Subarachnoid Haemorrhage in Malta – Are outcomes adversely affected due to lack of a local neurovascular service?

Malcolm Vella, Nicola Dingli, Josanne Aquilina, Anthony Galea Debono, Norbert Vella

Abstract

Objective: This study was performed to assess the incidence, treatment and outcome of non-traumatic Subarachnoid Haemorrhage (SAH) in an island which does not offer a neurovascular service and to determine whether such limitation is associated with a poor outcome.

Method: Data of adult patients with a diagnosis of non-traumatic SAH was analysed retrospectively over a two-year period from January 01, 2009 to December 31, 2010.

Results: The incidence of SAH in Malta is 3.16 cases per 100 000 population per year. An underlying aneurysm was found in 50% of all cases investigated with angiography. These patients were transported to the United Kingdom for definitve management and the outcome of all these patients at 6 months was excellent. (modified Rankin Scale of 0 or 1).

Conclusions: With the incidence of non-traumatic SAH being in the low range, setting up an interventional neuroradiology service in our country to treat aneurysmal SAH would not have the required numbers to maintain expertise and would probably translate into worse clinical outcomes. Despite having geographical and logistic limitations, our standards of care and survival rates are not below those of other international centres. Outcomes for patients with low initial Hunt and Hess scores have not been adversely affected by the lack of a local neurovascular service.

Malcolm Vella MD FEBN MRCP(UK)
Department of Neuroscience,
Mater Dei Hospital,
Msida, Malta

Nicola Dingli MD MSc MRCP(UK)*
Department of Neuroscience,
Mater Dei Hospital,
Msida, Malta
nicola.aquilina@gov.mt

Josanne Aquilina MD FRCP
Department of Neuroscience,
Mater Dei Hospital,
Msida, Malta

Anthony Galea Debono MD FRCP
Department of Neuroscience,
Mater Dei Hospital,
Msida, Malta

Norbert Vella MD FRCP
Department of Neuroscience,
Mater Dei Hospital,
Msida, Malta

**Corresponding author*

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Introduction

Subarachnoid haemorrhage (SAH) is a type of haemorrhagic stroke caused by bleeding into the subarachnoid space. The bleed can be secondary to trauma or non-traumatic. Aneurysmal SAH is reported to be the cause in about 80% of non traumatic bleeds. The rest are caused by perimesencephalic haemorrhage, vessel abnormalities such as arterio-venous malformations and other rarer causes.[1] Although SAH accounts for about 5% of all strokes, it is an important cause of stroke in young adults. The overall incidence is reported to be 6-10 per 100 000 per year. However, there is a significantly wide variation by region, as reported by a large World Health Organisation study where there was a 10-fold difference in incidence between countries from 2.0 per 100 000 in China to 22.5 per 100 000 in Finland.[2] At younger ages, the incidence is higher in men, but becomes more common in women after the age of 55.[3] SAH carries a significant mortality rate of up to 50% with 10-15% dying prior to reaching hospital. In

surviving patients, there has been a decrease in overall mortality reported over the past 2 decades.[4]

Malta has a population of 417, 432.[5] No data is currently available on the incidence and outcomes of SAH in Malta. The purpose of our study is to assess the incidence, treatment and outcomes of SAH in the Maltese population. Also, in view of the lack of neurovascular services available in the country and the need for patients to be transported to a centre in the UK for definitive treatment, we aim to assess whether this has negatively affected outcomes.

Study Methods

All patients admitted with a suspected SAH on the Maltese Islands are treated at the main public hospital, Mater Dei Hospital (MDH) by one of three consultant Neurologists. If patients present to a private clinic they are quickly transferred to this general hospital for further investigation and management. There are no other facilities on the island equipped to treat these patients.

Data of adult patients (>14 years of age) with a diagnosis of SAH from January 01, 2009 to December 31, 2010 was collected and analysed from four separate sources – (i) Patients who were admitted through the Accident and Emergency department of Mater Dei Hospital (MDH) with a diagnosis of suspected SAH from the casualty admission register; (ii) Patients who were discharged from Mater Dei Hospital with a diagnosis of SAH were identified from the hospital activity analysis, using ICD9 coding system; (iii) Patients who were referred abroad for treatment of aneurysms were obtained from the Treatment Abroad Committee; (iv) Patients whose cause of death on the death certificate was listed as "subarachnoid haemorrhage" from the Death Register. All patients with a traumatic SAH were excluded.

Only those patients who were not admitted to hospital because they died out-of-hospital or in the Accident and Emergency Department were solely identified from the death register. The rest of the patients were identified from more than one of the above mentioned sources, ensuring that data capture was thorough and complete. This data collection method guaranteed that no cases of SAH that were admitted to hospital were missed. All the case notes, radiology, blood and cerebrospinal fluid results of these patients were analysed.

Results

The final number of patients with definite spontaneous non-traumatic SAH over the two-year study period was 26. Therefore the incidence of SAH in the Maltese population is calculated to be about 3.16 per 100 000 population per year.

Patient Characteristics

Of these 26 patients, 18 (69%) were female and 8 (31%) were male. The mean age was 55 (range 34-87) with a peak between 40-59 years of age.

2 patients died before receiving medical attention and were certified dead from SAH according to their death certificate. One of these patients had a post-mortem examination which confirmed SAH secondary to a ruptured berry aneurysm. The other patient had a CT scan carried out 2 weeks earlier which revealed a giant anterior communicating artery aneurysm. No further action was taken in this case because of co-morbidities. SAH was listed as the cause of death on the death certificate. Another patient, a 60 year old, died soon after presentation at the emergency deparment. This patient also had a postmortem examination which confirmed SAH as the cause of death. The data of these 3 patients was not analysed further since the deaths were out of hospital or at the emergency department and no medical notes were available. (Figure 1)

Presentation

Almost all patients presented in the first 24 hours. One patient had symptoms suggestive of a sentinel bleed one week prior to presentation. All patients presented with an acute headache except the three who presented in a comatose or confused state. Other common symptoms at presentation were nausea and vomiting, confusion, reduced level of consciousness, motor weakness and seizures. Figure 2 demonstrates the Hunt and Hess scores on admission.[6]

***Figure 1**: Flow chart of patients with non-traumatic SAH*

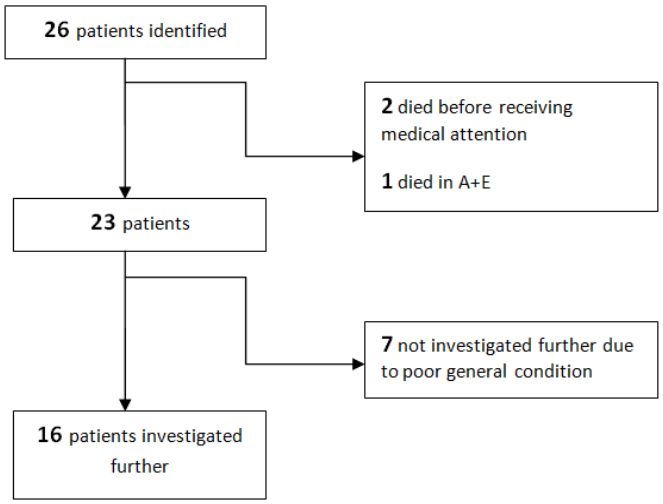
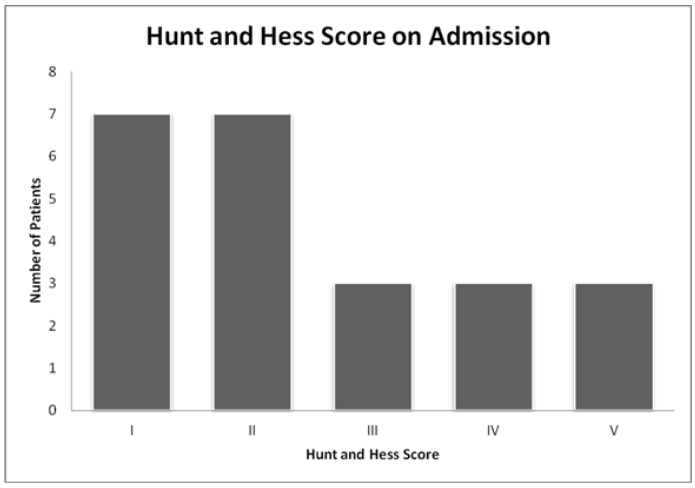


***Figure 2**: Hunt and Hess Score on Admission*



Risk factors

Risk Factors for SAH in our cohort were hypertension in 9 patients and smoking in 8 patients. One patient had immune thrombocytopenia and a myelodysplastic syndrome.

Investigations

Table 1 shows the investigations carried out on all patients with a diagnosis of spontaneous SAH. All patients had a non-contrast CT scan of the brain. SAH was confirmed in all cases except for one patient who had a normal CT. This patient had presented 5 days after the onset of headache.

A lumbar puncture was carried out only in two cases. In one case a suspicion was raised over the diagnosis of SAH from brain CT and in the other case the CT was normal. In both cases xanthochromia was present confirming the diagnosis of SAH.

Following a diagnosis of SAH from brain CT or lumbar puncture, 16 patients (70%), were investigated with further imaging modalities for the prescence of aneurysms. Further investigations consisted of a CT cerebral angiogram (CTA) in 9 patients; Magnetic Resonance Angiography (MRA) in 4 patients and Digital Subtraction Angiography (DSA) in 8 patients. The choice of the imaging modality after diagnosis of SAH was at the discretion of the caring consultant neurologist. If an aneurysm was identified on CTA or MRA, the patient was referred for coiling/clipping directly, and had a cerebral angiogram during pre-operative planning. If no aneurysm was identified on CTA or MRA, the patient was further investigated with formal cerebral angiography.

7 patients (30%) (patients 9, 10, 15, 20, 21, 22, 23 in Table 1), did not have further investigations carried out because they were deemed unfit due to their low GCS on presentation or because of significant co-morbities. These patients were treated conservatively.

Management

Most patients were admitted to the Neuromedical ward. Patients with a low GCS were admitted to Intensive Care. Treatment with nimodipine, lactulose and analgesia was initiated immediately in all cases upon diagnosis of SAH. Anticonvulsants were started only if the patient developed seizures.

Of the 16 patients (See Figure 1) that were investigated with further imaging modalities for the possibility of an underlying aneurysm, 8 patients (50% of those investigated) were found to have one or more aneurysms. These patients were referred to the United Kingdom (UK) for definitive treatment of the aneurysm within an average of 4.4 days (2-13 days) from the day of admission. Only one out of these 8 patients required ITU admission and was transfered to the UK after 13 days. The other 7 patients were transfered to the UK within an average of 3.1 days (2-4 days).

Table 2 shows the site and size of the aneurysms identified in 8 patients from CTA, MRA or cerebral angiography carried out in Malta and in the UK. Of note, 3 of these 8 patients had multiple aneurysms, although only the aneurysm suspected to have caused the SAH was treated with coiling or clipping. 6 patients with aneurysmal SAH were treated with coiling and aspirin ± clopidogrel for about 28 days. Only one patient underwent clipping of the aneursym. The decision to undergo coiling or clipping was decided by the caring Vascular Neurosurgeon in UK.

The time elapsed from diagnosis of SAH to definitive treatment of the aneurysm in the UK was 5.4 days (range 4-8 days).

Length of stay

The average total length of stay of patients with aneurysmal SAH from presentation until discharge from hospital was 17 days (14 - 20 days) with most patients being well enough to be discharged directly home from the UK hospital.

The average length of stay of patients with angio-negative SAH who survived the initial presentation was 21 days (8 – 65 days).

Outcome of SAH

Complications occurring in patients with aneurysmal SAH treated with coiling or clipping

There were no significant complications reported in the patients who underwent coiling or clipping except for a minor stroke in one patient, following which he made a full recovery. Another patient in this group developed Terson syndrome (vitreous haemorrhage associated with SAH). This patient also made a full recovery.

***Table 1**: Investigations carried out on patients with SAH*

Patient	Non-contrast CT	Lumbar Puncture	CT Angiogram	MRA	Cerebral Angiogram
1	SAH confirmed		Abnormal		
2	SAH confirmed		Abnormal		
3	SAH confirmed				Abnormal
4	SAH confirmed		Abnormal		
5	SAH confirmed			Abnormal	
6	SAH confirmed			Normal	Normal
7	SAH confirmed		Normal		Normal
8	SAH confirmed		Normal		Normal
9	SAH confirmed				
10	SAH confirmed				
11	SAH confirmed	Xanthochromia		Non-diagnostic	Normal
12	SAH confirmed		Normal		
13	Normal	Xanthochromia	Non-diagnostic		Normal
14	SAH confirmed				Abnormal
15	SAH confirmed				
16	SAH confirmed			Abnormal	
17	SAH confirmed		Abnormal		
18	SAH confirmed				Normal
19	SAH confirmed		Normal		
20	SAH confirmed				
21	SAH confirmed				
22	SAH confirmed				
23	SAH confirmed				

***Table 2**: Characteristics of the aneurysms and the management undertaken in UK*

Patient	Investigations in Malta			UK	Definitive Treatment
	CTA	MRA	Cerebral Angio	Cerebral Angio	
1	3mm Basilar Tip			3mm Basilar Tip 3mm Paraopthalmic	Coiling + Aspirin
2	6mm right Carotid Tip			P Comm	Coiling + Aspirin
3			6mm left P Comm	P Comm Left cavernous ICA Basilar fenestration	Coiling + Aspirin
4	6mm left MCA			N/A	Clipping
5		7mm left ACA		A Comm	Coiling + Aspirin
14			Basilar Tip	N/A	N/A
16		5mm A Comm		6mm A Comm	Coiling + Aspirin
17	4mm right vertebral 4mm left MCA			4mm right PICA 4mm left MCA	Coiling + Aspirin

MCA: middle cerebral artery
P Comm: posterior communicating artery
ACA: anterior cerebral artery
A Comm: anterior communicating artery
ICA: internal carotid artery
N/A: data not available

Complications occurring in patients with SAH who did not undergo coiling or clipping

2 patients (9%) had a subarachnoid re-bleed, which occured after one day post-admission in one patient and after 3 days in the other patient. 4 patients (17%) developed hydrocephalus and 3 of these patients underwent VP shunting. 3 patients (13%) developed seizures. 2 patients developed sepsis/ventilator associated pneumonia. 1 patient developed pulmonary embolism and another patient developed a massive middle cerebral artery infarction.

Post-treatment follow-up

Patient 14 (Table 2) who was referred to the UK for definitive treatment of the aneurysm was of British nationality and did not return to Malta after transfer to the UK and was therefore lost to follow-up. The other 7 patients who underwent coiling or clipping were followed up at Neurology out-patients for at least 6 months. All 6 patients who underwent coiling had a repeat cerebral angiogram at 3 to 6 months post-intervention. The angiogram revealed complete occlusion of the treated aneurysms in all cases. In one case the presence of another aneurysm was reported, but this was already reported in the CTA carried out on presentation with the SAH. Only the patient who underwent clipping of the aneurysm was not followed up with cerebral angiography.

Mortality

Excluding the British patient that was lost to follow-up, 22 patients were followed for at least 6 months after the initial presentation with SAH or until the time of death. Out of these 22 patients, 7 patients (32%) died. All deaths occured as in-patient with an average of 16 days (2 – 37 days). The cause of death was directly related to SAH in 4 patients (raised intracranial pressure/coning) and secondary to ventilator associated pneumonia, pulmonary embolism and stroke in 3 patients. All deaths occured in the patients who were

deemed not fit to undergo further investigations soon after admission (patients 9, 10, 15, 20, 21, 22, 23 in Table 1).

Table 3 shows the Modified Rankin Score 6 months after the initial presentation for the 22 patients that were followed up for at least 6 months.

***Table 3**: Modified Rankin Scale*

Scale	Description	No. of patients (/23)*
0	No symptoms	13
1	No significant disability. Able to carry out all usual activities, despite some symptoms	2
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities	0
3	Moderate disability. Requires some help, but able to walk unassisted	0
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted	0
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent	0
6	Dead	7

adapted from Farrell et al, 1991 (6)

* One patient lost to follow up

Discussion

MDH is the main acute hospital in the country. All patients diagnosed with SAH on the Maltese Islands are ultimately referred to MDH because it is the only hospital that offers the service of a critical care unit. The way the data was compiled in our study is representative of almost all the cases of SAH that occured in our country in the study period. The incidence of 3.16 per 100 000 population per year is on the low side of average incidence data. However, it further confirms the large variability across countries.[2] The Maltese population are mainly of Italian descent.[8]

Recent epidemiological studies from Italy have also shown similar data.[9-10] Reasons as to why the incidence is low could be due to the occurence of less risk factors, or genetics. Further demographics are all in keeping with international data, with the highest presentation being in the 40-59 years age group, and mainly female.

MRA and CTA are being increasingly used as imaging modalities for the detection of intracranial aneurysms.[11-12] Studies have reported sensitivity of CTA to be in the region of 95%, with a recent multicentre study reporting a sensitivity of 99%, comparable to DSA.[12] However, if CTA is inconclusive, conventional DSA is still recommended.[13] In our cohort, 50% of the patients investigated with angiography were found to have an aneurysm. This number is definitely an underestimate because it does not include those patients who did not undergo angiography. Theoretically, if all the patients who did not undergo angiography did actually have an aneurysm, this percentage would increase to 62%. Therefore comparison of the percentage of aneurysmal bleeds in our cohort with that of international figures unfortunately cannot be made.

In Malta we do not have the facility of a neurovascular service mainly because of the limited number of SAH cases treated at our main hospital. We also lack the facility and expertise of an interventional neuroradiology service and since the number of cases is small, offering such a service would undoubtedly pose higher risks for the patients. This practice is in line with the latest American Heart Association/American Stroke Association guidelines which highlight the importance of specialised centres in the management of these patients. The recommendation is for low-volume hospitals with less than 10 cases of aneurysmal SAH per year to transfer patients to centres dealing with over 35 cases per year as this has been shown to significantly improve outcomes.[13-14] Malta has had very close medical ties with Britain for the past several years. There is an agreement between Malta and the UK stating that Maltese patients are treated in specialised centres in the UK should that service not be available locally, or local expertise is lacking. In view of the limited numbers of SAH on our island, these patients' treatment falls under this agreement. Patients are transported by air to specialised UK centres accompanied by a doctor and nurse escort. No complications were reported to have happened on the 3 hour flight to the UK. Emergency air medical transfer of patients with acute intra-cerebral bleed for definitive neurosurgical care appears to be both safe and effective, and facilitates early definitive diagnosis and operative intervention.[15]

The International Subarachnoid Aneurysm Trial (ISAT) has shown a clear superiority of coiling over clipping in those aneurysms deemed to be suitable for both treatments and has definitively changed the practice in most neurovascular centres.[16] In our study, all patients

except one had the aneurysm treated by endovascular coiling. All these patients had a good outcome at 6 months. The decision as to which mode of treatment was employed was decided by the caring vascular neurosurgeon in the UK.

Ideally, patients with SAH should be treated as early as feasible.[13,17-18] Effort is made on our end to organise the transport of patients as soon as possible; however some delay is inevitable. Limitations to earlier treatment result from the logistics of the transfer itself as well as the clinical condition of the patient as some patients need stabilisation prior to air transfer. In our patients, intervention was done at a mean of 5.4 days, having taken a mean of 4.4 days from the time of initial presentation to transfer to the UK. However, interventions done on our patients at slightly later times did not result in poor outcomes.

There is no doubt that intervention on low-grade (Hunt and Hess score I-II) SAH patients reduces morbidity and mortality.[13,16] Studies have shown a beneficial outcome in a proportion of aneurysmal SAH patients admitted with a poor grade.[19-22] However, in some of these studies the authors have stated that there is an element of selection bias when choosing patients for intervention, whereby unstable patients were excluded.[19,21-22] As yet, intervention for this patient group has not become established practice in all centres. If it can be proven conclusively that all patients with non-traumatic SAH should be treated acutely then it is essential to have a 24 hour endovascular service. Meanwhile, for the low grade patients it may be appropriate to refer them to centers that treat a larger number of cases per year. Indeed, this was proven in our study.

This study was not designed to evaluate if the outcome of patients with aneurysmal SAH transferred to the UK is better than those treated locally, as we do not offer this neurovascular service. The main aim was to evaluate the need or otherwise for such a service to be developed in Malta. If the outcome for our patients needing transfer overseas for treament was shown to be poor, this would dictate the need for a local service. Unless the number of patients requiring endovascular treatment is significantly higher, it would not be justified to subject our patients to a poorer outcome due to limited expertise.

The main limitation of this study is the small number of patients with SAH seen in our country, making this study low-powered. The incidence of aneurysms is probably higher than reported as poor grade patients were deemed too unfit for further investigation. There is also underestimation if there were patients who died from SAH but this was not listed on the death certificate, especially if it was an out-of-hospital death and the cause of death is not attributed to SAH but to a cardiac or other event. Unfortunately, this will remain a limitation in all similar studies.

Conclusion

In this study we have shown that the incidence of non-traumatic SAH in Malta is in the range of low-incidence countries. Despite having small absolute numbers and logistic limitations for delivering definitive interventional treatment for aneurysmal bleeds, our standards of care and survival rates are not below those of other international centres for patients admitted with a low Hunt and Hess score. At present, the low number of non-traumatic SAH patients would not justify setting up an interventional neuroradiology service in our country to treat aneurysmal SAH. A local service would probably translate into worse clinical outcomes as the number of cases treated per year would be insufficient to maintain expertise.

Further studies on the outcome of patients treated at different centres are required to determine the minimum number of cases that need to be treated at a specific center to significantly reduce the morbidity and mortality associated with the treatment of aneurysmal SAH. This would potentially set a threshold to determine the number of specialised neurovascular centers required in different countries to achieve the best clinical outcome.

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