Use of a Large Angioplasty Balloon for Predilation is a Risk Factor for Embolic Complications in Protected Carotid Stenting

Akiyo SADATO, Tetsu SATOW, Akira ISHII, Takeshi OHTA, and Nobuo HASHIMOTO

Department of Neurosurgery, Kyoto University Graduate School of Medicine, Kyoto

Abstract

Periprocedural neurological complications (PNCs) after carotid stenting were retrospectively analyzed to determine the risk factors with the use of various protective devices. Forty-three lesions in 40 patients were treated by carotid stenting with distal balloon protection for nearly all postdilation procedures and some predilation procedures. The following variables were statistically analyzed for association with PNCs: diameter of the angioplasty balloon used for predilation, use of a distal protection balloon during predilation, use of a protection balloon during postdilation, lesion-bifurcation distance, length of the lesion, age, clinical presentation of the lesion (symptomatic or asymptomatic), and hypercholesterolemia. PNCs occurred in five patients, four with minor deficits and one with major deficits. Univariate analysis showed large diameter of the predilation angioplasty balloon (p = 0.0026), use of a protection balloon during predilation (p = 0.0075), lesion length (p = 0.0003), and lesion-bifurcation distance (p = 0.0006) were significantly associated with PNCs. Multivariate analysis of these four variables showed that use of a large angioplasty balloon for predilation was the only independent predictor (p = 0.004, odds ratio 34.00) for the occurrence of PNCs. Use of a large angioplasty balloon for predilation carries the risk of periprocedural embolic complications. Therefore, even when a protection device is used, predilation should be performed with a small balloon.

Key words: carotid stent, embolism, predilation, protection balloon

Introduction

Carotid angioplasty and stenting have recently emerged as alternatives to surgical treatment for high-grade stenoses in the carotid artery. Carotid stenting has a technical success rate of greater than 95%, but periprocedural neurological complications (PNCs) occur in 2% to 8% of cases. Most PNCs are supposedly caused by embolic plaque debris dislodged during the procedures. Various protection devices are now available to prevent embolic complications in the cerebral vasculature. However, embolic complications may not be completely avoided even with such devices. Therefore, the identification of the risk factors for embolic complications is very important. Two studies have investigated the risk factors for PNCs in carotid stenting with no protection devices, and found that advanced age, long lesion, symptomatic lesion, and absence of hypercholesterolemia are predictors of PNCs.

This study retrospectively investigated the use of distal protection balloons during pre- and postdilation in carotid stenting, as well as the use of larger angioplasty balloons for predilation, to assess the effect on the occurrence of PNCs.

Materials and Methods

I. Case profiles

In our institute, surgical or endovascular treatment is indicated for asymptomatic and symptomatic severe cervical carotid stenosis of more than 70% measured by the North American Symptomatic Carotid Endarterectomy Trial criteria. Carotid endarterectomy (CEA) is the procedure of choice, but endovascular stenting is selected for patients with relatively high risk for CEA such as advanced age (>75 years), unstable angina, high-positioned lesion, bilateral severe stenoses or contralateral occlusion, restenosis after CEA, and postradiation stenosis.
Carotid stenting has been performed on 47 lesions in 44 patients since 1999. Cases of restenosis after CEA or angioplasty (3 lesions) and postradiation stenosis (1 lesion) were excluded from the analysis. The remaining 43 lesions in 40 patients, 33 males and seven females aged 54 to 82 years (mean 70.6 years), were included in this study.

II. Stenting procedure

Two types of protection balloons were used in this study: a 2.4 Fr single-lumen balloon (Naviballoon D; Kaneka Medics, Osaka) (Fig. 1A) suitable only during postdilation, which was used throughout this series for 38 of 43 lesions; and a monorail-type balloon (Naviballoon M; Kaneka Medics) (Fig. 1B) suitable for predilation as long as the 0.010-inch wire can pass through the stenosis, which became available in October 2001 and was used for the predilation of 10 of 43 lesions.

All procedures were performed by the transfemoral approach under local anesthesia. An 8 or 9 Fr and a 5 Fr introducer were placed in the femoral arteries. Systemic heparinization was performed to raise the activated clotting time to over 250 seconds. An 8 or 9 Fr guiding catheter (Brite tip; Johnson & Johnson, New Brunswick, N.J., U.S.A.) was placed in the common carotid artery (CCA). Intravascular ultrasonography (IVUS) was performed first, and the stenting procedure was abandoned or postponed if echolucent plaque was detected.

Predilation was performed with an undersized angioplasty balloon with a diameter of 4.0 mm or less, usually 3.5 mm (SAVVY; Johnson & Johnson) in 35 lesions. However, after the monorail-type protection balloon became available, a larger angioplasty balloon with a diameter of 5 mm or more, usually 5 mm (SAVVY; Johnson & Johnson), was selected for eight lesions. The larger balloons were selected to establish a wider lumen at predilation to avoid narrowing or obstruction caused by the stent. The stent struts stick out toward the lumen and might disturb the removal of the stent-delivery sheath and following postdilation, especially if the plaque was located at a vascular curvature.

After predilation of the lesion, 20 ml of blood was aspirated through the guiding catheter, and if the internal carotid artery (ICA) was blocked with the distal protection balloon, followed by injection of 40 ml saline through the angioplasty balloon to wash away the plaque debris into the external carotid artery.

The protection balloon was not used during stent deployment. The stents used were Palmaz stent (Johnson & Johnson) in 10 lesions, SMART stent (Johnson & Johnson) in 22 lesions, and Acculink stent (Guidant, Temecula, Calif., U.S.A.) in 11 lesions.

Postdilation was performed if stenosis was still present (42 lesions). In principle, the distal protection balloon was used during postdilation (38/42 lesions). After postdilation, 20 ml of blood was aspirated, and then the debris was washed away into the external carotid artery with 40 ml saline injected through another 5 Fr catheter advanced just under the protection balloon.

After IVUS to ensure that the lesion was well dilated, heparin was reversed before removal of the femoral introducers. After hemostasis was completed, systemic anticoagulation was resumed with heparin and continued for 3 days (15,000 U/day, 10,000 U/day, and 5,000 U/day over a 24-hour period each day). Aspirin or ticlopidine administration was started at least 1 week prior to the procedure and both agents were given postoperatively.

III. Variables and measurements

This study investigated the following eight variables to study their association with PNCs: diameter of the angioplasty balloon used for predilation, use of a distal protection balloon during predilation, use of a protection balloon during postdilation, lesion-bifurcation distance, length of the lesion, age, clinical presentation of the lesion (symptomatic or asymptomatic), and hypercholesterolemia. The latter four variables are known to be significantly
associated with PNCs."

Medical records and angiograms were reviewed. PNCs were defined as any neurological deficits detected during the 48 hours after the stenting procedure. Hypercholesterolemia was defined as serum total cholesterol of above 220 mg/dl or use of antilipidemic medications.

Lesion length and the lesion-bifurcation distance were measured with a 0.035-inch calibrated wire with 3 mm-long radiopaque markers at intervals of 7 mm along the distal 10 cm (Interslupe; Clinical Supply Co., Hajima, Gifu) at angiography prior to the stenting procedure. The calibrated wire was positioned from the CCA to the external carotid artery, and angiography was performed. The angiographic and the fluoroscopic images were videotaped. The videotaped image including the calibrated wire parallel to both the anteroposterior and lateral image intensifiers was selected and transferred to a personal computer. Measurements were performed with NIH Image software (National Institutes of Health, Bethesda, Md., U.S.A.) using the markers of the calibrated wire as a reference. The lesion-bifurcation distance was defined as the distance between the distal end of the lesion and cervical carotid fork. This distance represents the length of the vascular stump where the distal protection balloon is used and thus the length of the dead space in the ICA from which plaque debris is to be cleared away. Four patients had lesions located in the CCA below the bifurcation. The lesion-bifurcation distance in these four cases was input as 0 mm, because the protection balloon is positioned just distal to the bifurcation and the length of the vascular stump is almost 0 mm.

The predilation angioplasty balloons were divided into small (<5 mm) and large (≥5 mm) diameters. The age, lesion length, and lesion-bifurcation distance were considered as continuous variables for the statistical analysis.

IV. Statistical analysis

Univariate analysis using the chi-square test for categorical variables and Student’s t-test for continuous variables was performed. Multivariate analysis was performed with the variables with p values of less than 0.05 by logistic regression analysis. The variables were subjected to backward stepwise regression analysis, and stepwise exclusion was performed by the criterion of p > 0.15. The remaining significant variables were included into the final logistic regression model and goodness of fit was calculated. Systat software (version 10.2; SPSS Inc., Richmond, Calif., U.S.A.) was used for all statistical analyses.

Results

I. Outcomes and complications

Successful dilation of the stenotic lesions, defined as less than 30% residual stenosis, was achieved in all lesions. All stents were deployed as intended. Symptomatic PNCs occurred in five lesions in five patients (11.6%). Three patients showed transient minor deficits (2 with upper limb motor weakness and one with aphasia), which disappeared within 2 weeks. Two patients developed permanent deficits, one with minor finger clumsiness and the other with major hemiparesis and total aphasia, affecting multiple major cerebral arterial territories. No neurological or non-neurological death occurred. Therefore, the occurrences of minor PNCs and major PNCs were 9.3% and 2.3%, respectively. The onset of the neurological symptoms occurred during the procedure in three patients, 5 hours after the procedure in one patient, and 20 hours after in one patient. Large balloons were used for predilation in the former four patients and a small balloon in the latter patient. Diffusion-weighted magnetic resonance imaging showed multiple fresh ischemic lesions in all five patients with symptomatic complications.

II. Statistical analysis

Table 1 presents the results of the univariate analysis of the eight variables. Large diameter of the predilation balloon (p = 0.0026), use of a protection balloon during predilation (p = 0.0075), lesion length (p = 0.0003), and lesion-bifurcation distance (p = 0.0006) were significantly related with the occurrence of PNCs.

The above four variables with p values of less than 0.05 were studied by multiple logistic regression analysis. Backward stepwise regression eliminated three of the four variables leaving only large diameter of the predilation balloon (p = 0.004). Final logistic regression with this significant variable revealed a regression coefficient of 3.526 and an odds ratio of 34.00 (95% confidence interval 3.012–382.844). The goodness of fit of the model with this variable was 1.328 (sensitivity 0.406, specificity 0.922). Figure 2 plots the correlation of lesion length, lesion-bifurcation distance, size of predilation balloon, and PNCs.

Discussion

The use of a large angioplasty balloon for predilation was the factor most associated with the occurrence of PNCs in this series. Dilation with a large balloon may cause dissection or rupture of the plaque, even if angiography does not show visible evidence, and
Table 1 Characteristics of the patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Overall (n = 43)</th>
<th>Periprocedural neurological complications</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes (n = 5)</td>
<td>No (n = 38)</td>
</tr>
<tr>
<td>Symptomatic, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>17 (39.5)</td>
<td>3 (17.6)</td>
<td>14 (82.4)</td>
</tr>
<tr>
<td>no</td>
<td>26 (60.5)</td>
<td>2 (7.7)</td>
<td>24 (92.3)</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>18 (43.9)</td>
<td>2 (11.1)</td>
<td>16 (88.9)</td>
</tr>
<tr>
<td>no</td>
<td>23 (56.1)</td>
<td>3 (13.0)</td>
<td>20 (87.0)</td>
</tr>
<tr>
<td>Size of predilation balloon, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>large (≥ 5 mm)</td>
<td>8 (18.6)</td>
<td>4 (50.0)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>small (&lt; 5 mm)</td>
<td>35 (81.4)</td>
<td>1 (2.9)</td>
<td>34 (97.1)</td>
</tr>
<tr>
<td>Use of protection balloon for predilation, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>10 (23.3)</td>
<td>4 (40.0)</td>
<td>6 (60.0)</td>
</tr>
<tr>
<td>no</td>
<td>33 (76.7)</td>
<td>1 (3.0)</td>
<td>32 (97.0)</td>
</tr>
<tr>
<td>Use of protection balloon for postdilation, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>38 (88.4)</td>
<td>5 (13.2)</td>
<td>33 (86.8)</td>
</tr>
<tr>
<td>no</td>
<td>5 (11.6)</td>
<td>0 (0)</td>
<td>5 (100.0)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>70.60 (6.77)</td>
<td>69.20 (7.46)</td>
<td>70.79 (6.76)</td>
</tr>
<tr>
<td>range</td>
<td>54–82</td>
<td>59–78</td>
<td>54–82</td>
</tr>
<tr>
<td>Lesion length, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>16.12 (6.40)</td>
<td>25.22 (6.31)</td>
<td>14.93 (5.43)</td>
</tr>
<tr>
<td>range</td>
<td>5.95–33.13</td>
<td>16.45–33.13</td>
<td>5.95–26.71</td>
</tr>
<tr>
<td>Lesion-bifurcation distance, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>14.75 (8.42)</td>
<td>26.34 (6.97)</td>
<td>13.23 (7.39)</td>
</tr>
<tr>
<td>range</td>
<td>0–35.60</td>
<td>19.47–35.60</td>
<td>0–25.51</td>
</tr>
</tbody>
</table>

*p-test was performed for continuous variables (age, lesion length, and lesion-bifurcation distance) and the chi-square test for categorical variables. **Data missing in two subjects. n: Number of lesions, SD: standard deviation.

Fig. 2 Graph showing the correlations of lesion length, lesion-bifurcation distance, and size of the predilation balloon with the occurrence of periprocedural neurological complications (PNCs).
- : PNC (+), large predilation balloon;
○ : PNC (+), small predilation balloon;
□ : PNC (−), large predilation balloon;
○ : PNC (−), small predilation balloon.

The embolic material within the torn plaque or irregular surface is then exposed to blood flow when the balloon is deflated and the plaque somewhat recoils. Even after the subsequently placed stent covers the torn plaque, the intraplaque material may continue to be exposed to blood flow and may release debris or induce thrombus formation. Under such conditions, temporary blockade of the ICA will not be adequate to avoid embolic complications. A small balloon may also cause dissection, but with a lower incidence and to a smaller extent.

The use of a large angioplasty balloon for postdilation may be a different situation. Dissection or rupture of the plaque may occur, but elastic recoil does not occur because of the stent, so the intraplaque material will not be exposed to the blood flow so much. Temporary blockade of the flow will be effective to avoid embolism in this situation.

Two previous studies identified other independent predictors for PNCs associated with carotid stenting. A study of 271 cases investigated 18 factors from clinical, morphological, and procedural features. Advanced age and presence of long and...
multiple stenoses were the independent predictors based on multivariate analysis. Another study analyzed 27 factors from clinical and morphological characteristics in 111 patients. Long lesion, symptomatic lesion, and absence of hypercholesterolemia were independent predictors.

In our study, none of the above showed an independent correlation with PNCs. In particular, lesion length and lesion-bifurcation distance, which is somewhat related to lesion length, were significant in univariate analysis, but the significance was not reproduced by multivariate analysis.

One of the reasons for these differences may be the procedural protocols. We used distal protection balloons for almost all of the postdilatations, whereas the previous studies did not use protection devices. Another procedural difference is that we used large balloons for predilation in the later part of the series. The occurrence of PNCs in a subgroup with predilation with small balloons was very low (1 minor transient deficit in 35 lesions) in our series. The protection balloon for postdilation may reduce the overall occurrence of PNCs provided that predilation is performed with a small balloon.

Another reason may be the limitations of the statistical analysis in our study, which was retrospective and the total number of the patients was quite small. Also, the large predilation balloon was used mostly in patients with a long lesion and long lesion-bifurcation distance. The effect of a large predilation balloon is large, so any influence of the long lesion and long lesion-bifurcation distance may have been obscured. These factors should be studied in a subset of cases in which a small balloon is used for predilation. This was not possible in this series because the occurrence of PNCs in the subset was too small.

Variable protection devices such as distal protection balloons and filter devices are now available, allowing the whole stenting procedure to be protected from predilation to postdilation. The occurrence of PNCs is 0% to 3% in protected procedures, and such devices are effective to reduce embolic complications. However, the protection devices do not yet adequately block the debris, based on clinical experience, postprocedural diffusion-weighted magnetic resonance imaging, and ex vivo experiments. Debris passing through the filter devices or around the devices cause embolic complications. Therefore, efforts should be continued to reduce embolism even with the use of protection devices.

This study suggests that even when such protection devices are used, predilation should not be performed with large balloons. Predilation with a small balloon that dilates the vessel just enough to allow passage of the stent is safer under any conditions. Large balloons should be used only after the lesion is stented.

References


Address reprint requests to: A. Sadato, M.D., Department of Neurosurgery, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogoin, Sakyoku, Kyoto 606-8507, Japan.

Commentary on this paper appears on the next page.
Commentary

Shortly after the publication of a number of studies demonstrating the benefit of carotid endarterectomy for both symptomatic and asymptomatic patients with high grade carotid stenosis, endovascular treatment of carotid stenosis has provided an alternative, less invasive option for managing these patients. Because of the rapid advances in endovascular technology, the ideal technical approach to carotid angioplasty and stenting has yet to be agreed upon. The authors have carefully analyzed a group of 40 patients in whom 43 carotid lesions were treated by angioplasty and stenting in order to identify those factors that influence the incidence of periprocedural neurological complications (PNCs). The authors analyzed eight variables, several of which have been previously demonstrated to be associated with a higher incidence of PNCs. Univariate analysis of these variables demonstrated that large diameter of the predilation balloon, use of a protection balloon during predilation, lesion length and lesion-bifurcation distance were significantly related to the occurrence of PNCs. Multiple logistic regression analysis left only large diameter of the predilation balloon as the factor most associated with occurrence of PNCs in this series. The authors are to be congratulated for expanding our knowledge of the technical factors that influence the outcome of endovascular treatment of carotid stenosis. Although the series is relatively small compared to the others that have analyzed PNCs, their thoughtful discussion assists in determining the role of endovascular treatment in selected patients with carotid stenosis.

Daniel L. BARROW, M.D.
Department of Neurosurgery
The Emory Clinic
Atlanta, Georgia, U.S.A.

This is an outstanding thoughtful article by Sadato and colleagues from Kyoto, which analyses in a scholarly way their experience with angioplasting/stenting for high-risk carotid cases. The authors state that carotid surgery remains their primary choice, but that for classically identified high-risk subgroups, they have chosen endovascular therapy as primary treatment. For this reason, as they point out, the number of patients in the study is modest; presumably many patients are having routine carotid surgery for their asymptomatic and symptomatic disease.

The study shows that large-balloon pre-stent angioplasty is associated independently with higher risk of peri-procedure neurological events, whether temporary or permanent. Of the many other risk factors evaluated, no other shows such an association. This differs somewhat from previous studies of endovascular treatment; in my mind these authors present compelling and credible evidence to support their observation. It is their theory that large balloon predilation fractures and dissects the plaque and that this effect is not negated by subsequent stent placement, thus embolic phenomena can occur in the post-treatment period. They observe, and feel strongly, that a smaller balloon for pre-dilation will prevent these neurologic events.

The strengths of the study are in the elegant statistical analysis, the consistent approach to indications and technical treatment, and the elegant presentation of the data. The weaknesses are the modest number of patients, the performance of stenting without protective devices (a practice which has now changed), and the lack of information as to whether these patients were asymptomatic or symptomatic pre-treatment. To their credit the authors recognize and address these weaknesses in their discussion, which is excellent.

I am convinced that this is a valid and scientifically credible study. I am not an endovascular surgeon, but I certainly would be inclined to re-evaluate my own practices based on this data, and I would encourage such specialists to do the same.

I congratulate the authors on an excellent study, beautifully analyzed and elegantly presented, and for the honesty in evaluating their individual strengths and weaknesses.

Christopher M. LOFTUS, M.D., F.A.C.S.
Department of Neurosurgery
Temple University School of Medicine
Philadelphia, Pennsylvania, U.S.A.