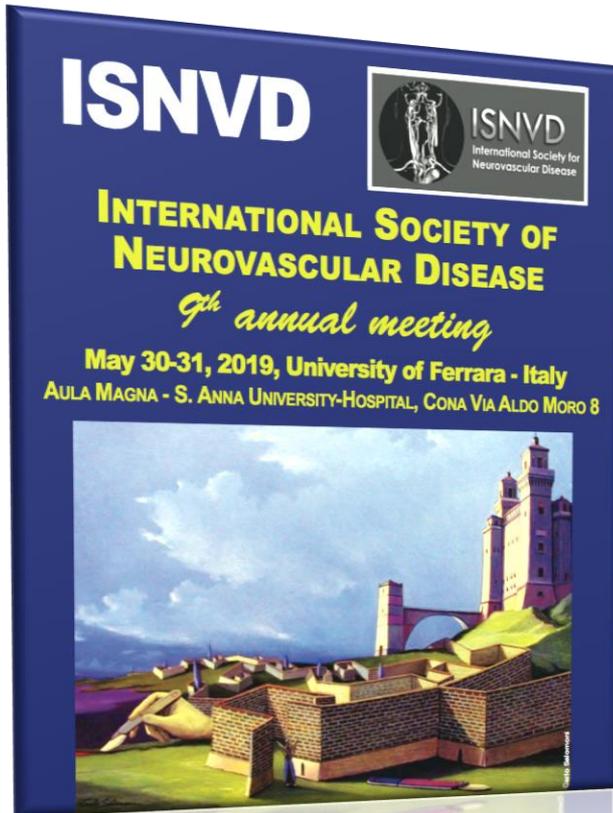




Vascular Surgery and Transplant Unit
University of Catania
Chief Prof. Pierfrancesco Veroux



HEADACHE SUSTAINED RELIEF FOLLOWING EXTRACRANIAL VENOUS ANGIOPLASTY

Alessia Giaquinta, MD PhD

May 30, 2019
S. Anna University Hospital, Ferrara

Disclosures

- I have the following potential conflicts of interest to report:
 - Receipt of grants/research support
 - Receipt of honoraria and travel support
 - Participation in a company sponsored speakers' bureau
 - Employment in industry
 - Shareholder in a healthcare company
 - Owner of a healthcare company

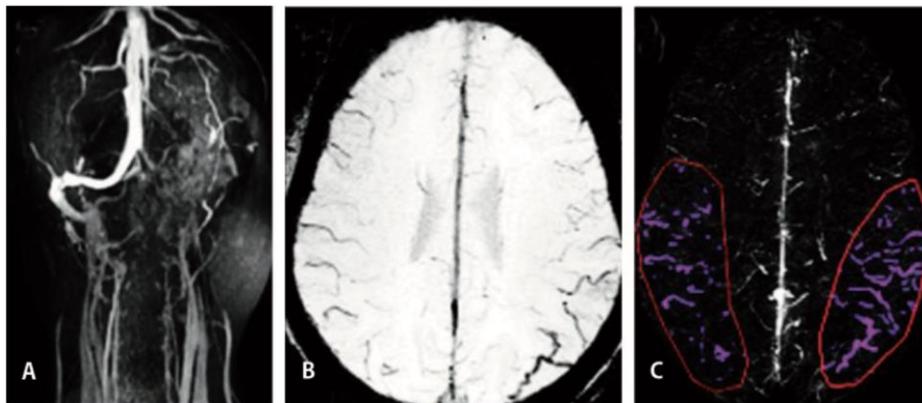
- I do not have any potential conflict of interest**



INSUFFICIENCY OF VENOUS DRAINAGE OF THE BRAIN AND HEADACHES

Headache is the 3th most prevalent illness in the world with an estimated 1 billion sufferers worldwide, including MS pts, with a vast proportion of pts reported to be poor responders to available therapies. In the past few years, attention has been focused on the role of insufficiency of venous drainage of the brain in diseases such as: MS, idiopathic intracranial hypertension and headache.

Venous insufficiency is the potential result of stenosis of the venous sinus.

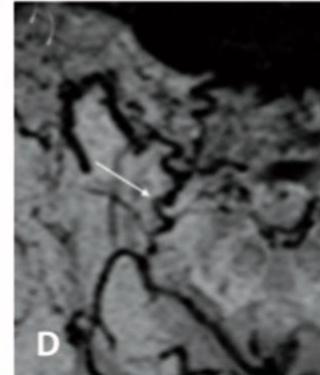
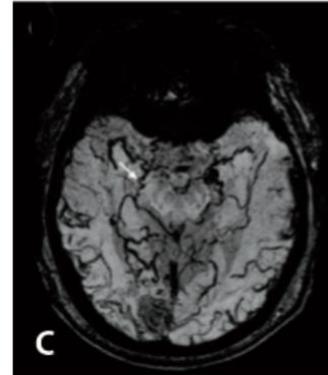
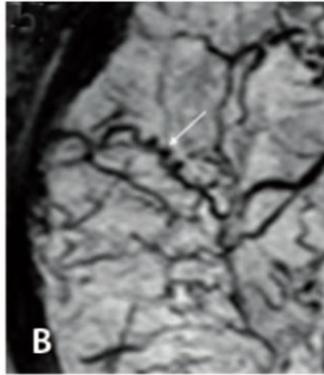
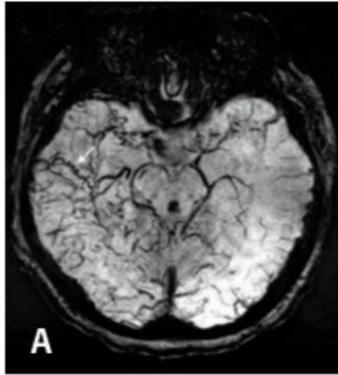


Occlusion of the left transverse sinus

The susceptibility value of the ipsilateral pial veins measured on the maximum intensity projected SWIM image was 159 ± 60 ppb which is higher than the contralateral veins (131 ± 43)

Courtesy of Mark Hackee

MRI (SWI MINIMUM INTENSITY PROJECTIONS) OF PATIENTS WITH DURAL SINUS OBSTRUCTION AND HEADACHE



Right transverse sinus obstruction demonstrates dilated veins and corkscrew effect in the ipsilateral hemisphere

Superior sagittal sinus obstruction demonstrates a more global dilation of veins showing the corkscrew effect.

Following increased intracranial venous pressure, a corkscrew effect can be visible in smaller draining veins which become dilated and are sometimes associated with nearby cerebral microbleeding

Courtesy of Mark Hackee



STENTING OF SUPERIOR SAGITTAL SINUS

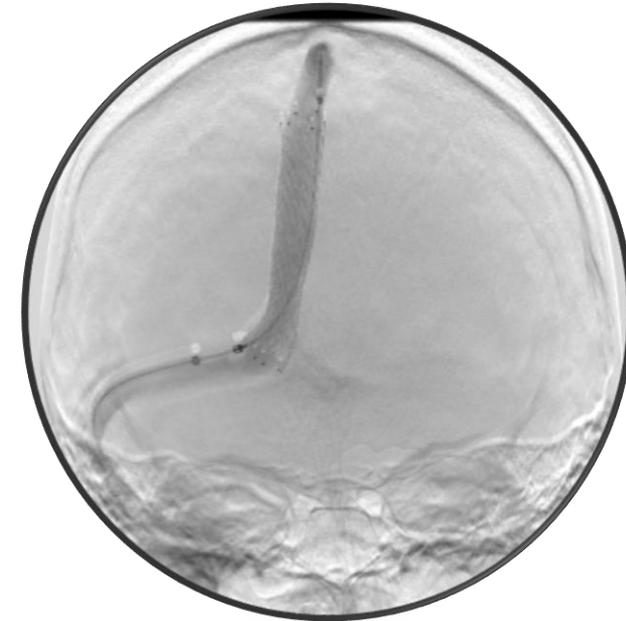
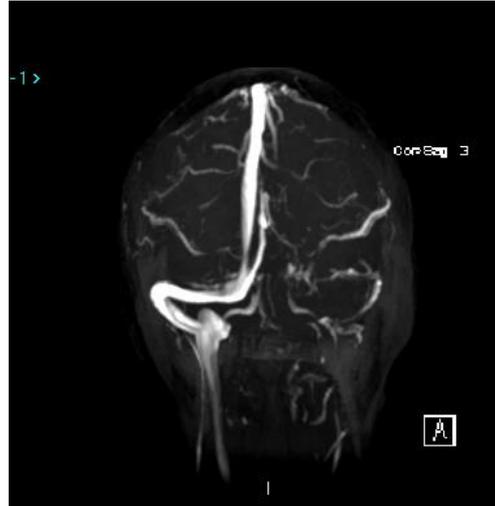
Understanding the complex pathophysiology of idiopathic intracranial hypertension and the evolving role of venous sinus stenting: a comprehensive review of the literature

Nisha Giridharan, BS,¹ Smruti K. Patel, MD,¹ Amanda Ojugbeli, BS,¹ Aria Nouri, MD, MSc,¹ Peyman Shirani, MD,^{1,2} Aaron W. Grossman, MD, PhD,^{1,2} Joseph Cheng, MD, MS,¹ Mario Zuccarello, MD,¹ and Charles J. Prestigiacomo, MD¹

Departments of ¹Neurosurgery and ²Neurology, University of Cincinnati College of Medicine, Cincinnati, Ohio

Idiopathic intracranial hypertension (IIH) is a disease defined by elevated intracranial pressure without established etiology. Although there is now consensus on the definition of the disorder, its complex pathophysiology remains elusive. The most common clinical symptoms of IIH include headache and visual complaints. Many current theories regarding the etiology of IIH focus on increased secretion or decreased absorption of cerebrospinal fluid (CSF) and on cerebral venous outflow obstruction due to venous sinus stenosis. In addition, it has been postulated that obesity plays a role, given its prevalence in this population of patients. Several treatments, including optic nerve sheath fenestration, CSF diversion with ventriculoperitoneal or lumboperitoneal shunts, and more recently venous sinus stenting, have been described for medically refractory IIH. Despite the availability of these treatments, no guidelines or standard management algorithms exist for the treatment of this disorder. In this paper, the authors provide a review of the literature on IIH, its clinical presentation, pathophysiology, and evidence supporting treatment strategies, with a specific focus on the role of venous sinus stenting. <https://thejns.org/doi/abs/10.3171/2018.4.FOCUS18100>

KEYWORDS idiopathic intracranial hypertension; benign intracranial hypertension; pseudotumor cerebri; venous sinus stenting; CSF diversion; optic nerve sheath fenestration



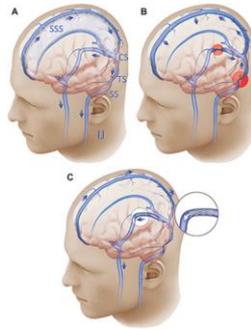
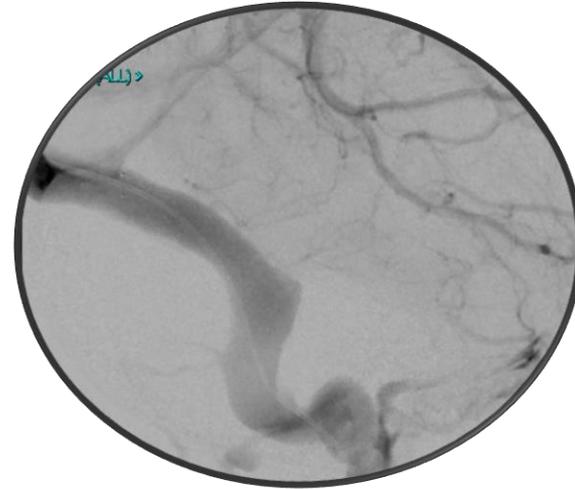
22 y/o female with headache, cognitive dysfunction, and right hemiparesis

STENTING OF TRANSVERSE SINUS

Endovascular Treatment of Idiopathic Intracranial Hypertension with Stenting of the Transverse Sinus Stenosis

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Kenkichi Takahashi, MD, PhD³, Toshihiko Kuroiwa, MD, PhD²

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³Department of Neurosurgery, Ohnishi Neurosurgical Hospital, Akashi, Japan

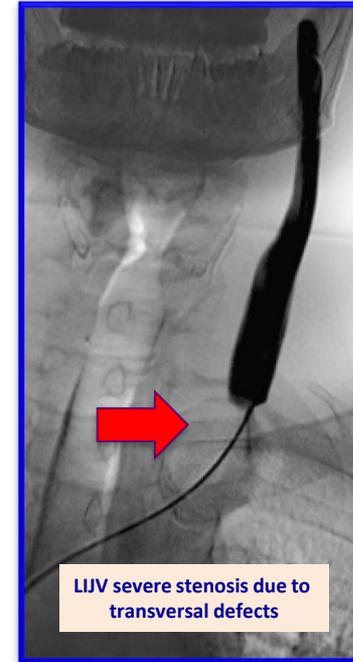
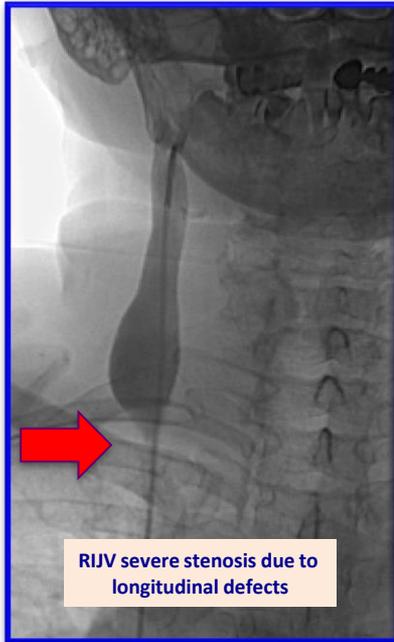


Conclusions Venous sinus stenting in patients with IIH who are refractory to medical therapy appears to have an excellent safety profile and is associated with significant improvements in headaches, pulsatile tinnitus, and papilledema.

37 yo female with **headache**
and cognitive dysfunction

INSUFFICIENCY OF VENOUS DRAINAGE OF THE BRAIN AND HEADACHES

but also of the major veins in the neck:
Internal jugular veins.



IJVS STENTING FOR NON THROMBOTIC STENOSIS

REVIEW ARTICLE

WILEY *CNS Neuroscience & Therapeutics*

Understanding jugular venous outflow disturbance

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Funding information

National Key R&D Program, Grant/Award Number: 2017YFC1308401; National Natural Science Foundation, Grant/Award Number: 8137289; Project of Beijing Municipal Top Talent of Healthy Work, Grant/Award Number: 2014-2-015

Summary

Extracranial venous abnormalities, especially jugular venous outflow disturbance, were originally viewed as nonpathological phenomena due to a lack of realization and exploration of their feature and clinical significance. The etiology and pathogenesis are still unclear, whereas a couple of causal factors have been conjectured. The clinical presentation of this condition is highly variable, ranging from insidious to symptomatic, such as headaches, dizziness, pulsatile tinnitus, visual impairment, sleep disturbance, and neck discomfort or pain. Standard diagnostic criteria are not available, and current diagnosis largely depends on a combinatory use of imaging modalities. Although few researches have been conducted to gain evidence-based therapeutic approach, several recent advances indicate that intravenous angioplasty in combination with stenting implantation may be a safe and efficient way to restore normal blood circulation, alleviate the discomfort symptoms, and enhance patients' quality of life. In addition, surgical removal of structures that constrain the internal jugular vein may serve as an alternative or adjunctive management when endovascular intervention is not feasible. Notably, discussion on every aspect of this newly recognized disease entity is in the infant stage and efforts with more rigorous designed, randomized controlled studies in attempt to identify the pathophysiology, diagnostic criteria, and effective approaches to its treatment will provide a profound insight into this issue.

KEYWORDS

diagnosis, jugular venous outflow disturbance, pathophysiology, tinnitus, treatment

Eur J Neurol. 2018 Feb;25(2):365–e13. doi: 10.1111/ene.13512. Epub 2017 Dec 7.

Intracranial hypertension induced by internal jugular vein stenosis can be resolved by stenting.

Zhou D^{1,2}, Meng R^{1,2}, Zhang X^{1,2}, Guo L^{1,2}, Li S^{1,2}, Wu W^{1,2}, Duan J^{1,2}, Song H^{1,2}, Ding Y^{2,3}, Ji X^{1,2}.

Author information

Abstract

BACKGROUND AND PURPOSE: Idiopathic intracranial hypertension (IIH) is characterized by abnormally elevated intracranial pressure (ICP) without identifiable etiology. Recently, however, a subset of patients with presumed IIH have been found with isolated internal jugular vein (IJV) stenosis in the absence of intracranial abnormalities.

METHODS: Fifteen consecutive patients were screened from 46 patients suspected as IIH and were finally confirmed as isolated IJV stenosis. The stenotic IJV was corrected with stenting when the trans-stenotic mean pressure gradient (Δ MPG) was equal to or higher than 5.44 cmH₂O. Dynamic magnetic resonance venography, computed tomographic venography and digital subtraction angiography of the IJV, Δ MPG, ICP, Headache Impact Test 6 and the Frisén papilledema grade score before and after stenting were compared.

RESULTS: All the stenotic IJVs were corrected by stenting. Δ MPG decreased and the abnormal collateral veins disappeared or shrank immediately. Headache, tinnitus, papilledema and ICP were significantly ameliorated at 14 \pm 3 days of follow-up (all $P < 0.01$). At 12 \pm 5.6 months of outpatient follow-up, headache disappeared in 14 out of 15 patients (93.3%), visual impairments were recovered in 10 of 12 patients (83.3%) and tinnitus resolved in 10 out of 11 patients (90.9%). In 12 out of 15 cases, the Frisén papilledema grade scores declined to 1 (0–2). The stented IJVs in all 15 patients kept to sufficient blood flows on computed tomographic venography follow-up without stenting-related adverse events.

CONCLUSIONS: Non-thrombotic IJV stenosis may be a potential etiology of IIH. Stenting seems to be a promising option to address the issue of intracranial hypertension from the etiological level, particularly after medical treatment failure.



HEADACHE TRIAL

*As such,
we designed a study
specifically aimed of
evaluating the impact of
balloon venoplasty of IJVs
on headache in MS patients.*



RESEARCH ARTICLE

Mid-term sustained relief from headaches after balloon angioplasty of the internal jugular veins in patients with multiple sclerosis

Clive B. Beggs^{1*}, Alessia Giaquinta², Massimiliano Veroux², Ester De Marco², Dovile Mociskyte², Pierfrancesco Veroux²

¹ Institute for Sport, Physical Activity and Leisure, School of Sport, Leeds Beckett University, Leeds, United Kingdom, ² Vascular Surgery and Organ Transplant Unit, Azienda Ospedaliero-Universitaria Policlinico, Catania, Italy



HEADACHE TRIAL

This was a single-center open label observational study with data collected prospectively but analyzed retrospectively

- **The study was unfunded**, with the Italian National Health System covering all the procedure costs.
- The patients and investigators were not paid for their participation.
- **The study had a specific approval by the Ethical Committee of the University Hospital of Catania** for the retrospective evaluation of morphological and hemodynamic changes in internal jugular outflow before and after balloon angioplasty.
- **All patients signed an informed consent form** on which the potential risks and benefits of the study treatment were detailed.
- **Patients were also conscious that venoplasty was not performed in order to treat MS.**



HEADACHE TRIAL - MATERIALS AND METHODS

JANUARY 2011 – DECEMBER 2015

From an original cohort of 364 MS patients who underwent venoplasty: **113 headaches positive patients** (82 relapsing remitting (RR), 22 secondary progressive (SP), and 9 primary progressive (PP)) met the inclusion criteria of this study:

- **Headaches resistant to best medical therapy**
 - **DUS Non thrombotic IJVs Stenosis > 50%**
 - **Moderate/Severe Insufficiency of IJV flow**
- **IJVs with stenosis suitable for Balloon Venoplasty**
 - **at least 12 months FU**



HEADACHE TRIAL - MATERIALS AND METHODS

✓ Headaches

✓ Midas: Migraine Disability Assessment Score

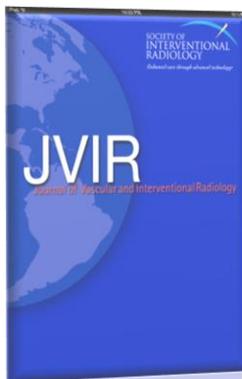
Symptoms were assessed and collected:

- the day before angioplasty: related to the last 3-month
- 3 month after angioplasty: related to the first 3-month after pta
- last follow up: related to the 3-month before the last visit



HEADACHE TRIAL - MATERIALS AND METHODS

All procedures were performed using a standardized and operator-independent catheter venography protocol.



CLINICAL STUDY

Internal Jugular Veins Outflow in Patients with Multiple Sclerosis: A Catheter Venography Study

Pierfrancesco Veroux, MD, Alessia Giaquinta, MD, Debora Perricone, MD, Lorenzo Lupo, MD, Flavia Gentile, MD, Carla Virgilio, MD, Anna Carbonaro, MD, Concetta De Pasquale, MD, and Massimiliano Veroux, MD, PhD

ABSTRACT

Purpose: To investigate an examiner-independent catheter venography protocol that could be used to reliably diagnose venous outflow abnormalities in patients with multiple sclerosis (MS) and chronic cerebrospinal venous insufficiency and to determine whether venous angioplasty is effective in the treatment of these abnormalities.

Materials and Methods: A total of 313 patients with MS and 12 patients with end-stage renal disease underwent echo-color Doppler sonography and catheter venography of the internal jugular veins (IJVs) to evaluate contrast medium clearance time. In patients with venous outflow anomalies, balloon angioplasty of the IJVs was performed.

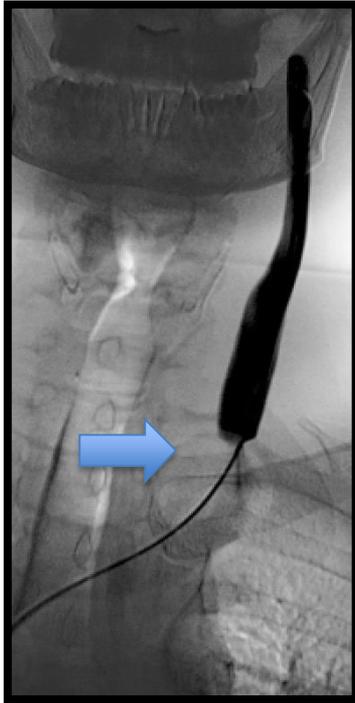
Results: A contrast medium clearance time cutoff value of 4 seconds or less provided the maximal combination of sensitivity and specificity for the right IJV (sensitivity, 73.4%; specificity, 100%) and left IJV (sensitivity, 91.4%; specificity, 100%). IJVs with a clearance time between 4.1 and 6 seconds had moderate delayed flow (MDF), and IJVs with a clearance time longer than 6 seconds had severe delayed flow (SDF); 89% of patients showed MDF/SDF through at least one IJV, 79% showed MDF/SDF through both IJVs, and only 5% showed normal flow in both IJVs. Balloon angioplasty was immediately able to improve flow in at least one IJV in 69% of patients, but venous flow was normalized in both veins in only 37% of patients; SDF persisted after angioplasty in 32% of patients.

Conclusions: There is a high prevalence of abnormal delayed flow through IJVs in patients with MS. Venous angioplasty was effective in only a minority of patients with SDF.

J Vasc Interv Radiol 2013; 24:1790–1797



Due to the fact that PTA of IJVs have been shown to be poor effective, patient selection is mandatory



CLINICAL RESEARCH STUDIES

Factors influencing the hemodynamic response to balloon angioplasty in the treatment of outflow anomalies of internal jugular veins



Alessia Ciaguirra, MD, PhD,* Clive B. Beggs, PhD,* Maximiliano Veroux, MD, PhD,* Ester De Marco, MD,* Adalberto Sanzone, MD,* Carla Virgilio, MD,* and Pierfrancesco Veroux, MD,* Catania, Italy, and Leeds, United Kingdom

ABSTRACT

Objective: Percutaneous transluminal angioplasty (PTA) of the internal jugular veins (IJVs) has been proposed in recent years to treat chronic cerebrovascular venous insufficiency, with discordant results. Moreover, very little is known about the efficacy of PTA in restoring a normal cerebral venous outflow. The aim of this study was to investigate the anatomic factors and patient characteristics that might influence the efficacy of PTA of the IJV.

Methods: There were 707 consecutive patients with venous outflow anomalies who underwent standardized, operator-independent catheter venography and PTA of the IJVs. Before and after PTA, morphologic and hemodynamic anomalies of the IJVs were documented. The primary end point of the study was to evaluate the morphologic factors influencing the efficacy of angioplasty in improving DV outflow.

Results: PTA resulted in an increased outflow through the IJVs in most patients. However, younger individuals with transverse endoluminal defects and higher pre-PTA flow are more likely to respond well to PTA compared with those who exhibit hypoplasia, stenosis, or longitudinal endoluminal defects.

Conclusions: This study identified the factors that influence and could predict the efficacy of PTA in the treatment of DV anomalies. *J Vasc Surg Venous and Lym Dis* 2015;7:77-83.

IMPROVES

the presence of transversal defect is the single most important criteria for determining whether or not PTA will be successful.



Factors influencing the hemodynamic response to balloon angioplasty in the treatment of outflow anomalies of internal jugular veins



Alessia Ciaquinta, MD, PhD,¹ Clive B. Beggs, PhD,² Massimiliano Veroux, MD, PhD,¹ Ester De Marco, MD,¹ Adalberto Sanzone, MD,¹ Carla Virgilio, MD,¹ and Pierfrancesco Veroux, MD,¹ Catania, Italy; and Leeds, United Kingdom

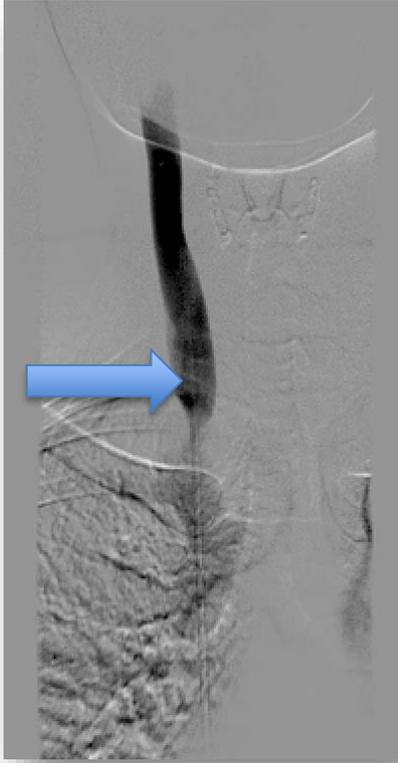
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LESS IMPROVERS

- Longitudinal leaflets



Factors influencing the hemodynamic response to balloon angioplasty in the treatment of outflow anomalies of internal jugular veins



Alessia Ciaquinta, MD, PhD,* Clive B. Beggs, PhD,* Massimiliano Veroux, MD, PhD,* Ester De Marco, MD,* Adalberto Sanzone, MD,* Carla Virgilio, MD,* and Pierfrancesco Veroux, MD,* Catania, Italy and Leeds, United Kingdom

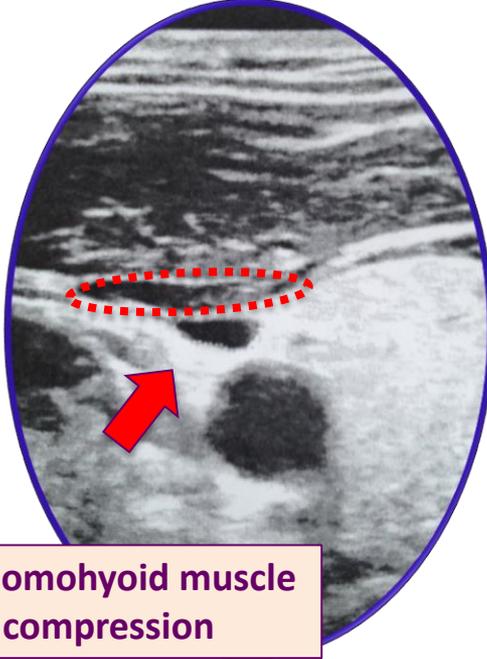
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Conclusions: This study identified the factors that influence and could predict the efficacy of PTA in the treatment of IJV anomalies. *J Vasc Surg Venous and Lym Dis* 2019;7:777-88.



RIJV omohyoid muscle compression

Exclusion Criteria

- hypoplasia
- extrinsic muscle compression



RESULTS:

The mean duration between the PTA procedure and last follow-up appointment was 1237 days (3.39 years)

Table 2. Demographic and clinical statistics for headache positive multiple sclerosis patients who received PTA treatment.

MS type	No.	Time (in days) to follow-up	Variable	Pre-PTA (mean)	Pre-PTA (sd)	3 months post-PTA (mean)	3 months post-PTA (sd)	2017 follow-up (mean)	2017 follow-up (sd)	Test Statistic	Signif. (p value)	Post-hoc 1 (p value)#	Post-hoc 2 (p value)^
RR	82	1296.5 (495.1)	Age at PTA	40.86	9.42	na	na	na	na	na	na	na	na
			Right IJV flow score	2.88	0.93	2.43	0.93	na	na	5.57**	<0.001**	na	na
			Left IJV flow score	3.05	0.90	2.59	1.02	na	na	5.64**	<0.001**	na	na
			MIDAS score	61.29	82.68	2.90	7.01	8.61	18.75	108 (2)*	<0.001*	<0.001	<0.001
SP	22	1284.3 (442.6)	Age at PTA	48.55	8.04	na	na	na	na	na	na	na	na
			Right IJV flow score	3.09	0.68	2.77	0.81	na	na	2.65**	0.016**	na	na
			Left IJV flow score	3.41	0.91	3.05	0.84	na	na	2.34**	0.035**	na	na
			MIDAS score	45.50	56.87	5.23	10.33	10.45	27.46	18.9 (2)*	<0.001*	<0.001	0.002
PP	9	1271.4 (461.7)	Age at PTA	44.67	8.80	na	na	na	na	na	na	na	na
			Right IJV flow score	2.89	0.93	2.00	0.87	na	na	2.20**	0.063**	na	na
			Left IJV flow score	3.11	0.93	2.44	0.88	na	na	1.98**	0.125**	na	na
			MIDAS score	44.00	40.24	5.89	11.34	10.33	13.25	4.8 (2)*	0.091*	na	na

NB. For ease of reference the post-PTA blood flow rate scores are shown in the '3 months post-PTA' columns. However, the post-PTA assessment of blood flow actually took place immediately following the procedure.

* Non-parametric repeated measures Friedman test (Friedman chi-square)

** Exact Wilcoxon-Pratt signed-rank test (Z statistic)

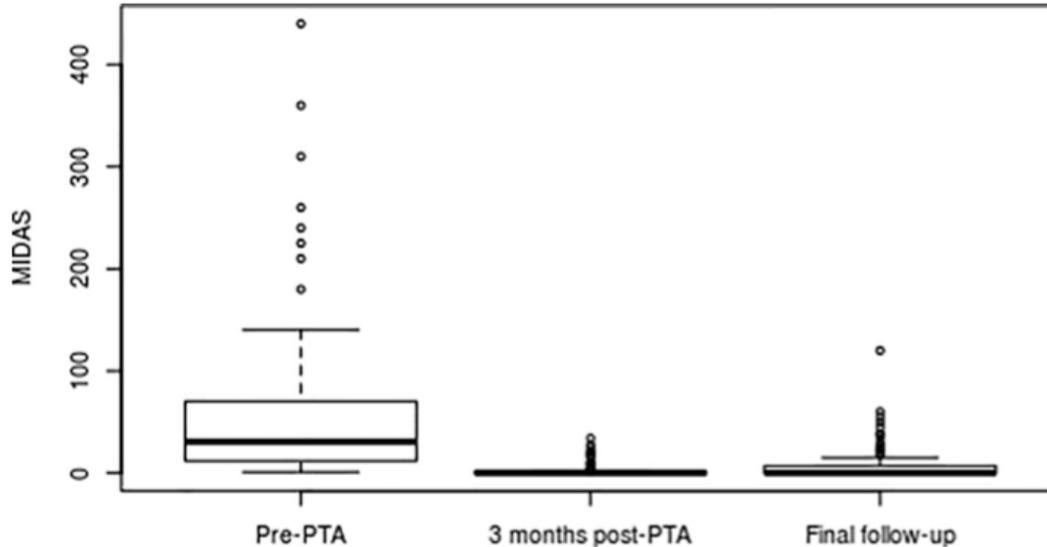
Post-hoc 1: Wilcoxon-Nemenyi-McDonald-Thompson post-hoc test comparing pre and 3 months post-PTA MIDAS scores.

^ Post-hoc 2: Wilcoxon-Nemenyi-McDonald-Thompson post-hoc test comparing pre PTA and 2017 follow-up MIDAS scores.



RESULTS:

- The clinical results showed a significant (86%) reductions ($p < 0.001$) in the MIDAS scores in the three months following PTA.
- The improvement in MIDAS score was maintained throughout the follow-up period in both the RR ($p < 0.001$; mean of 3.55 years) and SP ($p = 0.002$; mean of 3.52 years) MS patients.



CONCLUSION

- Patient selection is mandatory
- Balloon Venoplasty of IJVs appears to be associated with a large and sustained (>3 years) reduction in MIDAS score in MS patients
- Our findings suggest that PTA might be a useful intervention for treating MS patients with persistent headaches and non thrombotic stenosis of the IJVs





*Thank
you*

