Long-Term Results After Microvascular Decompression in Essential Hypertension

H. Frank, MD; H.P. Schobel, MD; K. Heusser, MD; H. Geiger, MD; R. Fahlbusch, MD; R. Naraghi, MD

Background and Purpose—In 1998, 8 patients with severe, intractable arterial hypertension and MR tomography–demonstrated neurovascular contact of a looping artery at the root entry zone of cranial nerves IX and X, causing neurovascular compression, underwent neurosurgical decompression. The short-term results showed a normalization of blood pressure with a markedly reduced antihypertensive drug regimen in 7 patients. To determine the longer-term outcome concerning blood pressure and secondary organ damage after neurovascular decompression, we studied these 8 operated patients prospectively for a mean follow-up of 3.5 years after surgical intervention.

Methods—Eight hypertensive patients who had undergone microsurgical decompression were monitored every 6 months after surgery to assess blood pressure (by 24-hour ambulatory pressure readings) and the need for antihypertensive medication. To evaluate secondary organ damage, echocardiographic assessment of left ventricular hypertrophy, fundoscopic assessment of hypertensive lesions, and analysis of renal function and proteinuria were done.

Results—Three of the 8 operated patients remained normotensive in the long-term period with decreased antihypertensive medication. Two patients required gradual increases of antihypertensive medication after the first postoperative year, after which arterial blood pressure levels were 10% to 15% lower than preoperative levels. Three patients suffered serious cardiovascular and renal complications, with the incidence of lethal intracerebral hemorrhage in 1 patient and end-stage renal disease in 2 patients, of whom 1 experienced sudden cardiac death.

Conclusions—The long-term results verify that microsurgical decompression is a successful alternative therapy in a certain subgroup of patients with arterial hypertension due to neurovascular compression. However, the relevance of the looping artery in the other cases, who did not improve, is not clear. Prospective studies to elucidate the pathophysiological role of neurovascular abnormalities and arterial hypertension are needed.

Key Words: blood pressure ■ decompression, surgical ■ microsurgery ■ nerve compression syndromes

In an earlier report in 1998,1 we showed an improvement of blood pressure by neurosurgical decompression in 8 patients with severe essential hypertension and neurovascular contact at the level of the root entry zone of cranial nerves IX and X at the rostral ventrolateral medulla (RVLM). On the basis of the short-term result of this prospective study showing a normalization of blood pressure together with a substantial reduction in antihypertensive medication in 7 patients 3 months after surgery, we cautiously concluded that this neurosurgical approach might offer a potentially new alternative therapy for patients with intractable hypertension and neurovascular compression (NVC) at the RVLM. However, initial positive effects of this procedure may not necessarily translate into a consistent long-term effect.2

Experimental and clinical data3–4 support the hypothesis that there is a subgroup of patients with essential hypertension who have a secondary form of hypertension related to NVC at the RVLM. Thus, it is now assumed that if a looping artery in the left lower brain stem (eg, the posterior inferior cerebellar artery) impinges on the surface of the RVLM, sympatoexcitatory neurons that are located closely adjacent to this zone might be activated by pulsatile compression.5–7

Given these limited data, it is critical to assess the value of microvascular decompression in the treatment of patients with severe hypertension and NVC on a longer-term basis. Therefore, the aim of this study was to present the long-term results (mean follow-up, 3.5 years) with regard to blood pressure control, secondary organ damage, morbidity, and mortality in our study group of 8 operated patients.

Subjects and Methods

Eight patients with preoperative severe hypertension who underwent microsurgical decompression were postoperatively monitored to analyze (1) the course of blood pressure levels (assessed by 24-hour ambulatory pressure readings); (2) the need for antihypertensive medication; (3) secondary organ damage, including echocardiographic assessment of left ventricular hypertrophy, fundoscopic assessment of hypertensive lesions, and laboratory screening of renal function and proteinuria.
blood pressure readings) and the need for antihypertensive medication; (2) the development of hypertensive organ damage (by analysis of renal function and degree of proteinuria, echocardiographic assessment of left ventricular hypertrophy, and fundoscopic assessment of hypertensive lesions); and (3) control of postoperative status of the brain stem area (assessed by MR tomography).

The following measurements were performed: physical examination, including determination of body mass index; 24-hour blood pressure measurements; blood tests (serum electrolytes, creatinine, urea, uric acid, glucose, cholesterol, triglycerides, blood cell counts); urine determinations (proteinuria, creatinine clearance test); electrocardiography; echocardiography (measurements according to the American Society of Echocardiography convention); fundoscopic examination; and MRI of the ventrolateral medulla at 6 and 12 months and every 6 months after neurovascular decompression. Normal blood pressure was assumed when mean arterial pressure was \( \leq 110 \) mm Hg systolic and \( \leq 75 \) mm Hg diastolic.

**Results**

Characteristics of the 8 patients who underwent neurovascular decompression are shown in Table 1. The postoperative long-term follow-up of blood pressure levels is shown in the Figure. Corresponding antihypertensive medication of each patient is presented in Table 2.

The individual courses were as follows: 12 months after surgery, 5 (patients 1, 2, 4, 5, and 7) of the 7 patients who were normalized in the short-term postoperative period remained normotensive, each with a markedly decreased antihypertensive regimen.

Two years after surgery, 3 of the initial 7 normalized patients (patients 2, 5, and 7) remained normotensive with a reduction in their antihypertensive drug therapy. Patients 1 and 4, however, experienced a successive increase in blood pressure.

Five patients had been followed up for 4 years after decompression. At this time, patients 1 and 7 were normotensive, with each patient taking 2 antihypertensive medications. Patient 5 showed moderate arterial hypertension (mean, 156/105 mm Hg), and patients 2 and 6 exhibited arterial hypertension (mean, 166/101 mm Hg) despite augmented antihypertensive medication.

Patient 3, a 42-year-old woman with malignant hypertension without any response to oral antihypertensive agents preoperatively, did not improve in the early period after surgical decompression. One year after surgery, near normalization of blood pressure levels (mean, 141/89 mm Hg) was achieved; however, the patient required a combined therapy of 6 antihypertensive drugs. Nevertheless, preexisting serious secondary organ damage worsened, and this patient finally lost renal function as a result of clinically suspected nephrosclerosis and received chronic intermittent hemodialysis.

TABLE 1. Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>Age, y</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Change in MAP, mm Hg*</th>
<th>Renal Function/Proteinuria</th>
<th>Fundoscopic Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M</td>
<td>59</td>
<td>29</td>
<td>31</td>
<td>-11</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>2/F</td>
<td>47</td>
<td>36</td>
<td>40</td>
<td>-24</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>3/F</td>
<td>41</td>
<td>31</td>
<td>33</td>
<td>-11</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>4/F</td>
<td>24</td>
<td>33</td>
<td>34</td>
<td>-13</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>5/F</td>
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<td>32</td>
<td>35</td>
<td>+7</td>
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<tr>
<td>6/F</td>
<td>40</td>
<td>27</td>
<td>21</td>
<td>-56</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>7/F</td>
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<td>40</td>
<td>41</td>
<td>-54</td>
<td>⇧</td>
<td>⇧</td>
</tr>
<tr>
<td>8/F</td>
<td>63</td>
<td>26</td>
<td>27</td>
<td>-6</td>
<td>⇧</td>
<td>⇧</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; MAP, mean arterial pressure; and LVH, left ventricular hypertrophy.

*Preoperative vs postoperative value.

Long-term course of systolic arterial pressure (SAP) (a) and diastolic arterial pressure (DAP) (b) (mean values of 24-hour readings). Pat. indicates patient; t, time.
treatment 14 months after decompression surgery. Two years later, she experienced sudden cardiac death due to an acute myocardial infarction.

Patient 6, a 41-year-old woman with severe hypertension and serious secondary organ damage including cerebral hemorrhage preoperatively, showed decreased blood pressure values during the first 6 months after surgery (mean, 146/89 mm Hg); however, she required a combination of 5 antihypertensive drugs. Then, when she experienced a weakness of the left trapezius muscle, a dislocation of the polytetrafluoroethylene (Teflon) felt, which was inserted neurosurgically to decompress the RVLM, was diagnosed with the use...
of MR tomography. Blood pressure levels were hypertensive at this time. Therefore, neurovascular decompression was repeated in this patient, and a new polytetrafluoroethylene felt was inserted. Three months after reoperation, blood pressure decreased by 25% compared with the preoperative values with a reduced antihypertensive regimen. However, subsequently blood pressure levels again increased, requiring a combined therapy of up to 9 antihypertensive agents. As a result of progressive hypertensive organ damage, patient 6 lost renal function and received long-term hemodialysis treatment 4 years after surgical decompression.

Patient 8, a 64-year-old woman with a history of apoplectic stroke who was normalized in the 3-month postoperative period under single therapy with a calcium channel blocker, showed a slight increase of 24-hour blood pressure 12 months after surgical decompression (mean, 156/86 mm Hg). After addition of a β-blocker, patient 8 remained normotensive 2 years after decompression surgery with a stable 2-fold anti-hypertensive regimen. However, patient 8 suffered a severe intracerebral hemorrhage (not associated with excessive blood pressure values) followed by a recurrent stroke and died 2.6 years after surgery.

Renal function remained stable in patients 1, 2, 4, 5, and 7 during the follow-up period, and existing mild proteinuria did not increase. Left ventricular hypertrophy, which was present in all cases preoperatively, decreased slightly in patients 1, 5, and 7 (Table 1).

Two patients (patients 5 and 6) suffered postoperatively from chronic headaches, probably as a result of cutaneous nerve irritation by scar formation.

**Discussion**

The long-term follow-up data of our neurosurgically decompressed hypertensive patients demonstrate success of this intervention in 3 of the 8 patients, with normalization of blood pressure and decreased need of antihypertensive medication. Another 2 patients, who were similarly improved during the first 12 months postoperatively, gradually required additional antihypertensive medication, finally reaching a drug level comparable to the preoperative level at the end of follow-up, at which time arterial blood pressure was 10% to 15% lower than preoperatively. The blood pressure of the remaining 3 patients, despite some initial improvement, could not be adequately controlled in the long term. These patients eventually suffered serious vascular and renal complications as a result of preexisting advanced hypertensive organ damage.

Taken together, the follow-up results of our prospectively studied patients who underwent microvascular decompression because of intractable, severe hypertension are in accordance with the results of a retrospective analysis by Levy et al., who demonstrated persistent normalization of blood pressure in 8 of 12 operated patients, partial success in 2 of 12 patients, and no success in 2 of 12 patients. Thus, it seems obvious that this novel, alternative approach to treat severe hypertension in patients who are refractory to medication may indeed represent a valuable choice for a specific subgroup of patients. However, our data, in combination with those by Levy et al., also clearly show that approximately a third of all patients do not benefit from this procedure. What are the reasons for this apparent discrepancy? Differences in the applied neurosurgical technique among the operated patients is probably not a relevant cause since this procedure was always performed by the same experienced neurosurgeons. Furthermore, MRIs were performed postoperatively to confirm the success of the surgery. Another reason for the potential lack of therapeutic success of microvascular decompression may be the fact that in some patients a long history of severe hypertension with advanced secondary organ damage may have already led to a “fixed” hypertension. At this phase of hypertension, adequate blood pressure control may not be achievable because of a progressively disturbed interplay among the many regulatory and counterregulatory neurohumoral mechanisms involved in blood pressure regulation. The third and probably most important reason for the failure of neurosurgical improvement of blood pressure control in some of our operated patients, however, is that the pathophysiological relevance of the neuroradiologically diagnosed looping artery at the RVLM for the development of arterial hypertension is not clear. Several MRI and microanatomic studies showed an association between neurovascular abnormalities at the left RVLM and hypertension. Recent MRI data, however, could not confirm this relationship, indicating nearly the same incidence of neurovascular contact at the RVLM in normotensives and hypertensives.

In conclusion, the long-term follow-up data of our study patients demonstrate that microvascular decompression of a
pathological neurovascular contact at the RVLM seems to be a safe and effective therapeutic alternative in a certain subgroup of patients with severe, intractable hypertension. Thus, our data support the hypothesis that there is a subgroup of patients with essential hypertension who have a secondary form of hypertension related to NVC at the ventrolateral medulla. However, before this surgical intervention can be recommended for general use among those patients with NVC, we need a better understanding of the underlying pathomechanisms and improved imaging techniques to more accurately define those patients who may benefit from this intervention. Until this is achieved, microvascular decompression should be performed only in prospective study protocols.

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References

Editorial Comment
Microvascular Decompression: Hype or Hoax?

The article by Frank et al is the latest in a long series of papers from a group of neurosurgeons in Erlangen, Germany, who have expanded the work of Peter Jannetta,1 the originator of the concept of vascular compression of the ventrolateral medulla as a primary cause of hypertension that can be relieved by decompression.

Unfortunately, as is true for every paper from the Jannetta group,2 the Erlangen group (including their article in this issue of Stroke),3 and Morimoto et al in Japan4 claiming cure of a large proportion of decompressed patients, these objections hold true.

First, the so-called refractory patients often were on suboptimal antihypertensive therapy preoperatively. In this series of 8 patients, 3 were on no diuretic preoperatively and 2 were on furosemide once daily, which is inadequate.5 In almost every series of refractory patients, the major cause is volume expansion from inadequate diuretic, and most of these patients can be controlled with adequate diuretic therapy.5

Second, most of the “cures” are not confirmed by the data. For example, in this series of 8 patients, 3 died from hypertension-related causes after having shown little response of blood pressure or reduction in the numbers of antihypertensive drugs (patients 3, 5, and 8); 1 developed end-stage renal failure (patient 6); 2 had only transient improvement in blood pressure (patients 2 and 4); and only 2 had good control of hypertension on less medication (patients 1 and 7). These results are similar to the only other published 4-year follow-up data, wherein 5 of 12 decompressed patients had “sustained improvements.”22

Third, there have been no comparisons of various hormonal and neurological measurements taken preoperatively and again after surgery to try to explain success or failure. The Japanese group6 and the Erlangen group7 have reported on the presence of sympathetic nervous system overactivity in patients with presumed compression but have not shown results of decompression.
I believe there may be a small number of patients with refractory hypertension who have compression and who can be relieved by decompression. However, in view of multiple reports on the inaccuracy of imaging techniques to visualize compression,6–12 and without any proven way to identify those who may respond to decompression, I believe no patient should be subjected to this procedure until a properly controlled trial is conducted. During a lecture at this medical school in Dallas in 1998, Dr Jannetta stated that such trials were underway. If and when they are reported, we will know if this is a real syndrome or another false cure for hypertension.

Norman M. Kaplan, MD, Guest Editor
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References
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