# Neurointerventional treatment of vasospasm

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***Objectives:*** *To review the historical development and current status of endovascular techniques used in the treatment of symptomatic vasospasm following aneurysmal subarachnoid hemorrhage.*
***Methods:*** *This article summarizes the relevant literature on neurointerventional therapy for vasospasm, namely instillation of intraarterial medication (papaverine, nicardipine, verapamil) and transluminal balloon angioplasty. The authors synthesize the available literature with their own experience using the various endovascular modalities to treat vasospasm at high volume cerebrovascular centers.*
***Technique:*** *Indications for the use of neurointerventional therapy as well as a summary of the technique for transluminal angioplasty to treat vasospasm as employed by the authors is described.*
***Discussion:*** *Neurointerventional treatment of vasospasm following aneurysmal hemorrhage has been proven to be a safe and successful technique for those patients suffering symptomatic vasospasm refractory to medical management. The techniques contunue to undergo refinement as endovascular technology advances. We currently favor the use of balloon angioplasty over intraarterial antispasmotics due to the increased durability and long-lasting effects of the former and lower risk profile.* [Neurol Res 2006; **28**: 769–776]

*Keywords: Vasospasm; neurointerventional; endovascular; subarachnoid hemorrhage; balloon angioplasty*



## INTRODUCTION

Cerebral vasospasm, defined as reversible vasoconstriction of the intracranial vasculature, remains the leading cause of stroke, morbidity and mortality after aneurysmal subarachnoid hemorrhage (SAH)[1]. Although the true etiology remains elusive, the incidence of radiographic or angiographic vasospasm as well as clinically significant symptomatic vasospasm has been well defined and predictable. Approximately 30–70% of those who suffer SAH will develop angiographic evidence of vasospasm, with approximately half of these developing concomitant delayed ischemic neurological deficits[2]. The severity of vasospasm and the incidence of CT demonstrable infarction and associated morbidity and mortality have been shown to be related to the amount of blood visualized on CT in the subarachnoid space at the time of the initial hemorrhage, described by the Fisher grade[3].

Although medical therapy, namely, the use of nimodipine and 'triple H' treatment (hypervolemia, hypertension and hemodilution), has been found to be beneficial for treatment of vasospasm in many patients, some continue to suffer vasospasm-related ischemia despite these efforts. Endovascular therapy, including intra-arterial administration of vasodilators and balloon angioplasty, has emerged as a more aggressive approach for such patients with good results[4]. Both endovascular methods (intra-arterial infusion of medication and angioplasty) have unique associated risks and benefits, and controversy exists over the best method[5]. Timing of endovascular treatment has also been controversial with some waiting until medical therapy has proven ineffective and others advocating a program of prophylactic balloon angioplasty in those deemed high risk to develop symptomatic vasospasm[6,7].

## HISTORICAL ASPECTS

The first report of balloon angioplasty was made by Zubkov *et al.*[8]. These investigators reported the reversal of angiographic vasospasm caused by SAH and clinical benefit in patients. Earlier sporadic reports had been published describing endovascular infusion of vasodilators for vasospasm, but these techniques had not been incorporated into treatment protocols for patients. In 1989, two groups in North America reported very promising results of the treatment of vasospasm in patients with aneurysms using newer soft silicone balloons and microcatheter techniques[9,10]. These reported results led to the widespread adoption of this technique by interventional neuroradiologists who were already using microcatheter techniques for balloon occlusion of aneurysms and embolization of intracranial vascular lesions. Subsequent reports followed the use of endovascular techniques to deliver papaverine selectively into intracranial vessels to treat vasospasm. The

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short lived action of papaverine has led to the experimental use of other selectively infused vasodilators and a trend towards using balloon angioplasty as a first line therapy for refractory vasospasm[11,12].

## DIAGNOSTIC CONSIDERATIONS AND MEDICAL MANAGEMENT PRECEDING ENDOVASCULAR INTERVENTION

In general, the diagnosis of cerebral vasospasm is made based on the clinical assessment of the patient and a series of ancillary tests. Accuracy of diagnosis is much more critical when endovascular therapy is entertained as the associated risks are higher than with medical therapy alone.

Cerebral vasospasm after SAH occurs in the overwhelming majority of patients between days 3 and 12 post-bleed, with a peak incidence on days 6–8[1,2]. The condition is marked by reversible arterial narrowing, usually of the medium to large intracranial vessels near the skull base, often involving vessels of or near the circle of Willis. However, smaller, more distal arteries are not infrequently involved. It is critical to differentiate between angiographic and symptomatic vasospasm, the latter being the more ominous and demanding more urgent remedy. At least half the patients who develop angiographic vasospasm will not develop symptoms[2,13]. It is only when cerebral blood flow (CBF) is greatly reduced and compensatory mechanisms such as autoregulation, collateral flow and increased oxygen extraction are exhausted, that ischemic deficit results[2].

The Fisher four-point grading scale is based on the extent of blood seen on the admission CT scan and has been shown to be a good prognostic indicator for the development of vasospasm[3,14]. Clinical or symptomatic vasospasm may present in different ways depending on the vascular territory involved and the area of brain deprived of blood. Any change in level of arousal or new focal neurological deficit is suspicious for symptomatic vasospasm, particularly once other causes such as hydrocephalus, infection and metabolic derangements have been ruled out.

In good grade patients, a rise in transcranial Doppler (TCD) velocities is responded to permissive hypertension (allowing the patient's blood pressure to rise on its own and withdrawing the patient's usual antihypertensive regimen, if one exists) initially and artificial hypertensive therapy if the TCD velocities demonstrate moderate to severe vasospasm[1,2,14,15]. As the indices of vasospasm by TCDs rise, patients are hydrated with saline and albumin to achieve a central venous pressure of 8–12 mmHg. Patients with significant cardiac histories are managed with Swan Ganz catheters, usually with the assistance of a cardiologist. As long as there is no neurological deterioration, this is the only therapy, which is tapered in response to decreasing TCD velocities. Computed tomographic angiography, single-photon emission computerized tomography (SPECT) and at times diagnostic angiography are often used even in patients who remain neurologically well if confirmation of the abnormal TCD readings are desired and would change the degree of therapy employed[2].

## ENDOVASCULAR THERAPY

### Intra-arterial antispasmotics

#### *Papaverine*

The largest experience with intra-arterial administration of antispasmotics has been with papaverine, a benzylisoquinoline alkaloid and a potent smooth muscle relaxant. Although the mechanism of action is not completely known, it is believed to inhibit phosphodiesterase activity in smooth muscle cells[2]. Since it was used for the first time to treat cerebral vasospasm in 1992, a wealth of data has been generated on its clinical use for this purpose[16–20].

Technically, the procedure is straightforward. After a diagnostic cerebral angiogram is performed to assess the degree and location of vasospasm, a microcatheter is navigated into the spastic vessels for the anterior circulation and just proximal to the area of spasm in the posterior circulation. Administration of 100–300 mg of the drug diluted in normal saline over 30–60 minutes is standard and may be repeated if different territories are involved[20,21].

Like all endovascular therapies for vasospasm, reported clinical success has been variable. Immediate angiographic relief from vasospasm is quite high with studies citing success anywhere from 57–90% of the time[16,18,21]. One study quantified blood vessel responsiveness based on angiography and found an average increase in vessel diameter of 26.5% in 34 patients undergoing 81 treatments[16].

More indirect measures of vasodilatory response using TCD ultrasound and other measures of CBF including $^{133}$Xenon and SPECT scans have also demonstrated the success of papaverine in achieving relief of vasospasm and resultant flow augmentation[5,18]. In one study observing TCD the day before and after intra-arterial papaverine (IAP), 41% displayed greater than 20 cm/s improvement in vasospasm parameters, with six individuals showing >50 cm/s change[17]. Vascular responsiveness to papaverine by TCD criterion was also found in two additional studies comparing angioplasty with papaverine therapy[5,22] or with the combination of the two modalities together[22]. Using thermal diffusion microprobes implanted into the white matter of affected vascular territories, Vajkoczy *et al.* were able to show that CBF was significantly improved in eight patients with vasospasm; the resultant increase is proportional to the degree of spasm and hypoperfusion before treatment[23]. In another study, jugular bulb vein oxygen saturation (Svj02) and arteriovenous differences in lactate were measured before and after papaverine usage in ten patients. Although there was no change in the lactate difference, improvements in Svj02 in 9/10 suggests improved global perfusion[24]. One review of the literature on CBF improvement after papaverine documented improvement in 60% of patients and in

31% of vascular territories in which the drug was administered[13].

Perhaps the biggest drawback to IAP use has been its temporary effect[16]. Because the vasodilatation after papaverine is not sustained, repeated endovascular instillations is often necessary. One review of the literature examining 401 patients found 663 treatments or an average of 1.7 intra-arterial sessions per patient[13]. In one study observing TCD velocities before and after papaverine therapy, although the velocities improved by 20% on average after papaverine infusion, these levels returned to pre-treatment values 1 day later[5]. Studies observing CBF have had similar results with one study demonstrating a return to baseline CBF just 3 hours post-treatment[23]. The efficacy of papaverine also seems to have a temporal window, in that patients with a longer duration of vasoconstriction appear less likely to respond[2]. Radiologic success does not necessarily correlate with neurological improvement, with one analysis showing that only 26% of patients demonstrated clinical improvement despite 78% of patients demonstrating some angiographic improvement[25]. One review of 346 patients treated with papaverine found clinical improvement in 148 (43%)[13].

Adverse effects associated with IAP have been well described, with systemic hypotension and raised intracranial pressure being the most serious. Both of these adverse side effects seem to be related to the rate of infusion[26]. Both hypotension and increased intracranial pressure (ICP) can be devastating to a patient with SAH, in whom compromised cerebral perfusion through stenotic vessels or increased ICP from hydrocephalus or brain swelling make any additional fluctuations in the cerebral perfusion pressure (CPP) undesirable. A myriad of additional complications related to IAP have been reported and include pupillary dilatation[27], aneurysm perforation[27], tachycardia, respiratory depression[28], exacerbation of vasospasm[29,30], seizures[31] and severe neurological deterioration associated with gray matter destruction seen on magnetic resonance imaging (MRI)[2,13,32]. Because of the temporary effect of IAP and the associated neurotoxicity, many have abandoned its use for vasospasm or use it selectively for patients in whom there is presumed distal small vessel vasospasm in which balloon angioplasty would be impossible. Papaverine may also be used in small amounts to transiently open vessels that would not allow passage of a microcatheter for more definitive therapies[2,25].

### *Nicardipine and verapamil*

Because of the myriad of side effects of IAP and its short-acting nature, some have tried endovascular intra-arterial administration of two additional calcium channel blockers (verapamil and nicardipine) to treat medically refractory vasospasm[11,12]. In one report, angiographic and TCD velocity improvement was documented in 18 patients (44 vessels treated) with refractory vasospasm treated with intra-arterial nicardipine (0.5–6 mg/vessel). Clinical improvement was seen in eight (42%), with only one instance of transient elevation of ICP and no systemic hypotension or other adverse events[11]. In another study, intra-arterial verapamil was administered to treat vasospasm after SAH in 29 patients. An average dose of 3 mg/patient being used, successful angiographic response was seen in all ten patients evaluated with immediate post-treatment angiography with an average vessel dilatation of 44 $\pm$ 9%; only six of these ten patients had intra-arterial verapamil as the sole endovascular therapy. Clinical improvement was noted in 5/17 patients or 29.4% of patients treated with intra-arterial verapamil alone[12]. No significant complications of the treatment were noted. Based on these studies, it seems that further validation of the safety and efficacy of both nicardipine and verapamil for this usage are warranted.

## Balloon angioplasty

### *Overview*

Transluminal balloon angioplasty (TBA) of cerebral vessels is currently the preferred technique for the treatment of medically refractory vasospasm[2,5,25]. Pioneered in 1984 by Zubkov, the treatment carries somewhat higher risks of a major complication such as vessel rupture compared with intra-arterial infusion of vasodilators[5,7,33]. When performed by experienced operators, however, the procedure can safely and reliably lead to vasodilatation of vessels in spasm with resultant angiographic and clinical improvement in a large proportion of patients[2,4,5,22,25,34,35]. Unlike papaverine infusion, the resultant vasodilatation is usually sustained and concomitant side effects such as raised ICP are not observed[5].

The pathophysiology underlying the success of balloon angioplasty is not completely known, but has been well studied both clinically and in experimental animal models[36–40]. Endothelial denudation, stretched smooth muscle fibers and ruptured internal elastic lamina have been demonstrated in canine basilar arteries after angioplasty. Using electron microscopy to study autopsied middle cerebral arteries in which TBA was performed, Yamamoto *et al.* documented torn and stretched collagen fibers and postulated that disrupted connective tissue within blood vessels was responsible for the sustained effect of TBA[39].

In his landmark paper, Zubkov described the use of balloon angioplasty for 105 cerebral arteries in 33 patients with no major complications[8]. In the decades that followed this seminal publication, numerous other groups have successfully used this technique and reported their clinical and angiographic success as well as their complications (*Table 1*)[4–10,22,33–35,41–45]. Since then, endovascular technology has progressed such that newer and safer balloons and catheters have been manufactured, perhaps explaining the increased popularity of this technique as the primary endovascular modality for refractory vasospasm. Expected results of TBA include clinical improvement, usually immediately noticeable, in 60–80% of patients, sustained angiographic dilatation that is almost uniformly achieved and

improvements in CBF as evidenced by SPECT and TCD studies[2,5].

### Clinical and radiographic results

Variable reports on the clinical efficacy of TBA exist (*Table 1*) and may be related to the differences in patient selection, timing of intervention and outcome assessment measures. In general, immediate neurological improvement can be expected in upwards of 60% of patients. We reported our early experience with TBA in which 41 patients were treated with a success rate (defined by an increase in Glasgow Coma Score by two points or significant improvement in speech or motor deficit) of 72%[4]. Subsequent reports on large numbers of vessels angioplastied from our group with increased usage documented clinical improvement in 74% (39 patients, 101 vessels[5]) and 61% (50 patients, 170 vessels[33]). One recent review of the English literature on this topic summated the patients treated with TBA for vasospasm in multiple papers and found a clinical improvement in 328 out of 530 patients treated[13]. Of note, one recent study looked at the results of TBA in the patients enrolled in the tirilizad in SAH trial and found no clinical benefit to TBA compared with a control population. These results are drastically different from the majority of other studies and can be explained by several methodological flaws inherent to that study, including lack of pre-treatment CT scan data (with 22/29 post-treatment scans showing infarcts), variable assessment of severity of vasospasm and inconsistent technique based on the collection of data from 15 different centers[34].

Like with IAP, clinical success does not always correlate with angiographic results. Multiple publications have cited a 100% success in angiographic response to TBA and this has been our experience (*Figure 1*)[4,9,10,46].

Numerous reports have confirmed the clinical and angiographic success of TBA using CBF physiologic measurements, including TCD[4,5,10,22,34], xenon-CT, xenon clearance and SPECT. TCD velocity improvement has been recorded to be 69% in one literature review incorporating 81 patients[13]. We were able to demonstrate an improvement in regional blood flow based on SPECT in eight out of ten patients in whom we studied both before and after TBA with this modality in an early study[4] and subsequently in 30/42 (71%) vessel segments using SPECT[5]. CBF as measured by xenon clearance in 12 patients undergoing TBA demonstrated increased flow in 7/12 (58%)[22].

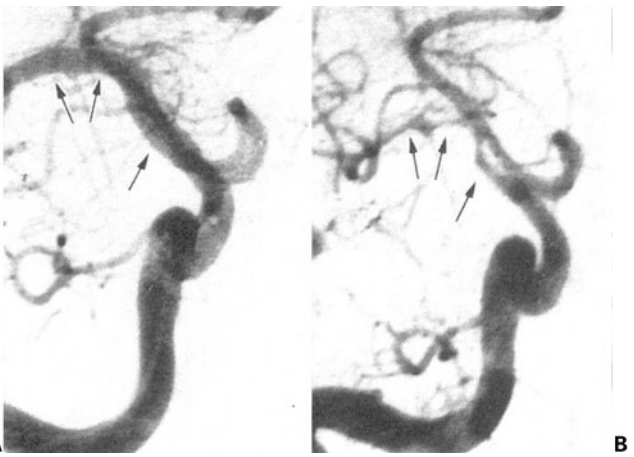


**Figure 1:** Right internal carotid artery injection digital subtraction angiography (oblique view) demonstrates angiographic changes after balloon angioplasty of the supraclinoid internal carotid artery (single arrow) and M1 segment (two arrows)

Little is known about the long-term effects of TBA. To determine whether there were any ill effects from the treatment during acute vasospasm, we obtained long term (average: 44 months) follow-up on 28 patients who had undergone TBA. No new neurological events were noted in the 21 patients studied and TCD documented normal velocities in all vessels. Cerebral autoregulation, assessed in the middle cerebral artery (MCA) with TCD,

**Table 1:** Results of select studies on balloon angioplasty for vasospasm

| Author | No. of patients | Angiographic results | Clinical results | Major procedural complications |
|---|---|---|---|---|
| Zubkov[38] | 33 | Successful in 100% | ? favorable | 0% |
| Higashida[15] | 13 | Successful in 100% | 69% improved | 7.7% |
| Newell[27] | 10 | Successful in 100% | 80% improved | 30% |
| Newell[26] | 41 | Successful in 100% | 72% improved | 9.8% |
| Nemoto[25] | 10 | Successful in 100% | 40% improved | 0% |
| Elliott[6] | 39 | Successful in 100% | 77% improved | 2.5% |
| Takahashi[35] | 22 | Successful in 100% | 70% improved | 4.5% |
| Bejjani[2] | 31 | Successful in 100% | 72% improved | 9.7% |
| Coyne[5] | 13 | Successful in 100% | 31% improved | 8% |
| Eskridge[7] | 50 | Successful in 100% | 61% improved | 10% |
| Firlik[11] | 14 | Successful in 93% | 92% improved | 7.7% |
| Fujii[14] | 19 | Successful in 83% | 63% improved | 5% |
| Rosenwasser[31] | 84 | Successful in 90% | 58% improved | 0% |
| Polin[29] | 38 | NA | 39% improved | NA |
| Muizelaar[24] | 13 | Successful in 85% | NAP | 7.7% |
| Oskouian[28] | 12 | Successful in 100% | 50% improved | 0% |

NA=not available; NAP=not applicable (angioplasty performed prophylactically in this study).

appeared to be normal, indicating that no long-term cerebrovascular occlusive disease had developed[25].

Complications of TBA include vessel rupture[33,47], vessel occlusion[10], hemorrhagic infarction of the vascular territory undergoing angioplasty[9], arterial dissection and hemorrhage from unsecured aneurysms[10]. The most serious, vessel rupture, is most often lethal and can be minimized by the use of soft compliant balloons, gentle inflation techniques (described below) and increased operator experience. Series by high volume centers have reported low complication rates, with two reports in the modern era documenting no neurological complications in their treatment of 115 patients[6,35]. Major complications were encountered in 5.0% of TBA procedures in one review with vessel rupture occurring in 1.1%[13].

Despite the inherent risks and the lack of a prospective controlled trial, TBA appears to be the best method of endovascular treatment for medically refractory vasospasm. In a study comparing TBA with IAP for medically refractory vasospasm, TCD velocity improvement was significantly greater and more sustained in the TBA cohort[5]. We have therefore adopted a practice of using TBA as a first line endovascular therapy in patients with refractory vasospasm with IAP used as an adjunct to facilitate TBA when the lumen diameter is too small to permit passage of the balloon catheter or in patients demonstrating distal, small vessel, vasospasm, in which TBA cannot be performed.

### *Technique*

Changes in the way we perform TBA for refractory vasospasm reflect our increased understanding of this disease process and the newer endovascular devices available[2,25]. We perform TBA under general anesthesia with full paralysis. A non-contrast CT scan of the head is obtained immediately before and after the procedure. CT scan of the head is mandatory before undertaking TBA, as it will show untreated hydrocephalus, aneurysmal rebleeding and completed infarction, which is a relative contraindication to TBA. Large territorial infarctions seen on CT scan and/or fixed neurological deficit that has persisted over several hours or more should make one reconsider TBA, as the chance for a reperfusion hemorrhage is increased. TBA can only be performed on the accessible large vessels at the base of the brain and is not effective for distal small-vessel vasospasm.

After placement of a 6 French vascular sheath into the common femoral artery, the patient is anticoagulated with 5000–7000 units of heparin and additional boluses of 1000 or 2000 units are periodically given to maintain the activated coagulation time at greater than 300 seconds. A 6 French guide catheter with a rotating hemostatic valve (to prevent untoward movements of the balloon microcatheter) is then advanced so that the tip sits within the distal cervical internal carotid artery (ICA) or distal dominant vertebral artery, depending on which part of the circulation is being treated.

If angiography demonstrates vasospasm in both the anterior and posterior circulation, the anterior circulation is treated first[2]. With the guide catheter in the distal ICA, fluoroscopic roadmapping technique in both the anteroposterior and lateral projections is used to navigate the balloon microcatheter into the vessel in vasospasm.

**Figure 2:** The progressive expansion of the compliant Sentry balloon (reprinted with permission from Target Therapeutics/Boston Scientific) frequently used to treat vasospasm

Balloon selection is somewhat a matter of choice and several balloons designed for this use exist. The balloon chosen must be compliant and pliable, and this usually indicates that the balloon is manufactured with silicone or polyethylene as opposed to latex, which is commonly used for balloon angioplasty of atheromatous disease. We prefer the Endeavor or Sentry balloon (Target Therapeutics/Boston Scientific, *Figure 2*) although the Hyperglide balloon (Microtherapeutics, Inc.) has been used with equal success. The Sentry balloon (usually 3.5 × 10 mm, although other sizes exist) is a single-lumen balloon-tipped microcatheter with an end hole that accepts 0.010–0.014 inch guidewires. For preparation, we simply flush the balloon with contrast material before pre-loading with the microguidewire. Although the balloon can be inflated and maintained with a maximal pressure of four atmospheres if the wire is kept inside, for treating vasospasm, we tend to use the balloon with the microguidewire removed. This permits lower pressures and allows spontaneous deflation of the system.

Once an appropriate roadmap is obtained, we navigate the Sentry balloon using a microguidewire. We then remove the microguidewire and attach a 3 cc syringe contrast to the end of the balloon microcatheter. For anterior circulation vasospasm, we start with placing the balloon in the M1 segment and slowly inflate the balloon under fluoroscopic guidance. Angioplasty is performed as a four-step progression, starting with gentle inflation of the balloon to ~25% of maximal balloon volume and then deflated. Repeated angioplasty is then performed with successive inflation to 50, 75 and ultimately 100% of the balloon's maximal volume and diameter[2]. Each inflation is held for

approximately 1–2 seconds with particular care to avoid overly rapid inflation. Caution must be used particularly with the first inflation of the balloon, where over-inflation or too rapid inflation is most often associated with arterial rupture. Arterial inflation must never be performed to a balloon diameter that exceeds the normal vessel diameter. We find it best to start the angioplasty distal on the M1 segment and successively move the balloon proximal. As we maneuver the balloon more proximally, we try to overlap the segments within the M1 to improve the overall angiographic appearance and avoid residual areas of focal stenosis.

Next, the balloon catheter is brought down into the supraclinoid ICA. Sometimes, it is the easiest to maintain partial inflation of the balloon as it is navigated into the supraclinoid ICA, to prevent it from sliding past the focal area of stenosis, which is sometimes exacerbated by a direct effect from pooled subarachnoid blood in dural folds in this area. Stepwise inflation is again the technique used, with some care to avoid complete deflation for the reason just mentioned. Consideration is sometimes given to balloon angioplasty of the A1 segment if the clinical situation dictates and only when prior angiograms confirm that the A1 is truly in spasm and not simply representative of a congenital hypoplastic or aplastic artery, which is common. Because of its small size, angioplasty of the A1, while technically feasible[48], is also the most risky and should be undertaken only by experienced operators and only if there is a strong clinical suspicion that the vasospasm from this vessel is symptomatic. Improved flow post-TBA of the ICA usually increases flow in distal vessels such as the A1. Because of the small size of the vessels relative to available balloons, we limit angioplasty to the MCA before its bifurcation into the M2 segments, the ICA and the A1 segments. IAP is infused in vessels if the spasm is so severe that the balloon cannot enter unless predilated or in patients in whom there is a concern that spasm distal to the vessels treatable with TBA is the cause of the neurological deterioration[25].

The technique of angioplasty is similar for the posterior circulation. Under roadmap guidance, the balloon microcatheter is directed into the basilar artery where angioplasty for the vertebrobasilar system usually begins. Dilatation of the P1 segments of the posterior cerebral artery (PCA) is performed only when there is a confirmation from prior angiography that these vessels are not congenitally narrowed. The balloon catheter is brought down in stepwise fashion into the vertebral artery, where continued angioplasty is performed, usually stopping at just proximal to the takeoff of the posterior inferior cerebellar artery. It is generally not necessary to dilate both vertebral arteries.

### *Timing*

As with neurological deficits from other causes, it appears that the sooner one treats active symptomatic vasospasm with TBA, the more likely there is to be a good recovery[6,33,35]. Of course, in part, this is related to the fact that continued vasospasm will often lead to cerebral infarction, which does not respond to angioplasty. It is even hypothesized that in those series in which low rates of clinical response to TBA are recorded that patients with completed infarction were included[6,43]. The optimal timing in relation to the development of symptoms has not been defined, with some advocating waiting for failure of 'triple H' therapy and others evaluating the use of prophylactic angioplasty for appropriate candidates[7].

The benefit of early treatment was documented by Bejjani *et al.*, who described the use of TBA in 31 patients with refractory symptomatic vasospasm and noted a significantly increased chance of good recovery in patients treated within 24 hours of symptom onset[35]. In our initial experience using TBA for vasospasm, we noted a tendency for better outcome in those patients treated within 12 hours of neurological deterioration[33]. In the most extensive study on this subject, Rosenwasser *et al.* studied the effect of timing of angioplasty after aneurysmal SAH in 84 patients. They found that patients treated within 2 hours of symptom onset ($n$=51) had a 70% rate of early favorable outcome compared with a 40% rate in those patients ($n$=33) treated after 2 hours[6].

These results strongly support the notion that angioplasty is more effective before permanent ischemic damage from vasospasm takes place. Because there can be a short time window between the onset of reversible neurological deficit and permanent neurological deficit, some have argued that pre-emptive angioplasty in high risk patients may be warranted. Muizelaar *et al.* designed a pilot study to test the hypothesis that it would be clinically beneficial to perform prophylactic angioplasty in the patients most susceptible to vasospasm, those suffering Fisher grade 3 SAH. They demonstrated that none of the 13 patients enrolled in this study and treated with prophylactic TBA suffered symptomatic vasospasm[7]. There was also no evidence for severe vasospasm in this cohort using TCD criteria. The success of this study was tempered by one procedural-related death associated with arterial rupture during TBA. Nonetheless, a larger prospective randomized study is underway to further define the role of prophylactic angioplasty in such patients.

## CONCLUSIONS

Endovascular therapy has proven to be an important adjunct in the treatment of medically refractory vasospasm. Although both intra-arterial administration of vasodilators and balloon angioplasty have been used as primary interventional modalities, we favor the use of balloon angioplasty as a first line agent because of its reproducible angiographic and clinical results, decreased complications when performed by experienced operators and sustained effect. Intra-arterial vasodilators continue to play an adjunct role in special circumstances and future studies on newer intra-arterially administered agents may increase their use. The results of the continuing trial on the prophylactic use of balloon angioplasty for Fisher grade 3 SAH as

well as the continued refinements in balloon and catheter technology should further define and advance the role of interventional procedures in the treatment of this condition.

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