Cerebrovascular accidents (CVAs) are associated with high rates of mortality and morbidity and impose a great burden on the economy, especially in developing countries. Carotid artery stenosis is thought to be responsible for about 20%–30% of all strokes. Although carotid endarterectomy (CEA) has been the gold-standard treatment for carotid stenosis, carotid artery stenting (CAS) has been proposed as a valid and reliable procedure for the treatment of carotid artery stenosis, especially in patients who are at high risk for general anesthesia and surgery. Postprocedural hypotension and bradycardia are important complications of CAS and are referred to as hemodynamic instability (HI). The pathophysiology of HI, which is also observed after CEA, is thought to be due to manipulation of the carotid sinus during stent deployment. The incidence and impact of HI on the short-term prognosis of patients have been of large debate. Attempts have been made to identify the predictive risk factors for the occurrence of HI.

Methods

Every patient who was a candidate for CAS at Shiraz University Hospitals between September 2008 and September 2009 without exclusion criteria was included in this study. Twenty-seven patients were selected based on NASCET (North American Symptomatic Carotid Endarterectomy Trial Collaborators) criteria as follows: those

Abbreviations used in this paper: BP = blood pressure; CAS = carotid artery stenting; CEA = carotid endarterectomy; CVA = cerebrovascular accident; ECG = electrocardiography; HI = hemodynamic instability; MI = myocardial infarction; TIA = transient ischemic attack; VR = Valsalva ratio.
who were symptomatic with 70% or more carotid artery stenosis and those who were asymptomatic with stenosis of more than 80% as determined by color Doppler ultrasonography. The degree of stenosis of all lesions was measured by digital estimation during pre- and postprocedural angiography. Written consent was obtained from all patients.

A bolus dose of aspirin (325 mg) and clopidogrel (300 mg) was administered to patients before the procedure. All medications including antihypertensive drugs were given on the morning of the procedure. Two interventionists (one of whom was a cardiologist) performed all carotid stent implantations. A complete history, including neurological and physical examinations, baseline electrocardiography (ECG), and supine blood pressure (BP), was obtained in all patients. After mild sedation with 2–3 mg intravenous midazolam, CAS was performed through a transfemoral approach. Complete 4-vessel brain angiography was performed before the procedure in each patient. All patients received an intravenous dose of 1 mg atropine. Different brands of stents were used, including WallStent (Boston Scientific), Crystallo Ideale (Invatec), and Acculink (Medlink). All stents were equipped with embolic protection devices: Filter EZ (Boston Scientific), Spider (Medlink), and MoMa (Invatec).

Exclusion criteria were the presence of hemodynamic instability and low BP at baseline, atrial fibrillation, recent transient ischemic attacks (TIAs) and CVAs occurring in the past week, and an inability for the patient to hold his or her breath for 30 seconds.

Hemodynamic instability was defined as: 1) any episode of hypotension (that is, systolic BP lower than 90 mm Hg or a decrease of 50 mm Hg or more from the baseline BP) after stent deployment or balloon inflation; or 2) any episode of bradycardia after stent deployment or balloon inflation described by a heart rate lower than 60 bpm, an R-R interval of greater than or equal to 25 msec, or a decrease of more than 30 bpm from the baseline heart rate according to ECG findings.

During the operation, patients were asked to perform a Valsalva maneuver by forceful expiration with an open glottis in supine position for 15 seconds against a resistance of approximately 40 mm Hg. This was performed by asking the patients to blow into a blunted tube with a pressure recorder on its end. The patient’s heart rate and BP were obtained before and immediately after the Valsalva maneuver. We also assessed the Valsalva ratio (VR) by dividing the length of the longest R-R interval on the ECG after the Valsalva maneuver by the shortest R-R interval during the maneuver and within the 45 seconds of peak heart rate. A VR of 1.1 or less was defined as a definite impaired autonomic function, that between 1.11 and 1.20 was defined as borderline, and that of 1.21 or more was defined as normal.

In all cases of HI, whether symptomatic or asymptomatic, an intravenous infusion of 300–400 ml of 9% saline was administered, and isolated bradycardia was managed using 0.5–1 mg atropine. In cases in which there was no response to initial treatment, intravenous dopamine drips starting with 5 μg/kg/min were begun and titrated until HI resolved. Persistent HI in patients was defined as unresponsiveness to treatment after 1 hour or requirement of dopamine drips for maintenance of hemodynamic status after the procedure and transferring to coronary care unit or ward.

The next day, the patient’s hemodynamic status and ECG results were reviewed, and abnormal findings, heart rate, BP, and VR were documented. Complete neurological examination to evaluate any new abnormal finding was performed in all patients by the same examiner.

All patients were contacted 1 month after CAS and were reexamined by the same interventionists as before. Any adverse outcomes were recorded, and a new color Doppler ultrasonography study was performed.

All available data from the carotid lesion morphology, degree of stenosis, and presence of calcification or tortuosity along with the location of lesion, risk factors for cardiovascular problems, history of a previous coronary artery disease or myocardial infarction (MI), and history of previous stroke or TIA, were gathered. Data are expressed as the means ± SDs, and variables were analyzed using the Pearson chi-square test and the Fisher exact test. A p value < 0.05 was considered statistically significant.

**Results**

Twenty-seven patients underwent successful CAS without any adverse neurological events. Seventeen were men (63%) and 10 were women (37%). The mean patient age was 69 ± 10.4 years (range 49–85 years). Among the patients, 4 (14%) suffered from significant bilateral carotid artery stenosis, while the remaining patients had unilateral lesions. The mean degree of stenosis was 88% ± 6.5% (range 75%–99%). Atherosclerosis risk factors are presented in Table 1.

According to our definition of HI, 17 patients (63%) developed the condition. Isolated bradycardia without hypotension was not reported in any case. Ten patients (37%) showed no signs of HI.

For patients with no HI, a mean decrease of 9 ± 12.7 mm Hg in baseline systolic BP was observed after stent deployment, while the mean decrease in the HI group was significantly higher (55 ± 18 mm Hg). The overall mean decrease in systolic BP during stenting in all patients was 38 mm Hg (Table 2). Twenty-six patients (96%) continued to maintain some degree of hypotension regardless of the occurrence of HI the day after stenting. Six patients (22%) developed persistent HI requiring dopamine infusion for a mean of 16 ± 6.2 hours after stenting. All patients were symptom free at the time of discharge with no adverse outcomes.

A comparison of demographic and procedural data between the HI and non-HI groups is given in Table 1. Among all available data, the degree of carotid artery stenosis was the single predictive factor and was statistically significant for the occurrence of HI (p = 0.006). Regarding the site and characteristics of the lesions, 26 patients (96%) had involvement of the carotid bifurcation, 8 patients (26%) had calcification, 22 patients (81%) had an eccentric lesion, 4 patients (15%) had significant clotting over the lesion, and 20 patients (74%) had a soft lesion.
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However, none of these characteristics were significantly different between the HI and non-HI groups (p > 0.05).

The mean VR at rest was 1.057 ± 0.12 (range 0.82–1.40). Twenty patients (74%) had a VR of 1.10 or less, and 2 (7%) had a VR of 1.21 or greater. The remaining patients (19%) had a VR in the borderline zone (between 1.11 and 1.20). Seventeen patients developed HI during stenting, and a decrease of 0.044 in VR was seen in all patients. While the mean VR at rest was 1.057 ± 0.12, the mean VR after stenting was 1.013 ± 0.12, indicating that at least some degree of autonomic dysfunction occurred overall. The mean VR at rest in the HI group was 1.00 ± 0.083 while it was 1.14 ± 0.12 in the non-HI group, which was significant (Table 3). Changes in systolic BP during the Valsalva maneuver at rest were 16 ± 12 mm Hg overall and failed to show any statistical significance between the HI and non-HI groups (p = 0.604). However, the decrease in BP after the Valsalva maneuver in the HI group was slightly greater than that in the non-HI group (13 ± 11 mm Hg in the non-HI group compared with 18 ± 12 mm Hg in the HI group).

Only 23 patients could attend follow-up visits in person. The other 4 patients were contacted by phone and underwent careful history taking. No adverse events such as death, MI, minor or major stroke, TIA, or any hospital admissions were reported. The mean follow-up period was 4.5 months after the procedure. Except for 1 case of a major CVA, no other patient developed any adverse

TABLE 1: Characteristics in 27 patients who underwent CAS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>HI Group</th>
<th>Non-HI Group</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean age (yrs)</td>
<td>69 ± 10.4 (49–85)</td>
<td>69 ± 10.3 (50–85)</td>
<td>70 ± 11 (49–85)</td>
<td>0.99</td>
</tr>
<tr>
<td>sex</td>
<td></td>
<td></td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>male</td>
<td>17 (63)</td>
<td>11 (64.7)</td>
<td>6 (60)</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>10 (37)</td>
<td>6 (35.3)</td>
<td>4 (40)</td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>18 (66.7)</td>
<td>12 (70.6)</td>
<td>6 (60)</td>
<td>0.683</td>
</tr>
<tr>
<td>hyperlipidemia</td>
<td>11 (40.7)</td>
<td>7 (41.2)</td>
<td>4 (40)</td>
<td>0.99</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>10 (37)</td>
<td>6 (35.3)</td>
<td>4 (40)</td>
<td>0.99</td>
</tr>
<tr>
<td>smoking</td>
<td>5 (18.5)</td>
<td>5 (29.4)</td>
<td>0 (0)</td>
<td>0.124</td>
</tr>
<tr>
<td>family history of MI or stroke</td>
<td>5 (18.5)</td>
<td>4 (23.5)</td>
<td>1 (10)</td>
<td>0.621</td>
</tr>
<tr>
<td>history of stroke or TIA</td>
<td>10 (37)</td>
<td>6 (35.3)</td>
<td>4 (40)</td>
<td>0.99</td>
</tr>
<tr>
<td>mean degree of stenosis (%)</td>
<td>88.3 ± 6.5 (75–99)</td>
<td>91 ± 4.7 (80–99)</td>
<td>83.5 ± 6.6 (75–95)</td>
<td>0.006</td>
</tr>
<tr>
<td>bilat lesion</td>
<td>4 (14.8)</td>
<td>1 (5.9)</td>
<td>3 (30)</td>
<td>0.128</td>
</tr>
<tr>
<td>mean systolic BP at rest (mm Hg)</td>
<td>161 ± 30.7 (95–230)</td>
<td>160 ± 32.5 (95–230)</td>
<td>163 ± 28.8 (120–210)</td>
<td>0.902</td>
</tr>
</tbody>
</table>

* Values represent the number of patients with percentages in parentheses, unless otherwise indicated. Mean values are presented as ± SDs with the ranges in parentheses.
† Fisher exact test. p < 0.05 is statistically significant.

TABLE 2: Comparison of BP and heart rate between the non-HI and HI groups*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-HI Group</th>
<th>HI Group</th>
<th>Total</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP at rest (mm Hg)</td>
<td>163.1 ± 28.8 (120 to 190)</td>
<td>160.3 ± 32.5 (95 to 230)</td>
<td>161.37 ± 30.7 (95 to 230)</td>
<td>0.902</td>
</tr>
<tr>
<td>SBP after Valsalva maneuver (mm Hg)</td>
<td>149.8 ± 26.9 (120 to 190)</td>
<td>142.2 ± 32.3 (90 to 220)</td>
<td>145 ± 30 (90 to 220)</td>
<td>0.505</td>
</tr>
<tr>
<td>SBP post–stent deployment (mm Hg)</td>
<td>154.1 ± 30.6 (120 to 195)</td>
<td>105.1 ± 25.1 (60 to 179)</td>
<td>123.2 ± 35.9 (60 to 195)</td>
<td>0.000</td>
</tr>
<tr>
<td>SBP the day after the procedure</td>
<td>120 ± 27</td>
<td>104.4 ± 17.2</td>
<td>110 ± 22.5</td>
<td>0.000</td>
</tr>
<tr>
<td>SBP at follow-up</td>
<td>125.6 ± 21.9 (85 to 160)</td>
<td>129 ± 17.3 (85 to 122)</td>
<td>127.8 ± 18.6 (85 to 160)</td>
<td>0.243</td>
</tr>
<tr>
<td>HR at rest (bpm)</td>
<td>82.3 ± 10.7 (71 to 100)</td>
<td>87.4 ± 15.1 (60 to 122)</td>
<td>85.5 ± 13.6 (60 to 122)</td>
<td>0.243</td>
</tr>
<tr>
<td>HR after stenting (bpm)</td>
<td>93.8 ± 18.3 (67 to 125)</td>
<td>93.5 ± 24.1 (50 to 150)</td>
<td>93.6 ± 21.8 (50 to 150)</td>
<td>0.863</td>
</tr>
<tr>
<td>SBP at rest − SBP after Valsalva (mm Hg)</td>
<td>13.3 ± 11 (–10 to 28)</td>
<td>18.1 ± 12.5 (3 to 50)</td>
<td>16.3 ± 12 (–10 to 50)</td>
<td>0.604</td>
</tr>
<tr>
<td>SBP at rest − SBP after stenting (mm Hg)</td>
<td>9 ± 12.7 (–17 to 25)</td>
<td>55.2 ± 18 (20 to 90)</td>
<td>38.1 ± 27.8 (–17 to 90)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

* HR = heart rate; SBP = systolic BP.
† Fisher exact test. p < 0.05 is statistically significant.
events. One patient (4.3%) maintained low BP (85/50 mm Hg) during the follow-up.

Discussion

Hypotension, bradycardia, and asystole have been reported as consequences of distension of the carotid bulb during CAS. In some reports, HI has been associated with neurological sequelae.\(^4\)\(^5\) However, HI does not occur after CAS in all patients; there are numerous debates in the literature regarding the incidence of this phenomenon and possible predictors. In addition, there have been efforts to determine the correlation between HI and increased mortality and morbidity in the short and long term in those who have undergone CAS. In one study of 51 patients in Italy, the presence of a fibrous plaque inside the carotid artery and the degree of stenosis before and after stenting were predictors of postprocedural hypotension and bradycardia. However, the authors could not establish any relationship between the incidence of HI and mortality and morbidity.\(^13\) In another study conducted in the US, significant postprocedural hypotension was noticed, but the condition was not associated with long-term adverse neurological outcomes.\(^14\)

Qureshi et al.\(^16\) performed a multicentric study including 71 cases of CAS. They reported incidences of hypotension and bradycardia to be 22.4% and 27.5%, respectively. A history of MI was found to be a predictive factor for postprocedural hypotension and bradycardia. Leisch et al.\(^9\) reported on the proximity of stenosis to the carotid bulb bifurcation as the most important predictor of HI. Other predictors were identified as existence of contralateral stenosis (> 60%), length of the stenosis, and balloon-to-artery ratio. Our results did not confirm their findings regarding contralateral stenosis as a predictive risk factor for HI. Although Qureshi et al.\(^16\) and Alpman et al.\(^2\) found that ischemic heart disease was frequently associated with postprocedural hypotension, our study failed to prove such a claim, and no relationship was found between the occurrence of HI and the presence of ischemic heart disease.

In 2006, a study on 500 CAS procedures performed in the US showed that HI occurred in 210 procedures (42%), and persistent HI defined as hypotension that only responded to vasopressors occurred in 84 patients (17%). Those with persistent HI were at a significantly higher risk of peri-procedural adverse outcomes including MI, stroke, or TIA.\(^3\)

The incidence of HI varies greatly in different studies from 1.7% to 42%. The incidence of HI in our study was roughly 63%, which is closer to the incidence reported by Gupta et al.\(^5\) The reason for the differences among these studies can be attributed to different definitions of HI. None of the demographic data or risk factors in our patients showed any correlation with susceptibility to hemodynamic instability. Our results suggest that the degree of carotid artery stenosis is highly related to occurrence of HI (p = 0.006).

It has previously been shown that VR can be of value during bedside detection of autonomic dysfunction, especially in patients with cardiovascular disease.\(^1\)\(^7\)\(^16\) To our knowledge, no study has evaluated the role of VR in predicting HI after CAS. Multivariate analysis of our data showed that there was a significant difference between the HI and non-HI groups with respect to the values of VR at rest and after stenting (p < 0.003).

Individuals in the HI group had significantly lower VRs at rest and before the procedure, and these patients maintained their low values throughout the next day. It can be assumed that patients with lower VRs at rest are more prone to HI after stenting, and this can play a major role as a predictive factor for occurrence of HI. The VR can be a very useful bedside method for prediction of HI after stent deployment; however, obtaining the value can sometimes be difficult depending on the patient’s cooperation. The VR decreased in all patients; however, a significant difference was found between the HI and non-HI groups.

According to our data, a patient with a VR of 1.10 or less at rest will probably develop HI after CAS, with a sensitivity of 94% and a specificity of 60%. The positive predictive value of VR for prediction of HI was 80%, and the negative predictive value was 85%. Having the VR at hand preprocedure can help to determine the high-risk group and prevent HI by proper administration of atropine and inotrope preoperatively.

Although our findings failed to correlate HI with short-term survival and there seems to be no association between the occurrence of HI after stenting and mortality or morbidity, the small size of the patient population may have biased the conclusion. Other studies also confirmed the absence of a correlation between HI and short-term survival or morbidity as we claimed in our study, but those studies also suffered from a small patient population.\(^15\)

Study Limitations

The most important limitation was our small patient population, which could affect the results, especially...
Hemodynamic instability following carotid artery stenting

those regarding the risk factors that might be considered as predictive factors for HI and the possible effect of HI on mortality and morbidity.

Conclusions

Hemodynamic instability occurs frequently after CAS, it but seems to be a benign phenomenon and does not increase the risk of mortality or morbidity in the short term. A VR at rest less than 1.10, baseline autonomic dysfunction, and degree of carotid artery stenosis can be used as measures for prediction of HI after CAS.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Kojuri. Acquisition of data: all authors. Analysis and interpretation of data: Kojuri, Zamiri. Drafting the article: Kojuri. Critically revising the article: Kojuri. Statistical analysis: Kojuri, Zamiri. Administrative/technical/material support: Kojuri, Zamiri. Study supervision: Kojuri.

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