

## Comparison of balloon angioplasty and papaverine infusion for the treatment of vasospasm following aneurysmal subarachnoid hemorrhage

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**Object.** The purpose of this study was to test the hypothesis that balloon angioplasty is superior to papaverine infusion for the treatment of proximal anterior circulation arterial vasospasm following subarachnoid hemorrhage (SAH). Between 1989 and 1995, 125 vasospastic distal internal carotid artery or proximal middle cerebral artery vessel segments were treated in 52 patients.

**Methods.** Blood flow velocities of the involved vessels were assessed by using transcranial Doppler (TCD) monitoring in relation to the day of treatment with balloon angioplasty or papaverine infusion. Balloon angioplasty and papaverine infusion cohorts were compared based on mean pre- and posttreatment velocity at 24 and 48 hours using the one-tailed, paired-samples t-test. Balloon angioplasty alone was performed in 101 vessel segments (81%) in 39 patients (75%), whereas papaverine infusion alone was used in 24 vessel segments (19%) in 13 patients (25%). Although repeated treatment after balloon angioplasty was needed in only one vessel segment, repeated treatment following papaverine infusion was required in 10 vessel segments (42%) in six patients because of recurrent vasospasm ( $p < 0.001$ ). Seven vessel segments (29%) with recurrent spasm following papaverine infusion were treated with balloon angioplasty. Although vessel segments treated with papaverine demonstrated a 20% mean decrease in blood flow velocity ( $p < 0.009$ ) on posttreatment Day 1, velocities were not significantly lower than pretreatment levels by posttreatment Day 2 ( $p = 0.133$ ). Balloon angioplasty resulted in a 45% mean decrease in velocity to a normal level following treatment ( $p < 0.001$ ), a decrease that was sustained.

**Conclusions.** Balloon angioplasty is superior to papaverine infusion for the permanent treatment of proximal anterior circulation vasospasm following aneurysmal SAH.

**KEY WORDS** • subarachnoid hemorrhage • vasospasm •  
transcranial Doppler ultrasound • balloon angioplasty • papaverine

CEREBRAL vasospasm remains a leading cause of increased morbidity and mortality rates following aneurysmal subarachnoid hemorrhage (SAH)<sup>20</sup> despite the apparent benefit of hypervolemic/hypertensive treatment<sup>43</sup> and calcium channel-blocking agents.<sup>42</sup> The development of noninvasive transcranial Doppler (TCD) evaluation of the cerebrovasculature has greatly facilitated the early diagnosis of vasospasm and the routine monitoring of arterial cerebral blood flow (CBF) velocity following treatment.<sup>39</sup> Successful resolution of medically refractory angiographically demonstrated vasospasm, with concomitant reversal of delayed neurological deficit, has been observed after balloon angioplasty treatment.<sup>9,15,36</sup> More recently, papaverine infusion has been used, with varying results in a small number of patients.<sup>18,19</sup> This study retrospectively compared balloon angioplasty with papaverine infusion for their efficacy in permanently reversing proximal anterior circulation vasospasm following SAH, as measured by TCD monitoring.

### Clinical Material and Methods

#### *Patient Population, Diagnosis, and Initial Management*

A retrospective review was made of the medical records of all patients diagnosed as having a ruptured cerebral aneurysm who were admitted to Harborview Medical Center at the University of Washington between September 1989 and July 1995. On admission, SAH caused by a ruptured aneurysm was confirmed by computerized tomography (CT) scanning or by lumbar puncture. Aneurysm location was assessed using four-vessel angiography or, in the case of moribund patients, by infusion CT scanning.<sup>23,38</sup> All patients admitted during this time period were considered surgical candidates and treated by a standardized protocol. Following preoperative resuscitation, patients were treated with early surgery, aggressive management of intracranial pressure (ICP) and vasospasm, and intensive perioperative care, as previously described.<sup>24-26</sup> Routine ICP and invasive hemodynamic monitoring and frequent CT scans of the head supplemented clinical evaluation. Phenytoin

TABLE 1  
Criteria for TCD evaluation of ICA or MCA vasospasm

Mean Velocity (cm/sec)	Intracranial/Extracranial Velocity Ratio*	Interpretation
<120	<3	normal or nonspecific elevation
≥120	3–6	vasospasm
≥200	>6	severe vasospasm

\* Quotient of distal intracranial ICA or proximal MCA velocity and the ipsilateral extracranial ICA velocity.

and nimodipine were routinely administered to achieve therapeutic levels. Volume expansion was initiated prophylactically.

#### Transcranial Doppler Evaluation

A baseline admission and repeated (usually daily) perioperative TCD examinations were obtained in all patients by experienced examiners using the standard technique.<sup>11</sup> The highest velocity in each vessel segment was recorded. Distal internal carotid artery (ICA) velocity was measured by transorbital or transtemporal TCD sonography, and middle cerebral artery (MCA) velocity was measured by transtemporal TCD. Each TCD examination included velocity measurements in both cervical ICAs via a submandibular approach. The quotient of the intracranial ICA or MCA velocity to the ipsilateral cervical ICA velocity (intracranial/extracranial ratio) allows for correction of systemic factors that alter volume flow.<sup>3</sup> The criterion for vasospasm of the distal ICA or proximal MCA was defined as a velocity greater than or equal to 120 cm/second with an intracranial/extracranial velocity ratio greater than or equal to 3 (Table 1). Treatment for hypertension supplemented prophylactic hypervolemia when symptomatic TCD vasospasm was diagnosed. Persistent symptomatic vasospasm was confirmed by angiography prior to treatment with balloon angioplasty or papaverine infusion. Transcranial Doppler sonography has the greatest accuracy for the diagnosis of vasospasm of the distal ICA and proximal MCA, and these vessel segments are the most amenable to balloon angioplasty. This study was therefore confined to assessing vasospasm in these vessel segments. Serial single-photon emission computerized tomography (SPECT) scans were used to assess the change in relative CBF in the affected territories in many of these patients.<sup>28,29</sup>

#### Treatment of Vasospasm

Aneurysms were obliterated in all patients prior to intra-arterial treatment of vasospasm. Balloon angioplasty was used to treat refractory vasospasm in all cases presenting before 1992. Since 1992, papaverine infusion has been used alone or in conjunction with balloon angioplasty in accordance with the clinical judgment of the treating interventional neuroradiologist (J.M.E.). Following confirmatory angiography, all accessible vasospastic segments were treated. Significant angiographic vasospasm was defined as a decrease of 25% or more in the diameter of a vessel segment when compared with the baseline angiogram, as previously reported.<sup>37</sup> Following balloon angioplasty in the symptomatic segments, papaverine infusion

was often used to treat contralateral vasospastic segments or to improve balloon access. Papaverine infusion alone was not usually used in the most severe cases. In the few cases in which increased TCD values were not accompanied by angiographic vasospasm, no treatment was administered. In cases in which patients were referred with unclipped aneurysms and severe, symptomatic vasospasm, balloon angioplasty and/or papaverine infusion was instituted immediately after aneurysm obliteration.<sup>27</sup>

#### Balloon Angioplasty

After full heparinization had been induced in the patient, a transfemoral approach was used to place an introducer catheter in the ICA. A low-pressure silicone angioplasty balloon was attached to a microcatheter of varying stiffness (Target Therapeutics Corp., San Jose, CA). With the aid of high-resolution digital fluoroscopy with digital road-mapping capabilities, the balloon was inflated and deflated in less than 5-second intervals, moving proximally to distally along the course of the spastic vessel.<sup>8,9</sup> Heparinization was reversed by administration of protamine sulfate after a posttreatment angiogram had been obtained.

#### Papaverine Infusion

Intraarterial papaverine was infused by placing a microcatheter just proximal to the spastic segment or, in some cases, more proximally in the ICA. Patients did not receive heparin prior to papaverine treatment. Doses of approximately 300 mg per vessel were infused over 20 minutes to 1 hour while changes in blood pressure and intracranial hypertension were monitored.<sup>33</sup> Posttreatment angiography was performed to assess the effects of treatment in all cases.

#### Comparison of Balloon Angioplasty and Papaverine Infusion

Vasospasm of the involved distal intracranial ICA or proximal MCA was assessed in relation to the day of treatment with balloon angioplasty or papaverine infusion by using TCD monitoring of both the absolute velocity of blood flow and the intracranial/extracranial velocity ratio. Pretreatment velocity (Day 0) was compared to the velocity at 24 (postoperative Day 1) and 48 hours posttreatment (postoperative Day 2) for each vessel segment using the one-tailed, paired-samples t-test. Vessels initially treated with a combination of the two methods were excluded from this analysis. Vessels treated successively with papaverine infusion and then balloon angioplasty, or with repeated treatment using either modality, were included in the original treatment cohort until the day of the subsequent treatment. Statistical analysis was performed using a commercially available software package (SPSS 6.1; SPSS, Inc., Chicago, IL).

#### Regional Cerebral Blood Flow Assessment

Single-photon emission <sup>99m</sup>Tc-hexamethylpropylene amine oxime (HMPAO) computerized tomography scans were obtained pre- and posttreatment in a subset of patients by means of methodology previously described.<sup>28,29</sup> The radiopharmaceutical material was injected intravenously within 30 minutes of reconstitution. Between 30 minutes and several hours postinjection, scanning was

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TABLE 2

*Clinical characteristics of 52 patients treated with papaverine infusion or balloon angioplasty\**

Characteristic	No. of Patients W/ Papaverine Infusion (%)	No. of Patients W/ Balloon Angioplasty (%)
age (yrs)		
mean $\pm$ SEM	52 $\pm$ 4	45 $\pm$ 2
range	27–53	22–73
sex		
female	9 (69)	25 (64)
male	4 (31)	14 (36)
grade at presentation		
I–III	10 (77)	26 (67)
IV–V	3 (23)	13 (33)
aneurysm location		
anterior circulation	12 (92)	33 (85)
posterior circulation	1 (8)	6 (15)
clinical deficit w/ vasospasm		
altered consciousness	9 (69)	20 (51)
weakness	1 (8)	6 (16)
combination or other	3 (23)	13 (33)
deficit resolution		
initial treatment	9 (69)	29 (74)
subsequent treatment	8 (62)	1 (3)
GOS ranking†		
favorable	8 (62)	26 (67)
unfavorable	5 (38)	13 (33)

\* GOS = Glasgow Outcome Scale; SEM = standard error of the mean.

† Favorable = good or moderately disabled; unfavorable = severely disabled, vegetative, or dead.

performed using low-energy, high-resolution collimation. Reconstructions were back-projection filtered, and attenuation correction was made using the Chang boundary method. Images were added to make contiguous slices comparable to the spatial resolution of the camera system and interpreted by a nuclear medicine physician experienced in brain SPECT imaging interpretation. The cerebellum was used as an internal reference point for comparison to the supratentorial uptake of radiopharmaceutical material. The paired SPECT studies of regional (r)CBF before and after vessel segment treatment with either balloon angioplasty or papaverine infusion were interpreted together in the transverse, coronal, and sagittal planes. The blood flow in the territory supplied by the treated vasospastic vessel was summarized as decreased, unchanged, or improved.

### Results

#### Clinical Data

During the study period from September 1989 to July 1995, 587 patients were surgically treated for a ruptured cerebral aneurysm. Seventy-eight patients developed medically refractory, symptomatic vasospasm. In the 52 patients initially treated by either balloon angioplasty (39 patients) or papaverine infusion alone (13 patients), a total of 125 anterior circulation distal ICA or proximal MCA vessel segments were evaluated. A combination of both modalities was used to treat the remaining 26 patients. The proximal MCA accounted for the majority of vessel segments treated in both the balloon angioplasty (56%) and the papaverine infusion cohorts (63%). The incidence of SAH was not significantly different among treatment groups. Age, gender, SAH grade at presentation, aneu-

rysm location, and clinical deficit associated with anterior circulation vasospasm were similar in the two treatment groups (Table 2).

#### Velocity Measurement by Means of TCD After Treatment of Vasospasm

**Balloon Angioplasty.** In 101 vessel segments in 39 patients treated with balloon angioplasty, the mean combined TCD-measured blood flow velocity in the distal ICA and proximal MCA increased from a baseline of  $95 \pm 12$  to  $166 \pm 9$  cm/second just before treatment. This decreased significantly to  $92 \pm 4$  cm/second following balloon angioplasty and remained stable ( $p < 0.001$ ; Fig. 1 *left*). The intracranial/extracranial ratio also decreased significantly, from  $5 \pm 0.3$  just before treatment to  $2.5 \pm 0.1$  after treatment ( $p < 0.001$ ; Fig. 1 *right*). When distal intracranial ICA and proximal MCA segments treated by means of balloon angioplasty were analyzed separately, these relationships persisted. Distal intracranial ICA flow velocity decreased from  $118 \pm 77$  to  $81 \pm 6$  cm/second ( $p < 0.001$ ) and the intracranial ICA/extracranial ICA ratio decreased from  $3.5 \pm 0.3$  to  $2.1 \pm 0.2$  ( $p < 0.001$ ). Proximal MCA flow velocity decreased from  $206 \pm 8$  to  $100 \pm 5$  cm/second ( $p < 0.001$ ), and the proximal MCA/extracranial ICA ratio decreased from  $6.1 \pm 0.4$  to  $2.7 \pm 0.2$  ( $p < 0.001$ ).

**Papaverine Infusion.** In 24 vessel segments in 13 patients treated with papaverine infusion, the mean TCD-measured blood flow velocity was  $158 \pm 8$  cm/second just before treatment, and although this value decreased significantly, to  $127 \pm 13$  cm/second ( $p = 0.008$ ; Fig. 2 *left*) on posttreatment Day 1, the mean velocity failed to reach normal levels and increased toward pretreatment levels by posttreatment Day 2 ( $p = 0.133$ ). The associated intracranial/extracranial ratio decreased from  $4.1 \pm 0.4$  pretreatment to  $3.7 \pm 0.5$  on posttreatment Day 1 ( $p = 0.23$ ; Fig. 2 *right*), but increased above the pretreatment value by posttreatment Day 2 ( $p = 0.31$ ). Correlation of the TCD intracranial/extracranial ratio with recurrent symptomatic angiographic vasospasm after papaverine infusion is illustrated in Fig. 3. When distal ICA segments and proximal MCA segments treated with papaverine infusion were analyzed separately, the mean distal ICA velocity and ratio failed to demonstrate a significant response at 1 or 2 days posttreatment. Although proximal MCA flow velocity decreased from  $166 \pm 10$  cm/second just before papaverine treatment to  $135 \pm 15$  cm/second on posttreatment Day 1 ( $p = 0.018$ ), it failed to reach normal levels, increasing to  $140 \pm 13$  cm/second by posttreatment Day 2 ( $p = 0.028$ ).

#### Response to Treatment

Angiographic response at the time of initial treatment was observed in all patients treated with either balloon angioplasty or papaverine infusion. However, a failure to respond clinically coupled with recurrent elevation of TCD-measured flow velocity necessitated retreatment for vasospasm. This occurred in patients initially treated with papaverine infusion significantly more often than in patients initially treated with balloon angioplasty ( $p < 0.001$ , Fisher's exact test; Table 3). Thirteen vessel segments (54%) in eight patients (62%) initially treated with papaverine infusion alone required retreatment: six vessel segments in three patients were treated with repeated

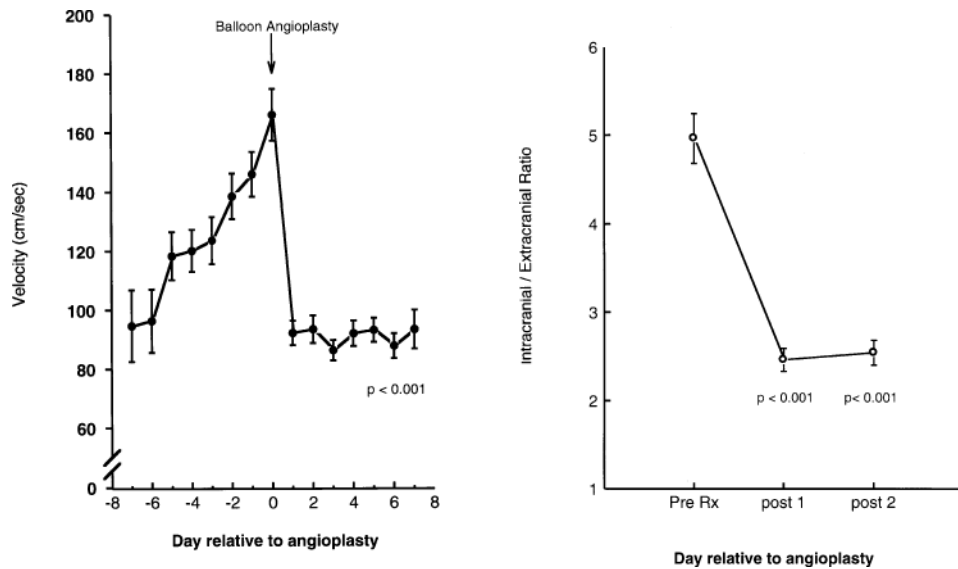


FIG. 1. *Left:* Graph showing the results of treatment of vasospasm with balloon angioplasty in 101 distal ICA or proximal MCA vessel segments in 39 patients that resulted in a sustained decrease in the mean TCD-measured flow velocity to normal levels. *Right:* Graph showing a sustained decrease in the mean TCD-measured flow velocity ratio (MCA or distal intracranial ICA/extracranial ICA) in patients treated with balloon angioplasty.

papaverine infusion; three segments in two patients with balloon angioplasty; and four segments in three patients with both modalities simultaneously (Table 3). Only one patient (3%) initially treated with balloon angioplasty alone required retreatment. Overall, a favorable clinical outcome was achieved in 26 patients (67%) initially treated with balloon angioplasty (Table 2). Whereas eight patients (62%) initially treated with papaverine infusion ultimately achieved a favorable outcome, retreatment with balloon angioplasty and/or papaverine infusion was necessary in five (63%) of these patients. Response to vaso-

spasm treatment was associated with a favorable clinical outcome ( $p < 0.001$ , Fisher's exact test; Table 2). Complications of balloon angioplasty included one death in a patient treated for vasospasm after partial clipping of an anterior communicating artery aneurysm. There were no deaths or clinically evident complications in patients treated with papaverine.

*Evaluation of CBF by SPECT Scanning*

Both pre- and posttreatment SPECT evaluations obtained within 24 hours of treatment were available for

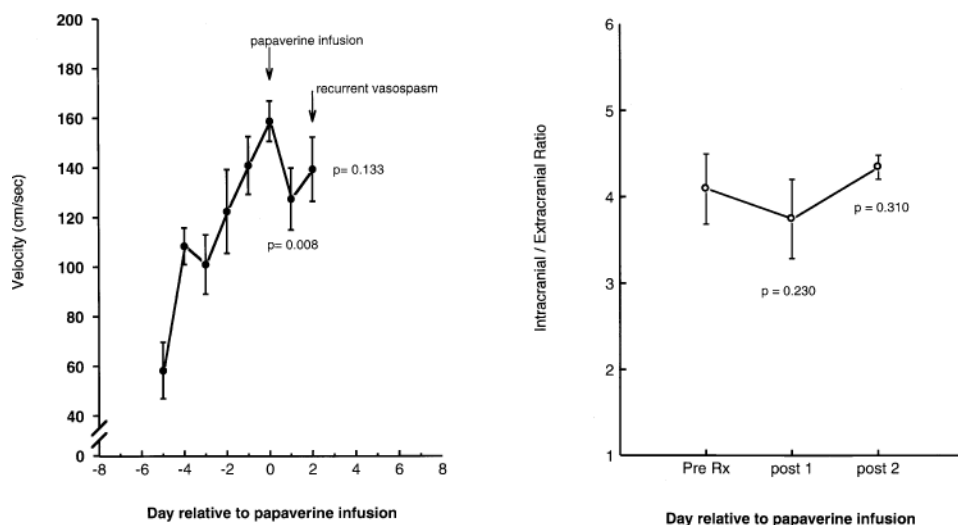


FIG. 2. *Left:* Graph showing results of treatment with papaverine infusion in 24 distal intracranial ICA or proximal MCA vessel segments in 13 patients that resulted in an initial transient decrease in mean velocity that failed to reach normal levels and increased toward pretreatment levels within 2 days. *Right:* Graph showing that the mean TCD velocity ratio (MCA or distal intracranial ICA/extracranial ICA) also decreased transiently in patients treated with papaverine infusion, returning to pretreatment levels within 2 days.

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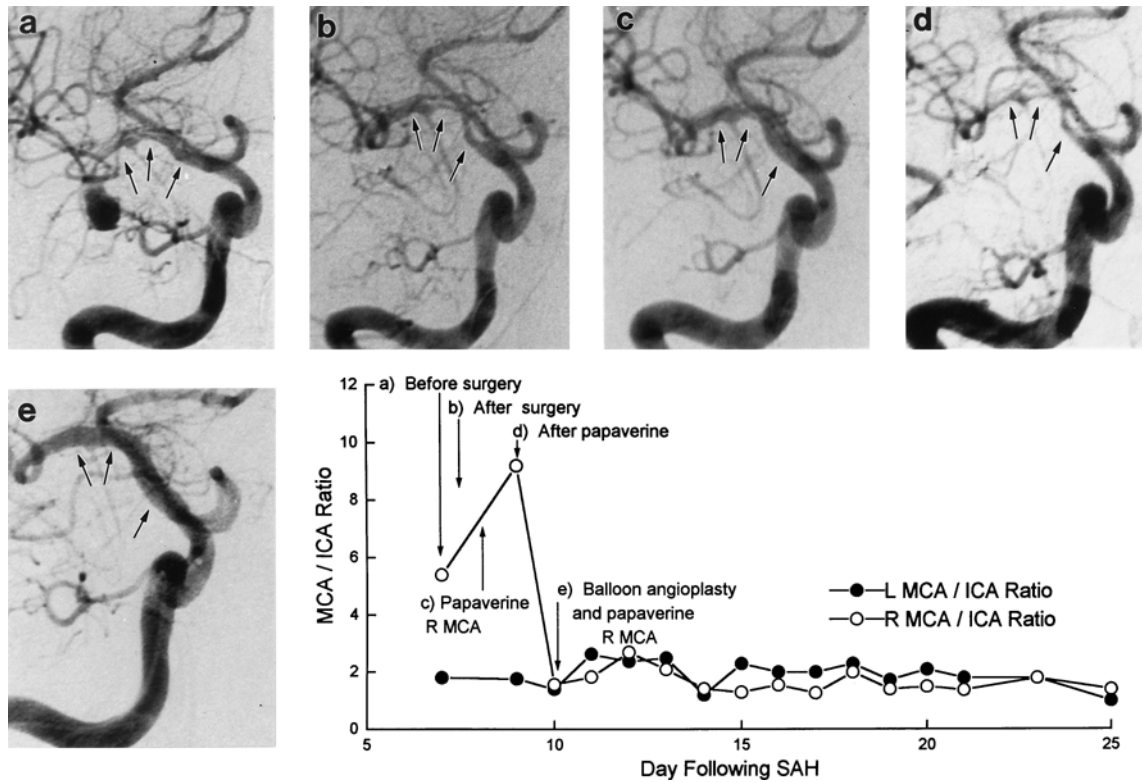


FIG. 3. Correlation of angiographically confirmed vasospasm with MCA/extracranial ICA velocity ratio in a representative case of a 47-year-old woman who suffered a Grade II SAH from an MCA aneurysm and in whom severe vasospasm was documented at the time of presentation. a: Initial angiogram obtained at presentation showing an unclipped MCA aneurysm and severe vasospasm of the MCA trunk (arrows). b: Angiogram obtained immediately after surgery illustrating aneurysm obliteration and persistent vasospasm of the MCA (arrows). c: Angiogram obtained immediately after papaverine infusion showing improved caliber of the MCA (arrows). d: Middle cerebral artery velocity and ratio were higher than preoperative values the day after papaverine treatment, prompting a repeated angiogram that shows recurrent severe vasospasm of the MCA (arrows). e: Angiogram obtained after balloon angioplasty and papaverine treatment illustrating increased diameter at the MCA (arrows), which correlated with a persistently decreased MCA/extracranial ICA velocity ratio, indicating sustained reversal of vasospasm.

assessing a total of 58 anterior circulation vessel territories in 37 patients (Table 4). Prior to treatment, patients in the papaverine-treated group demonstrated decreased SPECT perfusion in 14 vessel segment territories (88%). This was similar to the balloon angioplasty group, in which 86% of vessel segment territories were decreased before treatment. Following treatment, five vessel segment territories (31%) showed improvement within 24 hours after papaverine infusion, whereas 30 vessel segment territories (71%) improved after balloon angioplasty. This difference was statistically significant ( $p = 0.007$ , Fisher's exact test).

### Discussion

The purpose of this study was to determine if balloon angioplasty is superior to papaverine infusion for the permanent reversal of anterior circulation vasospasm following aneurysmal SAH. Transcranial Doppler sonography was used to compare and sequentially monitor the effect of each treatment on vessel caliber. Balloon angioplasty proved to be superior to papaverine infusion in producing a sustained reduction of elevated blood flow velocities associated with vasospasm to normal levels. Balloon an-

gioplasty was also associated with fewer treatment failures than papaverine infusion.

### Transcranial Doppler Response to Treatment

Before accepting the results of this study, it is useful to review the value and limitations of TCD sonography in detecting and monitoring vasospasm. Well-suited for the noninvasive detection of vasospasm,<sup>35</sup> TCD monitoring is

TABLE 3  
Summary of vasospasm treatment in 125 distal ICA and proximal MCA vessel segments\*

Modality	No. of Vessel Segments Treated		
	Initial Treatment	Repeated Treatment	Crossover Treatment
papaverine infusion	24	10 (42%)	7 (29%)†
balloon angioplasty	101	1 (1%)	0 (0%)‡

\* Clinical response to vasospasm treatment associated with favorable clinical outcome ( $p < 0.001$ , Fisher's exact test).

† Crossover treatment to balloon angioplasty.

‡ Crossover treatment to papaverine infusion.

TABLE 4  
*Evaluation of CBF by SPECT scanning at 24 hours after  
 treatment of anterior circulation vasospasm*

Variable	Papaverine Infusion (13 patients)	Balloon Angioplasty (24 patients)
pretreatment perfusion		
decreased	14 (88%)	36 (86%)
normal	2 (13%)	6 (14%)
change in perfusion posttreatment		
decreased	4 (25%)	7 (17%)
unchanged	7 (44%)	5 (12%)
improved*	5 (31%)	30 (71%)
total territories treated	16	42

\* Statistically significant difference ( $p = 0.007$ , Fisher's exact test) achieved in improvement of balloon angioplasty—over papaverine infusion—treated patients.

not only technically feasible in the vast majority of cases, but it is also directed toward the proximal basal vessel segments where vasospasm occurs.<sup>37</sup> In some cases, vasospasm may be limited to distal vascular distributions and can be missed by TCD examination.<sup>37</sup> Vasospastic MCAs, as visualized by angiography, consistently demonstrate flow velocities greater than 120 cm/second, with velocity being inversely related to arterial diameter.<sup>1,2,13</sup> Although angiographic responses to balloon angioplasty<sup>8,9,15,36,47</sup> and papaverine infusion<sup>7,9,18</sup> have both been reported to be successful, these observations have been predominantly made immediately following treatment. In this study, the use of TCD evaluation allowed daily monitoring throughout the intensive care unit stay as well as frequent examinations throughout the postoperative period. This monitoring protocol allowed comparison between treatment efficacy of balloon angioplasty and papaverine infusion on vessel caliber. Balloon angioplasty has been reported to be successful when used either soon after the onset of neurological deficit or in a delayed fashion.<sup>4</sup> It has been suggested that papaverine is most effective when used soon after the onset of vasospasm before arteries lose their ability to return to their normal caliber.<sup>18</sup> Because it is impractical to repeat angiography at frequent intervals, daily TCD evaluation following treatment offers an ideal approach to the monitoring of the posttreatment interval in which recurrent elevation of flow velocities is most often associated with the recurrent vasospasm that can adversely affect outcome.<sup>17,21</sup>

In the present study, balloon angioplasty resulted in an immediate and permanent decrease in TCD-measured flow velocity and reversal of vasospasm in affected ICA and MCA segments. Papaverine infusion also resulted in an initial decrease of TCD-measured velocities; however, reversal of vasospasm was transient in the majority of cases, rendering it much less effective as a treatment for vasospasm when used alone. Only one vessel segment initially treated with balloon angioplasty required repeated treatment, whereas 42% of vessel segments initially treated with papaverine required repeated infusion and 29% required subsequent balloon angioplasty.

#### *Why is Balloon Angioplasty Superior to Papaverine Infusion?*

In the majority of cases we found that balloon angio-

plasty provided permanent TCD-confirmed reversal of vasospasm after a single treatment, whereas the effects of papaverine were often transient, requiring multiple treatments. Such multiple treatments increase the potential for complications as well as cost associated with papaverine when used alone as a therapeutic strategy.

Although the reasons for the more sustained effect of balloon angioplasty treatment are not yet known, there is increasing evidence that anatomical and physiological mechanisms of action may be involved. Stretched and torn collagen fibers,<sup>45</sup> endothelial denudation and rupturing of the internal elastic lamina,<sup>6,10,41</sup> thinning of the tunica media,<sup>6,16</sup> and alteration of smooth-muscle cells<sup>6</sup> have all been associated with permanent reversal of vasospasm in a variety of models. In addition, impaired vasoreactivity to a wide range of vasoconstrictors has been observed following balloon angioplasty.<sup>6</sup> There is mounting evidence that vasospasm results from calcium-mediated smooth-muscle contraction during an early active phase and may be subsequently sustained by noncontractile processes.<sup>12</sup> It is possible that impairment of the vasoreactivity of smooth muscle may contribute to the early phase of persistent dilation following balloon angioplasty and that structural changes may account for its long-term efficacy.

The transient effects of papaverine infusion may be largely due to its action as a nonspecific smooth-muscle relaxant. The use of papaverine has been limited by both dose and mode of delivery. Although repeated infusions of intrathecal papaverine can reverse angiographically demonstrated vasospasm,<sup>22,40</sup> this treatment is limited by its attendant elevated rates of morbidity. Preliminary studies of a sustained-release papaverine preparation have been reported.<sup>14</sup> Although the use of intraarterial papaverine in combination with other agents such as sodium nitropruside or adenosine has been reported,<sup>34</sup> vasospasm was reversible only if treated within 2 days of SAH. Thus, it is likely that papaverine is most useful only when administered soon after SAH; unfortunately, in the clinical setting this may occur after the time during which vasospasm becomes medically refractory.

#### *Role of Papaverine*

Although we found papaverine infusion alone to be less effective than balloon angioplasty for the treatment of vasospasm, a small initial infusion often facilitated access for balloon angioplasty procedures. Whereas the use of papaverine must be tempered by its attendant risk of hemodynamic complications,<sup>33</sup> it remains potentially useful for the treatment of vasospastic vessel segments that cannot be treated with balloon dilation, such as the anterior cerebral artery, MCA branches, and distal distributions. Further studies in which serial blood flow measurements are made are needed to establish papaverine's long-term effect in these vessels.

#### *Complications of Treatment*

The complications of balloon angioplasty and papaverine infusion should be considered in conjunction with their efficacy. With experience and attention to several caveats, the complications associated with balloon angioplasty can be minimized. It is important to obliterate the ruptured aneurysm before performing balloon angioplasty on a feeding vessel to prevent aneurysm rebleeding.<sup>9</sup>

## Comparison of angioplasty and papaverine

Therefore, when patients present with an unsecured aneurysm and symptomatic vasospasm, one treatment option is to proceed on an emergency basis with aneurysm obliteration followed by immediate balloon angioplasty.<sup>27</sup> Vessel rupture is another serious complication of balloon angioplasty,<sup>30</sup> occurring when the balloon is overdistended or positioned too distal in a vessel.<sup>9</sup> Balloon angioplasty therefore remains safest when limited to proximal vessel segments.

Papaverine infusion for the treatment of cerebral vasospasm might seem more attractive based on arguments that papaverine is safer because its infusion is less technically demanding than balloon angioplasty. This assumption, however, may not be true. Reported complications of papaverine infusion include monocular blindness,<sup>7</sup> brainstem dysfunction (including respiratory arrest),<sup>5,31</sup> focal neurological deficits that resolved on cessation of papaverine infusion,<sup>18,19</sup> and formation of crystal emboli.<sup>32</sup> Moreover, as the present study indicates, papaverine infusion does not provide permanent reversal of vasospasm, thus requiring repeated infusions with the associated risks of repeated angiography. We have previously reported that significant elevations in blood pressure and ICP, often accompanied by a decrease in cerebral perfusion pressure, were common complications of papaverine infusion not normally found with balloon angioplasty procedures.<sup>33</sup> When papaverine is required, it is therefore our policy to intubate the patient and use slow infusions with both arterial pressure and ICP monitoring.

### *Evaluation of CBF Changes by SPECT Scanning*

Single-photon emission computerized tomography scanning is one of several methods available to evaluate rCBF in patients with vasospasm following SAH.<sup>44</sup> In poor-grade patients it can be difficult or impossible to discern whether vasospasm is accompanied by a worsened neurological condition despite maximum medical treatment.<sup>9</sup> We have found <sup>99m</sup>Tc-HMPAO SPECT scanning of the brain to be a useful adjunct to TCD and neurological examinations in deciding when to perform angioplasty in this situation. Additionally, SPECT scanning has proven to be of interest in assessing changes in relative CBF following treatment with balloon angioplasty<sup>29</sup> and papaverine infusion.<sup>28</sup>

In the present study, an improved relative CBF, assessed by SPECT scans at 24 hours after treatment of vasospasm, was observed following treatment with balloon angioplasty significantly more often than with papaverine infusion; 71% of vessel segment territories demonstrated improved CBF 24 hours after balloon angioplasty, whereas only 31% of vessel segment territories showed improvement following papaverine infusion. Unfortunately, few studies were available for analysis of results 48 hours or more posttreatment. These results are consistent with our TCD observations that balloon angioplasty is superior to papaverine infusion when used alone for the treatment of vasospasm.

Although SPECT scanning assesses only relative CBF, Yonas, et al.,<sup>46</sup> made absolute CBF measurements using Xe-CT CBF evaluation and documented decreased CBF specific to territories supplied by vasospastic vessels. Nine of 14 patients who were persistently symptomatic despite maximum medical treatment demonstrated a CBF below 15 ml/100 g/minute in two or more adjacent 2-cm

cortical regions in the affected territory. Eight of these nine patients ultimately developed infarcts. No patient whose CBF remained above 18 ml/100 g/minute developed an infarct secondary to vasospasm. Used in combination with routine TCD detection of vasospasm, Xe-CT CBF or SPECT evaluation may prove valuable in deciding not only which patients will ultimately benefit from balloon angioplasty but may also help predict when earlier intervention during the asymptomatic period might be beneficial. Additionally, CBF imaging techniques such as Xe-CT and SPECT assess tissue perfusion, complementing the assessment of vessel diameter provided by TCD evaluation.

## Conclusions

Transcranial Doppler sonography was used to compare the efficacy of balloon angioplasty with papaverine infusion in the permanent reversal of anterior circulation vasospasm following aneurysmal SAH. We conclude that balloon angioplasty is superior to papaverine infusion in providing permanent reversal of vasospasm.

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