Surgical Management of Intractable Meniere's Disease

Pietro De Luca¹, Massimo Ralli^{2*}, Claudia Cassandro³, Francesca Yoshie Russo², Federico Maria Gioacchini¹, Matteo Cavaliere¹, Marco Fiore⁴, Antonio Greco², Ettore Cassandro¹, Alfonso Scarpa¹

ABSTRACT

Meniere's Disease (MD) is an inner ear disorder characterized by spontaneous recurrent vertigo, fluctuating sensorineural hearing loss, aural fullness and low-pitch tinnitus. Therapeutic management of MD includes dietary restriction and medical therapy. A minority of cases is characterized by frequent vertigo attacks, progressive hearing loss and persistent tinnitus even through the continuous medical treatments; this condition is called intractable MD and requires a therapeutic escalation from non-invasive medical treatment to surgical intervention. Invasive procedures include endolymphatic sac surgery, vestibular nerve section and labyrinthectomy. These procedures have a very high success rate on symptom control but may have a severe impact on the hearing function. However, the simultaneous combined approach of demolitive surgery and cochlear implantation may be a valid approach to treat symptoms of intractable MD and preserve hearing function. In the present study, we review current literature focusing on intractable MD to describe and discuss advantages and disadvantages of established and newly proposed surgical treatments for intractable MD.

Keywords: Meniere disease, Intractable meniere, Vertigo, Hearing loss, Tinnitus.

¹Department of Medicine and Surgery, University of Salerno, Salerno, Italy ²Department of Sense Organs, Sapienza Università di Roma, Rome, Italy ³Department of Otolaryngology, University of Turin, Turin, Italy ⁴Institute of Cell Biology and Neurobiology - IBCN CNR, Italy

*Send correspondence to Massimo Ralli

Department of Sense Organs, Sapienza University of Rome, Italy, Viale del Policlinico 155, 00162 Roma, Italy. Email: Massimo.ralli@uniroma1.it; Tel: +39 0649976808 Paper submitted on March 24, 2022; and Accepted on April 25, 2022

INTRODUCTION

Meniere's Disease (MD) is an idiopathic inner ear disorder, first described by Prosper Meniere in 1861, characterized by spontaneous recurrent vertigo, fluctuating Sensorineural Hearing Loss (SNHL), aural fullness and low-pitch tinnitus¹⁻³. One of the most debilitating aspects for MD patients is the recurrence of acute and long-term vertigo attacks that are often debilitating and may severely affect quality of life⁴⁻⁶, similarly to other conditions⁷⁻¹³.

The pathologic mechanism of MD is still unclear; however, Endolymphatic Hydrops (EH) of the scala media of the cochlea is one the currently known pathophysiological mechanisms that underlie MD^{3,14-18}. EH seems to be due to an overproduction of endolymph and/or a decrease in the absorption of endolymph based on histopathological studies. Several theories have been proposed to explain the cause of MD, including viral infections and immune system-mediated mechanisms^{19,20}. An autoimmune origin of MD based on inner ear antigens has been reported in up to one third of patients, although the immunological mechanisms involved are not clear^{19,21-25}.

MD diagnosis is based on the criteria of the Baràny Society²⁶.

There are several therapeutic options for MD, but none is unanimously considered effective by the scientific community²⁷. First-line treatment commonly includes dietary modifications such as restriction of salt, caffeine and alcohol intake; however, there is no evidence from randomized controlled trials that supports the effectiveness of such approach in MD^{28,29}. The restriction of glucose intake for MD has been recently proposed³⁰; in a review from our group, we remarked the possible role of hyperinsulinemia in subjects affected by MD. There is actually strong evidence that the saccule, which is the main labyrinthine structure affected by pathological damage due to EH, has a large number of insulin receptors. This observation was confirmed by the examination of cadaveric subjects and in vivo analysis by cervical Vestibular Evoked Myogenic Potentials (cVEMPs)³¹.

Several drugs have been proposed for the treatment of MD. Dimenhydrinate and benzodiazepines have been proposed for acute attacks, while betahistine, betablockers and diuretics as prophylactic therapy, although evidence of their efficacy is lacking (3). Specially processed cereals (SPC) that increase endogenous antisecretory factor synthesis have been proposed to improve symptoms of MD with controversial results³².

If of first-line treatment which does not guarantee a good symptom control, intratympanic administration of drugs such as corticosteroids or gentamicin has been proposed as a treatment option³³. Corticosteroids can lower the risk of hearing damage^{34,36}, but showed less efficacy to control vertigo attacks compared to gentamicin^{37,38}. Gentamicin has been proven as an effective treatment for vertigo in MD with a potential risk of hearing loss³⁹⁻⁴². The dosage and administration method for gentamicin is still debated.

Some authors suggest the use of low-dose gentamicin in which the drug is injected once and further treatments are only performed in cases of recurrent vertigo attacks; others prefer high-dose gentamicin, titration or continuous administration in which the drug is injected until vestibular weakness is reached⁴³⁻⁵¹. Hearing loss and healthy-side vestibular dysfunction are potential risks of gentamicin treatment due to its ablative nature and ototoxicity^{52,53}.

A minority of cases is characterized by frequent vertigo attacks, progressive hearing loss and persistent tinnitus even through continuous medical treatments; this condition is called intractable MD54 and requires a different treatment approach. Management of MD should follow a therapeutic escalation from non-invasive medical treatment to surgical intervention including ablation. Invasive procedures, such as vestibular nerve section or labyrinthectomy, may be suggested in case of medical treatment failure. Surgery must be preceded by hearing assessment, ipsi and contralateral vestibular function assessment and medical imaging⁵⁵. Recently, an electronic questionnaire formulated by Quaranta et al and sent to Italian otolaryngologists showed that refractory case of MD are treated initially with intratympanic steroids followed by gentamicin; in case of failure of intratympanic treatment, vestibular nerve section is the treatment of choice56,57.

In the present study, we review current literature to describe and discuss advantages and disadvantages of established and newly proposed surgical treatments for intractable MD.

Surgical Management of Meniere Disease: Several surgical approaches have been described for intractable MD. Endolymphatic sac surgery was first described by Portman in 1926⁵⁸; and several variations on this surgical technique have been suggested. They include simple decompression, cannulation of the endolymphatic duct, endolymphatic drainage to the subarachnoid space, wide decompression that includes the sigmoid sinus, drainage to the mastoid, and removal of the extraosseus portion of the sac. Prostheses to allow flow selectively in either the mastoid or subarachnoid direction have also been proposed, including simple silastic sheet apposition to tubes and one-way valves.

Endolymphatic Sac Surgery: The role of endolymphatic sac surgery in intractable MD cases has been widely discussed. A Brazilian retrospective study from Bento et al⁵⁹ included 95 patients who underwent endolymphatic sac drainage. In patients with unilateral MD, the authors described a satisfactory vertigo control in 94.3% of patients, a significant improvement in cochlear function in 14%, and hearing preservation or even improvement in 88% of patients with intractable MD. In patients with bilateral MD, vertigo control was obtained in 85.7% of patients, cochlear function improved in 28% and hearing preservation or even improvement was reported in 71% of patients. The authors concluded that endolymphatic sac drainage can be considered a good surgical option

for patients with intractable MD, with a high percentage of vertigo control and hearing preservation. The results were also supported by a study from Flores Garcia et al⁶⁰; the authors confirmed that endolymphatic sac surgery including its variants can be a good option for patients with incapacitating endolymphatic hydrops.

Nevertheless, the efficacy of this procedure remains controversial, and the evidence to support this surgery is low. Thomsen et al⁶¹ conducted a double-blind, placedcontrolled study which compared mastoidectomy alone and endolymphatic shunt; results showed no significant differences between the two surgical approaches. Recently, Gibson et al⁶² compared endolymphatic shunt surgery and intratympanic gentamicin in patients with MD: the authors demonstrated that endolymphatic shunt surgery had a successful vertigo control comparable with intratympanic gentamicin, with a lower incidence of audio-vestibular complications. A Cochrane review by Pullens et al⁶³ over two randomized controlled studied showed no significant effects of endolymphatic sac surgery on symptom control, and concluded that there was no sufficient evidence for the beneficial effect of this treatment. A systematic review by Devantier et al.64 concluded that there is still a lack of high-quality research that supports the role of endolymphatic sac surgery in providing a significant amount of symptomatic relief for patients with MD. In addition, Taeko et al.¹⁶ studied 21 patients who received endolymphatic sac surgery and found no correlation between the changes in hearing function and the volume of endolymphatic hydrops after surgery. Furthermore, intra-sac steroid injection during surgery did not result in further improvement in patient outcomes⁶⁵. In a study performed by Higashi-Shingai et al two years after sac surgery, the authors showed that sac surgery could reduce vestibular endolymphatic hydrops⁶⁶. However, histologic evidence revealed that hydrops is not relieved after shunt placement⁶⁷ and that there was no relationship between changes in hearing function and volume of endolymphatic hydrous after endolymphatic sac drainage.

Mattingly et al evaluated the use of intraoperative Electrocochleography (ECochG) in patients with MD undergoing endolymphatic sac surgery. The authors detected only small objective changes in the low-frequency SP magnitude (500 Hz) immediately after surgery, but not in other frequencies or measures tested, suggesting that only minimal electrophysiological changes occurred in the cochlea as result of endolymphatic sac surgery⁶⁸.

Vestibular Nerve Section: Vestibular nerve section is widely used for symptom control in patients with intractable MD and is the fifth line of management for MD according to the European Statement on Meniere's disease⁶⁹.

Several studies focused on the efficacy and safety of this technique, demonstrating that vestibular nerve section, with differences based on the surgical approach, can reach a complete vertigo control in 85% to 95% of patients

and hearing preservation in 80% to 90% of patients after the procedure⁷⁰⁻⁷². Although the procedure showed a higher vertigo control rate compared to endolymphatic shunt, it was more invasive and technically challenging procedure. Two retrospective studies from Lemnos et al.⁷³ and Chen et al.⁷⁴ showed that vestibular nerve section can be considered an effective treatment in the case of intractable MD, with good functional results and low failure rate.

The risk of hearing loss in vestibular nerve section procedure has been shown to be lower compared to gentamicin injection⁷⁵, although the risk of hearing loss following gentamicin treatment seems to be most significant with high-dose protocols.

Labyrinthectomy: Labyrinthectomy is the most destructive procedure for treatment of MD because of the total damage of hearing and vestibular function. Indications of this procedure include patients without residual hearing or subjects that did not benefit from conservative treatment options. The procedure has a higher rate of vertigo improvement compared to vestibular nerve section⁷⁶ and has been reported to improve quality of life in the majority of patients⁷⁷. The procedure is mainly performed using a transmastoid exposure, although a transcanal approach has been described and is rarely used.

To treat the total hearing loss following the procedure, Heywood and Atlas proposed a simultaneous cochlear implantation and labyrinthectomy. They performed the surgery on two female patients with advanced MD and described several benefits of the simultaneous procedure such as the prevention of implantation of a fibrous or ossified cochlea, the decrease in the duration of deafness, and the use of a single operative procedure⁷⁸. Todt et al reported a labyrinthectomy performed after cochlear implantation⁷⁹; to date this is the only report in the literature.

Other Surgical Treatments: Some authors suggest the insertion of a ventilation tube in the tympanic membrane as first choice of treatment for refractory MD⁸⁰. A British work by Kanegaonkar et al, treated 33 patients with early grommet insertion with intratympanic steroid injection, combined with customized vestibular rehabilitation; they suggested that this combination may provide an alternative first-line strategy for MD, preventing further true MD attacks. Compared to established surgical treatments of MD such as endolymphatic shunt surgery and vestibular neurectomy, transtympanic ventilation tube placement is a procedure with extremely low risks and comorbidities. In selected patients, ventilation tube placement might anticipate and postpone more invasive treatments⁸¹.

In the recent years, new surgery techniques for intractable MD have been proposed. Endolymphatic duct blockage has been first proposed in 2015⁸² and consists in a non-ablative surgical technique. The initial results of this surgical option showed no clinical cochlear

and vestibular damage and a significantly better control of the vertigo attacks in comparison to the traditional endolymphatic sac surgery⁸³. In addition, there were no significant complications or side effects, as confirmed by some recent works^{83,84}.

Another novel technique that has been proposed is tenotomy of the tendons of the stapedius and tensor tympani muscles. The use of this technique, proposed by a Belgian Otolaryngology Unit leaded by De Valck⁸⁵, had some benefits in intractable MD patients as demonstrated by studies from Reichmayr et al⁸⁶, Albu et al⁸⁷ and Loader et al⁸⁸. Results included an improvement not only of vestibular symptoms, but also of hearing thresholds.

Zhang et al proposed a triple semicircular canal plugging for the treatment of intractable MD; according to the authors, this surgery offered a total control rate of vertigo and could represent an effective therapy for the advanced state of this disorder⁸⁹.

An interesting and recent study from Attanasio et al speculated the association between MD and chronic cerebrospinal venous insufficiency and evaluated the efficacy of bilateral percutaneous transluminal angioplasty of the jugular/azygos veins compared to medical therapy. The encouraging responses to vascular interventional therapy on MD symptoms suggest that this may be a promising treatment option for interpretation and treatment of this complex disease.

CONCLUSION

According to International Guidelines, surgical therapy for MD is recommended only for refractory disease, and therefore represents the third (or even the fifth) line of management.

Currently, the most popular surgical procedures used to control vertigo attacks are also the most invasive and have a significant impact on auditory function. However, the simultaneous combined approach of demolitive surgery and cochlear implantation may be a valid approach to treat symptoms of intractable MD and preserve hearing function.

STATEMENT DISCLOSURE

The authors declare that they have no conflicts of interest

CONFLICTS OF INTEREST AND SOURCE OF FUNDING

The authors declare that they have no conflicts of interest. The authors have not received financial support for this research.

REFERENCES

- 1. Hallpike CS. Meniere's disease. Postgrad Med J 1955;31(357):330-40.
- Ciorba A, Skarżyński PH, Corazzi V, Bianchini C, Aimoni C, Hatzopoulos S. Assessment tools for use in patients with Meniere disease: an update. Medical science monitor: Int Med J Experimental and Clin Res. 2017;23:6144.

- Nakashima T, Pyykkö I, Arroll MA, Casselbrant ML, Foster CA, Manzoor NF, et al. Meniere's disease. Nature reviews Disease primers. 2016;2(1):1-8.
- 4. Orji FT. The influence of psychological factors in Meniere's disease. Ann of Med and Health Sci Res. 2014;4(1):3-7.
- Petri M, Chirilă M, Bolboacă SD, Cosgarea M. Health-related quality of life and disability in patients with acute unilateral peripheral vestibular disorders. Brazilian J Otorhinolaryngol. 2017;83:611-8.
- Di Stadio A, Ricci G, Ralli M, Paolo T, Agostini G, Faralli M. Head-shaking nystagmus in the early stage of unilateral Meniere's disease. The J Int Adv Otolo. 2019;15(3):425.
- Bruscolini A, Sacchetti M, La Cava M, Nebbioso M, Iannitelli A, Quartini A, et al. Quality of life and neuropsychiatric disorders in patients with Graves' orbitopathy: current concepts. Autoimmun Rev. 2018;17(7):639-43.
- Passali GC, Ralli M, Galli J, Calo L, Paludetti G. How relevant is the impairment of smell for the quality of life in allergic rhinitis?. Current Opinion in Allergy and Clinical Immunol. 2008;8(3):238-42.
- Ralli G, Milella C, Ralli M, Fusconi M, La Torre G. Quality of life measurements for patients with chronic suppurative otitis media: Italian adaptation of" Chronic Ear Survey". Acta Otorhinolaryngologica Italica. 2017;37(1):51.
- Ralli M, Quaranta N, Canale A, Röösli C, Milella C, De Robertis V, et al. Cross-cultural adaption and validation of the Zurich chronic middle ear inventory translated into Italian (ZCMEI-21-It)—a prospective multicenter study. Otol & Neurotol. 2019;40(3):351-8.
- Bakir S, Kinis V, Bez Y, Gun R, Yorgancilar E, Ozbay M, et al. Mental health and quality of life in patients with chronic otitis media. Eur Arch of Oto-rhino-laryngol. 2013;270(2):521-6.
- Ciorba A, Bianchini C, Pelucchi S, Pastore A. The impact of hearing loss on the quality of life of elderly adults. Clinical Interventions in Aging. 2012;7:159.
- 13. Furuta M, Yamashita Y. Oral health and swallowing problems. Current Phys Med and Rehabili Reports. 2013;1(4):216-22.
- Ralli M, Greco A, Altissimi G, Turchetta R, Longo L, D'Aguanno V, et al. Vestibular Schwannoma and Ipsilateral Endolymphatic Hydrops: An Unusual Association. Int Tinnitus J. 2017;21(2).
- Gürkov R, Pyykö I, Zou J, Kentala E. What is Meniere's disease? A contemporary re-evaluation of endolymphatic hydrops. J Neurol. 2016;263(1):71-81.
- Ito T, Inui H, Miyasaka T, Shiozaki T, Fujita H, Yamanaka T, et al. Relationship between changes in hearing function and volumes of endolymphatic hydrops after endolymphatic sac drainage. Acta Oto-Laryngol. 2019;139(9):739-46.
- 17. Kimura RS. Experimental pathogenesis of hydrops. Arch of Oto-Rhino-laryngol . 1976;212(4):263-75.
- Ralli M, Nola G, Sparvoli L, Ralli G. Unilateral enlarged vestibular aqueduct syndrome and bilateral endolymphatic hydrops. Case Reports in Otolaryngol. 2017.
- Greco A, Gallo A, Fusconi M, Marinelli C, Macri GF, De Vincentiis M. Meniere's disease might be an autoimmune condition?. Autoimmun Rev. 2012;11(10):731-8.

- 20. Berlinger NT. Meniere's disease: new concepts, new treatments. Minnesota Med. 2011;94(11):33-6.
- 21. Ralli M, Di Stadio A, De Virgilio A, Croce A, de Vincentiis M. Autoimmunity and otolaryngology diseases. J Immunol Res. 2018.
- Russo FY, Ralli M, De Seta D, Mancini P, Lambiase A, Artico M, et al. Autoimmune vertigo: An update on vestibular disorders associated with autoimmune mechanisms. Immunologic Res. 2018;66(6):675-85.
- 23. Ralli M, D'Aguanno V, Di Stadio A, De Virgilio A, Croce A, Longo L, Greco A, et al. Audiovestibular symptoms in systemic autoimmune diseases. J Immunol Res. 2018.
- Kangasniemi E, Hietikko E. The theory of autoimmunity in Meniere's disease is lacking evidence. Auris Nasus Larynx. 2018;45(3):399-406.
- 25. Mancini P, Atturo F, Di Mario A, Portanova G, Ralli M, De Virgilio A, et al. Hearing loss in autoimmune disorders: Prevalence and therapeutic options. Autoimmunity Rev. 2018;17(7):644-52.
- Lopez-Escamez JA, Carey J, Chung WH, Goebel JA, Magnusson M, Mandalà M, et al. Diagnostic criteria for Meniere's disease according to the Classification Committee of the Barany Society. HNO. 2017;65(11):887-93.
- 27. Clyde JW, Oberman BS, Isildak H. Current management practices in Meniere's disease. Otol & Neurotol. 2017;38(6):e159-67.
- Hussain K, Murdin L, Schilder AG. Restriction of salt, caffeine and alcohol intake for the treatment of Ménière's disease or syndrome. Cochrane Database of Systematic Rev. 2018(12).
- Hussain K, Murdin L, Schilder AG. Restriction of salt, caffeine and alcohol intake for the treatment of Ménière's disease or syndrome. Cochrane Database of Systematic Rev. 2018(12).
- 30. Gioacchini FM, Albera R, Re M, Scarpa A, Cassandro C, Cassandro E. Hyperglycemia and diabetes mellitus are related to vestibular organs dysfunction: truth or suggestion? A literature Review. Acta Diabetolo. 2018;55(12):1201-7.
- 31. Scarpa A, Gioacchini FM, Cassandro E, Tulli M, Ralli M, Re M, et al. Clinical application of cVEMPs and oVEMPs in patients affected by Meniere's disease, vestibular neuritis and benign paroxysmal positional vertigo: a systematic review. Acta Otorhinolaryngol Italica. 2019;39(5):298.
- 32. Scarpa A, Ralli M, Viola P, Cassandro C, Alicandri-Ciufelli M, lengo M, et al. Food-induced stimulation of the antisecretory factor to improve symptoms in Meniere's disease: our results. Eur Arch of Oto-Rhino-Laryngol. 2020;277(1):77-83.
- 33. Schoo DP, Tan GX, Ehrenburg MR, Pross SE, Ward BK, Carey JP. Intratympanic (IT) therapies for Menière's Disease: some consensus among the confusion. Current Otorhinolaryngol Reports. 2017;5(2):132-41.
- 34. Patel M. Intratympanic corticosteroids in Ménière's disease: A mini-review. J Otol. 2017;12(3):117-24.
- Ren H, Yin T, Lu Y, Kong W, Ren J. Intratympanic dexamethasone injections for refractory Meniere's disease. Int J of Clin and Experimental Med. 2015;8(4):6016.
- Cavaliere M, De Luca P, Scarpa A, Ralli M, Bottiglieri P, Cassandro E, et al. SCORE risk scale as a prognostic factor after sudden sensorineural hearing loss. Eur Arch of Oto-Rhino-Laryngol. 2020;277(3):953-4.

- Naples JG, Henry L, Brant JA, Eliades SJ, Ruckenstein MJ. Intratympanic Therapies in M énière Disease: Evaluation of Outcomes and Early Vertigo Control. The Laryngoscope. 2019;129(1):216-21.
- 38. Patel M, Agarwal K, Arshad Q, Hariri M, Rea P, Seemungal BM, et al. Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's disease: a randomised, double-blind, comparative effectiveness trial. The Lancet. 2016;388(10061):2753-62.
- Syed MI, Ilan O, Nassar J, Rutka JA. Intratympanic therapy in Meniere's syndrome or disease: up to date evidence for clinical practice. Clin Otolaryngol. 2015;40(6):682-90.
- Pullens B, van Benthem PP. Intratympanic gentamicin for Meniere's disease or syndrome. Cochrane Database Syst Rev. 2011(3):CD008234.
- Diamond C, O'Connell DA, Hornig JD, Liu R. Systematic review of intratympanic gentamicin in Meniere's disease. Database of Abstracts of Reviews of Effects (DARE): Qualityassessed Rev [Internet]. 2003.
- 42. Minor LB. Intratympanic gentamicin for control of vertigo in Meniere's disease: vestibular signs that specify completion of therapy. The Am J Otol. 1999;20(2):209-19.
- Liu H, Zhang T, Wu Q, Zhang Y, Dai C. End-point indicators of low-dose intra-tympanic gentamicin in management of Ménière's disease. Acta Oto-Laryngol. 2017;137(2):136-43.
- 44. Liu B, Leng YM, Shi H, Zhou RH, Liu JJ, Zhang WJ, et al. Modified titration intratympanic gentamicin injection for unilateral intractable Meniere's disease. J Huazhong Univ of Sci and Technol [Medical Sciences]. 2015;35(5):747-51.
- Watson GJ, Nelson C, Irving RM. Is low-dose intratympanic gentamicin an effective treatment for Ménière's disease: the Birmingham experience. The J Laryngol & Otol. 2015;129(10):970-3.
- 46. Quaglieri S, Gatti O, Rebecchi E, Manfrin M, Tinelli C, Mira E, et al. Intratympanic gentamicin treatment 'as needed'for Meniere's disease. Long-term analysis using the Kaplan–Meier method. Eur Arch of Oto-Rhino-Laryngol. 2014;271(6):1443-9.
- 47. Gode S, Celebisoy N, Akyuz A, Gulec F, Karapolat H, Bilgen C, et al. Single-shot, low-dose intratympanic gentamicin in Ménière disease: role of vestibular-evoked myogenic potentials and caloric test in the prediction of outcome. Am J Otolaryngol. 2011;32(5):412-6.
- 48. Buki B. Results of electrocochleography in Meniere's disease after successful vertigo control by single intratympanic gentamicin injection. Audiol Neurootol. 2011;16:49-54.
- 49. Nguyen KD, Minor LB, Della Santina CC, Carey JP. Time course of repeated intratympanic gentamicin for Ménière's disease. The Laryngoscope. 2009;119(4):792-8.
- 50. Salt AN, Gill RM, Plontke SK. Dependence of hearing changes on the dose of intratympanically applied gentamicin: a metaanalysis using mathematical simulations of clinical drug delivery protocols. The Laryngoscope. 2008;118(10):1793-800.
- 51. Helling K, Schönfeld U, Clarke AH. Treatment of Meniere's disease by low-dosage intratympanic gentamicin application: effect on otolith function. The Laryngoscope. 2007;117(12):2244-50.

- 52. Vlastarakos PV, lacovou E, Nikolopoulos TP. Is gentamycin delivery via sustained-release vehicles a safe and effective treatment for refractory Meniere's disease? A critical analysis of published interventional studies. European Arch of Oto-Rhino-Laryngol. 2017;274(3):1309-15.
- 53. Scarpa A, Ralli M, Cassandro C, Gioacchini FM, Alicandri-Ciufelli M, Viola P, et al. Low-dose intratympanic gentamicin administration for unilateral Meniere's disease using a method based on clinical symptomatology: Preliminary results. Am J Otolaryngol. 2019;40(6):102289.
- 54. Kitahara T. Evidence of surgical treatments for intractable Meniere's disease. Auris Nasus Larynx. 2018;45(3):393-8.
- 55. Nevoux J, Franco-Vidal V, Bouccara D, Parietti-Winkler C, Uziel A, et al. Diagnostic and therapeutic strategy in Menière's disease. Guidelines of the French Otorhinolaryngology-Head and Neck Surgery Society (SFORL). Eur Ann of otorhinolaryngol, head and Neck Diseases. 2017;134(6):441-4.
- Quaranta N, Picciotti P, Porro G, Sterlicchio B, Danesi G, Petrone P, et al. Therapeutic strategies in the treatment of Menière's disease: the Italian experience. Eur Arch of Oto-Rhino-Laryngol. 2019;276(7):1943-50.
- 57. Scarpa A, Ralli M, De Luca P, Savignano L, Gioacchini FM, Cassandro E, et al. Letter to Editor concerning the "Therapeutic strategies in the treatment of Meniere's disease: the Italian Experience". Eur Arch of Oto-Rhino-Laryngol. 2020;277(6):1847-8.
- 58. Portmann M. The Portmann procedure after sixty years. The Am J of Otol. 1987;8(4):271-4.
- 59. Bento RF, Cisneros JC, Fonseca AD. Endolymphatic sac drainage for the treatment of Ménière's disease. The J Laryngol & Otol. 2017;131(2):144-9.
- Flores Garcia ML, Llata Segura C, Cisneros Lesser JC, Pane Pianese C. Endolymphatic Sac Surgery for Meniere's Disease - Current Opinion and Literature Review. Int Arch Otorhinolaryngol 2017;21(2): 179-83.
- Thomsen J, Bretlau P, Tos M, Johnsen NJ. Placebo effect in surgery for Meniere's disease. A double-blind, placebocontrolled study on endolymphatic sac shunt surgery. Arch Otolaryngol 1981;107(5):271-7.
- 62. Gibson AW, Moon IJ, Golub JS, Rubinstein JT. A comparison of endolymphatic shunt surgery and intratympanic gentamicin for meniere's disease. The Laryngoscope. 2020;130(10):2455-60.
- Pullens B, Verschuur HP, van Benthem PP. Surgery for Ménière's disease. Cochrane Database of Systematic Revi. 2013(2).
- 64. Devantier L, Schmidt JH, Djurhuus BD, Hougaard DD, Händel MN, Liviu-Adelin Guldfred F, et al. Current state of evidence for endolymphatic sac surgery in Menière's disease: a systematic review. Acta Oto-Laryngologica. 2019;139(11):953-8.
- 65. Bojrab DI, LaRouere MJ, Babu SC, Sargent EW, Chan EY, Hong RS. Endolymphatic sac decompression with intrasac dexamethasone injection in Meniere's disease. Otolo & Neurotol. 2018;39(5):616-21.
- 66. Higashi-Shingai K, Imai T, Okumura T, Uno A, Kitahara T, Horii A, et al. Change in endolymphatic hydrops 2 years after endolymphatic sac surgery evaluated by MRI. Auris Nasus Larynx. 2019;46(3):335-45.

- 67. Chung JW, Fayad J, Linthicum F, Ishiyama A, Merchant SN. Histopathology after endolymphatic sac surgery for Ménière's syndrome. Otology & neurotology: official publication of the American Otological Society, Am Neurotol Society [and] Eur Academy of Otolo and Neurotol. 2011;32(4):660.
- Mattingly JK, Zhan KY, Hiss MM, Harris MS, Dodson EE, Moberly AC, et al. Intraoperative electrocochleography in patients with Menière's disease undergoing endolymphatic sac decompression and shunt surgery. Otolo & Neurotol. 2019;40(9):1208-16.
- Magnan J, Ozgirgin ON, Trabalzini F, Lacour M, Escamez AL, Magnusson M, et al. European Position Statement on Diagnosis, and Treatment of Meniere's Disease. J Int Adv Otol 2018;14(2):317-21.
- Colletti V, Carner M, Colletti L. Auditory results after vestibular nerve section and intratympanic gentamicin for Ménière's disease. Otolo & Neurotolo. 2007;28(2):145-51.
- 71. Silverstein H, Jackson LE. Vestibular nerve section. Otolaryngologic Clinics of North Am. 2002;35(3):655-73.
- 72. Thomsen J, Berner B, Tos M. Vestibular neurectomy. Auris Nasus Larynx. 2000;27(4):297-301.
- Lemnos L, Aubry K, Moreau JJ, Caire F, Salle H. Postoperative compensation after neurotomy in Meniere's disease: Retrospective study of 15 cases. Neurochirurgie. 2019;65(1):20-6.
- 74. Chen BS, Roberts DS, Lekovic GP. Vestibular neurectomy for intractable vertigo: case series and evaluation of role of endoscopic assistance in retrolabyrinthine craniotomy. J Neurolo Surg Part B: Skull Base. 2019;80(04):357-63.
- 75. Kaylie DM, Jackson CG, Gardner EK. Surgical management of Meniere's disease in the era of gentamicin. Otolaryngol— Head and Neck Surg. 2005;132(3):443-50.
- Diaz RC, LaRouere MJ, Bojrab DI, Zappia JJ, Sargent EW, Shaia WT. Quality-of-life assessment of Ménière's disease patients after surgical labyrinthectomy. Otolo & Neurotol. 2007;28(1):74-86.
- Heywood RL, Atlas MD. Simultaneous cochlear implantation and labyrinthectomy for advanced Ménière's disease. The J Laryngol & Otol. 2016;130(2):204-6.
- 78. Thomsen J, Bonding P, Becker B, Stage J, Tos M. The nonspecific effect of endolymphatic sac surgery in treatment of Meniere's disease: a prospective, randomized controlled study comparing" classic" endolymphatic sac surgery with the insertion of a ventilating tube in the tympanic membrane. Acta oto-laryngologica. 1998;118(6):769-73.
- Todt I, Wilms K, Sudhoff H. Labyrinthectomy after cochlear implantation: a case of a novel approach for vertigo control. Case Reports in Otolaryngol. 2019.
- 80. Park JJ, Chen YS, Westhofen M. Meniere's disease and middle ear pressure-vestibular function after transtympanic tube placement. Acta oto-laryngologica. 2009;129(12):1408-13.
- Saliba I, Gabra N, Alzahrani M, Berbiche D. Endolymphatic duct blockage: a randomized controlled trial of a novel surgical technique for Ménière's disease treatment. Otolaryngol-Head and Neck Surg. 2015;152(1):122-9.
- 82. Saliba I, Asmar MH. Endolymphatic duct blockage for refractory Ménière's disease: assessment of intraoperative

CSF leak on short-term surgical outcomes. Acta Oto-Laryngologica. 2018;138(10):886-92.

- Gabra N, Asmar MH, Berbiche D, Saliba I. Endolymphatic duct blockage: quality of life assessment of a novel surgical technique for Ménière disease. Eur Archof Oto-Rhino-Laryngol. 2016;273(10):2965-73.
- 84. De Valck CF, Van Rompaey V, Wuyts FL, Van de Heyning PH. Tenotomy of the tensor tympani and stapedius tendons in Meniers's disease. Acta oto-rhino-laryngologica belgica. 2009;5(1):1.
- 85. Reichmayr C, Sterrer E, Bachtiar A, Layr M, Loader B. Tenotomy of the middle ear muscles. Wiener klinische Wochenschrift. 2019;131(3):87-91.
- 86. Albu S, Babighian G, Amadori M, Trabalzini F. Endolymphatic sac surgery versus tenotomy of the stapedius and

tensor tympani muscles in the management of patients with unilateral definite Meniere's disease. Eur Arch Otorhinolaryngol 2015;272(12): 3645-50.

- 87. Loader B, Beicht D, Hamzavi JS, Franz P. Tenotomy of the stapedius and tensor tympani muscles reduces subjective dizziness handicap in definite Meniere's disease. Acta Oto-Laryngologica. 2013;133(4):368-72.
- Zhang D, Lv Y, Han Y, Li Y, Li X, Wang J, et al. Long-term outcomes of triple semicircular canal plugging for the treatment of intractable Meniere's disease: A single center experience of 361 cases. J Vestibular Res. 2019;29(6):315-22.
- Attanasio G, Califano L, Bruno A, Giugliano V, Ralli M, Martellucci S, et al. Chronic cerebrospinal venous insufficiency and menière's disease: Interventional versus medical therapy. The Laryngoscope. 2020;130(8):2040-6.