlusion, neurological function must be monitored, either by neurological examination or by an electrophysiological method. If deficits do not occur after some hypotension, in principle, the artery could be occluded without producing neurological deficits. Nowadays, the delay in the venous phase of angiography is also used to predict the probability of ischemia. When the occlusion test is positive, an extra-intracranial by-pass should be performed to carry out the occlusion safely. This treatment algorithm is being used more and more frequently in our country.

A theoretical advantage of surgery is the washing of cisternal blood, which theoretically can reduce the incidence of postoperative ischemia. This premise could not be demonstrated, it has even been seen that the aggressive risk of surgical clogging increases the surgical risk[4]. The average stay in ICU collected in the diverse literature analyzed is 1.8 and 1.7 days for patients operated surgically operated and treated by endovascular embolization respectively. In the present study, the previously published trend in which embolized patients usually have a shorter stay in the ICU is reversed. Unfortunately, we do not have a sufficiently large sample of patients operated on to ensure this trend. The stay in the ICU usually reflects the level of complexity of the patients treated. In relation to the time of delay between bleeding and treatment there have been no statistically significant differences in our work, although there is a tendency to have longer periods for surgery. This trend agrees with that described in the literature. In addition, the International Subarachnoid Aneurysm Trial (ISAT) also confirms this data. The period between diagnosis and treatment has been longer for surgery (p <0.0001). Because the morbidity assessment of the treatments was not the primary objective of this study, it has been counted as present or absent regardless of the type of associated morbidity. Therefore, no distinction has been made between complications such as post-procedure vaso-spasm, rebleeding, infection, deep vein thrombosis or others. Considering this, the global number of complications is similar in both types of treatment. In the review of the literature we find that it is a highly controversial topic, and we find enormously different results according to the different published studies and the surgical or endovascular treatment preferences of the different neurosurgical hospitals.[7,8]

The effectiveness of the treatment of aneurysms is marked by two aspects: to reduce the risk of rebleeding and achieve a definitive treatment of the aneurysm, that is, to achieve its complete exclusion from the cerebral circulation. The risk of rebleeding in embolized aneurysms decreases to 0.9 to 2.9%, although other studies have estimated a risk of 1.4% per year of re-rupture. It seems that one of the most important factors in the occurrence of a recurrence or hemorrhage after endovascular treatment is the size and shape of the treated aneurysm. For aneurysms greater than 2 cm, rebleeding is common, reaching 33% in one study. The recurrence of aneurysms is also greater in large aneurysms, mainly because the frequency of incomplete treatments is greater.[9] When the treatment is incomplete, the frequency of growth of the rest of the aneurysm is high, reaching figures of up to 49%. The treatment is infrequently complete in global series of aneurysms, this being the result in up to 55% of cases. The size of the aneurysm and neck appear to have an important role in the outcome. The worst results are obtained in wide necks and larger sizes. The risk of recurrence of the aneurysm is also high in aneurysms treated in a complete manner, being the risk factors for its growth the larger size of the aneurysm or its situation with respect to blood flow such as the middle brain or basilar.[10,11]

Although the follow-up of embolized aneurysms has traditionally been carried out using angiography, it seems that cranial MRI can serve as an alternative to angiography, leaving only the angiography for the case of obvious filling in the MRI. The need for follow-up of patients treated by embolization is evident, and for this reason we recommend carrying out long-term control tests on these patients.[4–6] Although the frequency of re-canalizations and aneurysm growth treated by endovascular treatment remains high, new technical advances will probably determine better results in this regard. On the other hand it seems clear that the use of this technology has reduced the mortality of patients with SAH and therefore should be used in those cases in which better results are achieved. The treatment of cerebral aneurysms should be performed by an experienced team consisting of neurosurgeons trained in the treatment of cerebral vascular pathology and experienced interventionists.[12] The treatment must therefore be carried out in centers that have both specialists working together. It is increasingly evident that the increase of experience in the treatment of this pathology improves the results. In addition, centers that include endovascular treatment treat patients earlier and have better overall results.[13] The recommendation in this regard is to concentrate the treatment of these patients in centers that have both techniques, although the effect of treatment concentration is lower in ruptured aneurysms. The best indication should also be established depending on the characteristics of the patient, their clinical status and comorbidity, the characteristics of the aneurysm to be treated and the center's own experience. Although strict indications cannot be extracted from the literature review, some general indications may be suggested. The ISAT study, which included patients who could be treated by both endovascular and surgical treatment, showed that although mortality was similar in both treatment groups, the morbidity associated with endovascular treatment was lower.[14]

Therefore, endovascular treatment should be used when the results with both techniques are judged equivalent by the treatment team. Some neuropsychological studies and quality of life in our environment in patients treated with one or another therapeutic modality appreciate a minimal and little difference in favor of embolization. Several prospective studies have shown a similar rate of bleeding. After an SAH there is a risk of rebleeding of 3-4% in the first 24 hours, followed by a cumulative risk between 1-2%/day during the first four weeks. In the cases that were treated conservatively, the incidences of rebleeding registered in the first month ranged between 20-30%, stabilizing after the third year. In the Cooperative Study with a greater follow-up, they found a rebleeding index of 2.2% per year after 6 months of bleeding during the first 10 years, falling to 0.86% per year starting in the second decade. Mortality associated with rebleeding is estimated at 74%.[6] The fundamental treatment to prevent rebleeding is the occlusion of the aneurysm (surgical / embolization). The use of fibrinolytics in high doses during the first 72 hours of bleeding reduces the risk of rebleeding without an increase in ischemic complications.[15] This strategy could be useful in cases where it is necessary to carry out a hospital center transfer for the treatment of the aneurysm. Given the selection bias demonstrated by the low incidence of SAH and the low mortality rate, together with the small sample of patients operated on in our study, it could be argued that the conclusions on re-bleeding lose their statistical validity. However, the re-bleeding rates are not different from those found in the literature, and the historical bias of our study would in principle penalize the operated patients, since these are much lower. It must be borne in mind that in the University Hospital of Getafe over the last decade, conventional surgery has been replaced by endovascular embolization. These results indicate that endovascular embolization is an excellent treatment for aneurysmal subarachnoid haemorrhage, but that its absolute indication against surgery cannot be conclusively determined.[10]

Therefore, any decision making in the type of treatment should include a comparison of the natural risk with the efficacy, morbidity and mortality associated with the procedure depending on the location, size and morphology of the aneurysm without forgetting the patient's will. As a reflection of the future, the surgical results will worsen as the number of surgeries is divided among a growing number of neurosurgeons. If the number of embolizations per radiologist is significantly greater than that of clipping by neurosurgeon, better results in endovascular treatment are expected due to the difference in experience. Less experience in surgery means increased surgical risk. Regarding the prognostic factors, clinical and radiological criteria are clearly established, according to the most recent studies, which allow orientation in the face of the ideal treatment, as well as the opportune moment or "timing", so controversial in the neurosurgical field[15]. It is important to highlight the novelty of blood volume measurement in CT, something that clearly conditions the final result. The logistic regression models allow us to know, introducing the variables analyzed, the "theoretical" final evolutionary prognosis of the patient, and according to this, decide what is the ideal treatment for each patient and the moment of it, always following the principles of "optimism" "Logical that make all the valid therapeutic possibilities are administered, even if the patient is in a bad clinical and neurological situation. Therefore, the present study reconciles economic, social and environmental sustainability in the diagnosis and therapeutic management of patients suffering from aneurysmal subarachnoid hemorrhage.

Conclusion

1. Subarachnoid hemorrhage is more frequent in males (1.2 / 1), predominantly in patients between the ages of 45 and 55 years. The incidence in our environment can be established in 1.5 cases per 100,000 inhabitants per year, below the figures collected in scientific publications. TheSAH is a devastating entity that requires urgent multidisciplinary action. The Glasgow scale for the modified Coma (WFNS) and the Glasgow Evolutionary scale correlate well with the clinical situation and with the final prognosis of the patient suffering from SAH. Endovascular embolization treatment, as currently described in the literature, seems to improve the prognosis and overall survival of patients suffering from aneurysmal rupture. The most influential parameters in the final prognosis in patients suffering from SAH are the neurological situation at admission (WFNS), the amount of blood in the skull CT (Fisher's Scale) and age.

2. As soon as the diagnosis has been made and the patient has stabilized in his cardiovascular and respiratory functions, he should be transferred to a center that has adequate diagnostic and therapeutic options (Neurosurgery, Interventional Neuroradiology and Neurological ICU). The admission of the patient in the ICU is fundamental for an adequate treatment of the pain, to avoid causal factors of secondary brain injury and to initiate the administration of nimodipine precociously. Hypotension and hypovolemia should be avoided from the first moments with adequate replacement of isotonic saline sera.

3. All patients should be examined with CT, immediately after being received in the hospital, as well as proceed to their admission to the ICU and subsequent arteriography. The measurement of the volume of blood in the CT is useful, being demonstrated that to greater volume of blood, worse prognosis. In the clinical management of SAH, patients can be classified according to the risk factors they present, according to the neurological situation, age and medical history and the characteristics found in the CT (Fisher's Scale).

4. CT is the diagnostic test of choice when this pathology is suspected; once the diagnosis is confirmed, in the same act a CT angiography of Willis polygon can be performed that will define the presence and characteristics of most aneurysms. If the patient is in a neurological emergency due to a large hematoma with mass effect, with these examinations of adequate quality, he can undergo surgery.

5. Early exclusion of aneurysms from the circulation should be attempted to avoid rebleeding. It is important to perform cerebral arteriography and, if an aneurysm responsible for bleeding susceptible to embolization is discovered, perform the endovascular treatment in the same act. If the aneurysm is not susceptible to embolization, urgent surgery should be scheduled, at least in patients in good clinical condition.

6. As a general principle, during the patient's stay in the ICU, their present situation should be treated, prevent, if possible, early detection and treat the many and serious neurological and systemic complications to which these patients are exposed.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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