Wilson CD, Safavi-Abbasi S, Sun H, Kalani MYS, Zhao YD, Levitt MR, et al.: Meta-analysis and systematic review of risk factors for shunt dependency after aneurysmal subarachnoid hemorrhage. J Neurosurg: 1–10, 2016

Hydrocephalus generally complicates 20-30% of aneurysmal subarachnoid hemorrhages (aSAHs), which leads to increased patient morbidity and longer hospital stays and risk factors for development of hydrocephalus are still inconsistent in the literature. The goal of this meta-analysis by Wilson et al (2016) was to determine the risk factors for shunt dependency and calculate the magnitude of effect for each risk factor.

The authors found eight risk factors that increased the chance a patient will have shunt dependent hydrocephalus (Table 1). A higher Fischer Grade of 3 and 4 compared to grade 1 and 2 was the strongest risk factor for shunt dependency. This was followed by acute hydrocephalus on presentation and in-hospital complications, which included nosocomial meningitis, pneumonia, vasospasm and ischemic stroke. Intraventricular blood, especially blood in the 4th ventricle, was a risk factor for hydrocephalus. A high Hunt & Hess score at admission, re-bleeding event, posterior circulation aneurysm and age greater and equal to 60 years of age were also significant risk factors.

This meta-analysis provides a comprehensive literature review of the risk factors of shunt dependent hydrocephalus in SAH patients. All but three risk factors can be immediately evaluated upon patient presentation allowing clinicians to better predict patient's clinical course.

Table 1. Literature summary of major risk factors for shunt dependency

Risk Factor	Meta-Analysis Odds Ratio (CI 95%)
High Fischer Grade	7.74 (4.46-13.41)
Acute hydrocephalus at admission and EVD challenge	5.67 (3.96-8.12)
In-hospital complication	4.91 (2.79-8.64)
Intraventricular blood	3.93 (2.80-5.52)
High Hunt & Hess Score at Admission	3.25 (2.51-4.21)
Rehemorrhage	2.21 (1.24-3.95)
Posterior circulation aneurysm location	1.85 (1.35-2.53)
Age >=60 years	1.81 (1.5-2.19)

Johansson E, Ambarki K, Birgander R, Bahrami N, Eklund A, Malm J: Cerebral microbleeds in idiopathic normal pressure hydrocephalus. Fluids Barriers CNS 13:1449–4, 2016

In recent years, small vessel disease has been proposed to play a role in the pathophysiology of iNPH. Cerebral microbleeds (CMB) are iron deposits in the brain located around small vessels. They have been associated with cognitive decline and several other causes of dementia. The authors performed a retrospective case-control study to assess the association between INPH and CMBs. Fourteen consecutive patients undergoing surgery for iNPH had pre-operative MRI scans assessed for the presence of CMBs. Forty-one healthy controls (HeCo) also had MRI scan performed with subsequent assessment for CMB. The main outcome measure was the presence of 2 or more CMBs.

In this series, the authors found the frequency of >2 CMB to be 43% in patients with iNPH and only 10% of healthy controls (p=01). When only subjects with CMBs were taken into account, the median number of CMB in INPH patients was 8 while the median in HeCo was 1 (p=0.005). The authors conclude that patients with iNPH are more likely to have > 2 CMBs relative to HeCo. They suggest these preliminary findings support the hypothesis of a vascular component to the pathophysiology of NPH.

This is a small retrospective case-control study of the association between CMB and INPH. There are significant limitations, which may weaken the strength of the authors conclusion. First, only 14 patients with INPH are included in the patient group and the average age of the INPH patients was significantly older (76.4 vs 70.5; p=-.001), with age being a known risk factor for the presence of CMBs. The patients in the iNPH group were also more likely to be on ASA or anticoagulation (4 vs 0; p=0.003), which provides another confounding variable. Further investigation into the relationship between CMB and INPH should be undertaken, with a larger sample size and a healthy control group that is appropriately matched to the case group.

Del Bigio MR, Di Curzio DL: Nonsurgical therapy for hydrocephalus: a comprehensive and critical review. Fluids Barriers CNS 13:1–20, 2016

Presently, the only recommended treatment of hydrocephalus is CSF diversion surgery. However, over the past six decades, pharmacologic alternatives have been identified and some have been tried in humans for the management of hydrocephalus. Del Bigio and Di Curzio present an extensive review of the pharmacologic management of hydrocephalus in animal models and humans. Leading from a pathophysiological standpoint, the treatment modalities have been grouped into four main categories: CSF production; CSF pathway modulation; Cerebral blood flow and pulsation; and brain protection. Table 1 below demonstrates a road map on the pharmacologic modalities that was presented in the paper. The authors concluded that, while there is yet no established benefit of medical therapy for the treatment of hydrocephalus, some have shown promising results on the prevention of hydrocephalus as a compliment to shunting.

Table 2: Summary of pharmacological therapies for hydrocephalus

	Pathophysiology	Agent
CSF production	Osmotic agents and CSF pressure	Theobromin sodio salicylate Isosorbide Glycerol Mannitol
	Interference with CSF production	Acetazolamide Furosemide-Acetazolamide Digoxin Triamterene Glucocorticoids Choroid plexus cauterization
CSF pathway modulation	Enzymatic dissolution or thrombolysis of intracranial hemorrhage	Tissue plasminogen activator (tPA) Urokinase Streptokinase
	Interference of meningeal inflammation	Methylprednisolone Dexamethsone
	Interference of subarachnoid fibrosis	Transforming growth factor beta (TGF-b TGF receptor 1 inhibitor SD208) Deferoxamine
	Reversal of extracellular matrix accumulation in subarachnoid space	Hyaluronidase
Cerebral blood flow and pulsation	Vasoactive drugs	Nimodipine Magnesium sulfate Isosorbide dinitrate Dihydroergotamine
	Vascular endothelial growth factor (VEGF)	VEGF-2
Brain protection	Anti-inflammatory interventions and microglia	Minocycline Ibuprofen Pioglitazone Infliximab
	Antioxidative interventions	Gallocatechin gallate N-acetylcystein Melatonin catechin polyphenols Edaravone
	Neuron and axon protection	Memantine Morinda citrifolia Tacrolimus Cyclosporin A Calpain inhibitor I
	Cerebral Stimulants	Bifemelane Bromocriptine Ephedrine
	Protection in developing brain	
	Cell transplantation	