Editorial

Hypertension and neurovascular compression

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High blood pressure affects nearly 25% of the world’s population, and is a major risk factor for stroke, myocardial infarction, heart failure, and aortic aneurysm. In 5%–10% of hypertensive individuals, an endocrine, renal, or neoplastic cause is found, but the vast majority of cases are idiopathic. Because the medulla is responsible for control of blood pressure, brainstem pathological conditions may be responsible for essential hypertension in some patients. Bilateral lesions in the middle third of the nucleus solitarius produce persistent hypertension in pigeons, and pulsatile compression of the lateral medulla in nonhuman primates is able to produce reversible hypertension. In humans, certain tumors of the inferior cerebellum have led to refractory hypertension that resolves after resection, and arterial decompression of the brainstem in hypertensive patients undergoing microwascular decompression for other indications has been observed to normalize blood pressure postoperatively. Based on the theory that hypertension may result from neurovascular compression (NVC) through mechanisms similar to trigeminal neuralgia and hemifacial spasm, it has been postulated that a subset of patients with medically refractory hypertension may benefit from surgical exploration of the lateral brainstem to resolve compression by the vertebral artery or one of its branches. This idea has failed to gain much traction in the neurosurgical and medical communities.

The discovery of NVC as the putative cause of trigeminal neuralgia was based on Walter Dandy’s observations among 215 patients with trigeminal neuralgia. In 1934, Dandy observed the following:

In the routine treatment of trigeminal neuralgia by division of the posterior root, either totally or subtotally, and using the sub-cerebellar approach, I have been impressed with the frequency of certain anatomical findings which, I believe, must have a bearing on the production of this pain.... These are the arteries and veins which impinge upon and frequently distort the sensory root.

The development of high-resolution MR imaging techniques has recently made it possible to perform a virtual exploration of the posterior fossa with a high degree of detail. Such observations correlate well with surgical findings, and significant differences have been seen in patients with and without trigeminal neuralgia. Therefore, it is possible to determine nonoperatively whether there is an association between arterial brainstem compression and other diseases, essentially repeating Dandy’s series noninvasively. Since 1994, a number of such studies have been performed, some of which have identified a significant association between hypertension and NVC. Association does not necessarily imply cause; it is also possible that hypertension produces arterial compression (for example, by lengthening of arteries) or that both are independently caused by an unrecognized third factor. However, if even a fraction of the increased odds of arterial compression in a randomly selected sample of hypertensive individuals occurs because compression causes hypertension, potentially millions of individuals would become candidates for brain surgery.

In their meta-analysis, Boogaarts and colleagues examined this controversial proposal by analyzing studies of the prevalence of arterial compression on MR images to determine whether there is an association between essential hypertension and arterial brainstem compression. They found a total of 14 such studies conducted over 13 years, in which a variety of MR sequencing paradigms and outcome assessments were used. When the results of all studies are combined, there appears to be a strongly significant relationship. However, considered individually, half of the studies did not find an association, and those that did tended to be earlier, retrospective, unblinded, and with a small sample size. When only prospective studies are included, no significant association is found. Seven studies used a second comparison group of patients with hypertension from a known cause (“secondary hypertension”) to determine whether any observed arterial compression resulted from hypertension rather than the reverse. Five of these 7 studies found that there was indeed a greater association in patients with primary hypertension, but these same 5 (and not the other 2) were among those that also found a significant difference when compared to normotensive individuals.

One possible explanation for the heterogeneity of findings is the wide diversity of imaging parameters and definitions of NVC among the studies. Another intriguing possibility is publication bias, as demonstrated in the funnel plot in Fig. 2 of the current study. A funnel plot compares each study’s reported effect size (x axis) to an estimate of the precision of the effect size measurement.
for that study, such as sample size, variance, or standard error (y axis). If all research examining a particular problem has been published, it would be expected that points would spread out symmetrically along the bottom of the plot (that is, studies with greater variance demonstrate variable results) and converge near the top. A funnel plot can be asymmetrical for many reasons, but one common cause is the “file drawer” effect—smaller studies with negative results considered unworthy of publication by authors or journal editors were simply filed away, leading to an overestimation of the true effect size when the literature is considered as a whole. In this particular case, the studies near the top of the plot essentially identified no difference at all (OR 1.0), and the reports that do identify an effect are located in the lower right area of the plot, raising the suspicion that there may have been other studies that identified no association or a negative association between hypertension and arterial brainstem contact that were never published.

Altogether, the disparity of findings among these studies provides less compelling evidence than Dandy’s observations in patients with trigeminal neuralgia. It is certainly possible that some individuals have hypertension due to arterial compression of the lateral brainstem, and imaging may someday play an important role both in proving this association and in selecting patients for surgical treatment. However, the available literature does not conclusively support the existence of an association between the two. Refinement of imaging techniques is likely to provide a more satisfying answer to this question in the future.

Disclosure

The authors report no conflict of interest.

References


Response

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I thank my colleagues Drs. Selman and Miller for their positive remarks on our article. Future studies should indeed clarify the relationship between hypertension and NVC. Improvement of the imaging techniques and clear definitions of NVC are mandatory for obtaining interpretable results.

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