Original Article

Predictors of Conservative Treatment Outcomes for Adult Otitis Media with Effusion

#Zhen Zhong ⓘ, #Junbo Zhang ⓘ, Lei Ren ⓘ, Yuhe Liu ⓘ, Zhen Zhen ⓘ, Shuifang Xiao ⓘ

Department of Otorhinolaryngology, Head and Neck Surgery, Peking University First Hospital, Beijing, China

ORCID iDs of the authors: Z.Z. 0000-0001-5372-0309; J.Z. 0000-0002-5681-0147; L.R. 0000-0003-2711-0798; Y.L. 0000-0002-7470-1905; Z.Z. 0000-0001-6280-8679, S.X. 0000-0003-1554-9859.

OBJECTIVES: Conservative treatments are usually the preferred choices for newly diagnosed adult otitis media with effusion (OME). This study was performed to explore the efficacy of conservative treatments, including medication and eustachian tube auto-inflation (ETA), for treating OME in adults and to analyze its predictors.

MATERIALS and METHODS: A total of 107 adult patients with OME were included. All patients completed two weeks of conservative treatments including medication alone or the combination of medication and ETA.

RESULTS: The numbers of patients with only one and both ears affected were 79 and 28, respectively, and therefore, 135 affected ears were included. After treatment, 75 affected ears were classified as responders (55.6%), while 60 ears were classified as nonresponders (44.4%). Four predictive factors, including age, air-bone gap (ABG), tubomanometry value (TMM), and the treatment plan (all p<0.05) were found in treatment outcomes. Patients with age ≤50 years (vs. age>50 years), ABG <17 dB (vs. ABG≥17dB), TMM values of 2-6 (vs. TMM values of 0-1), and patients who received combined treatments, including medication and ETA (vs. patients who received medication only), were more likely to be responders (all p<0.05).

CONCLUSION: For OME in adult patients, younger age, smaller ABG, higher TMM value, and combined treatment including medication and ETA are good predictors for treatment success.

KEYWORDS: Otitis media with effusion, eustachian tube auto-inflation, tubomanometry, eustachian tube, medication

INTRODUCTION

Otitis media with effusion (OME) is characterized by the presence of fluid in the tympanic cavity without any symptoms of infection. The main symptoms of OME in adults are ear fullness, earache, hearing loss, tinnitus, etc. Although some patients can recover by themselves, there are a great number of them who need treatment. This disease may decrease the quality of life when treated inappropriately and may cause long-term complications when deferred, leading to chronic OME such as adhesive otitis media, tympanosclerosis, and ossicular necrosis [1]. Therefore, adult OME patients who cannot not heal themselves should be treated in a timely manner.

Conservative treatments including medication and eustachian tube auto-inflation (ETA) are usually the preferred choices for newly diagnosed OME patients [2, 3]. The use of ETA in the short term appears favorable for children and adults [2]. Invasive treatments, such as tympanocentesis or myringotomy tube insertion, are more efficient options and are usually proposed in cases where conservative treatments have failed [4]. Currently, there are no standard criteria for patient selection for different treatments. As a result, some patients who need invasive treatments may receive unnecessary prophase conservative treatments, resulting in a waste of time and medical resources. Therefore, it is meaningful to predict the potential outcomes of conservative treatments, which might be useful for choosing treatment options in such patients without incurring excessive delays. For example, patients with low probability of success with conservative treatments should be directly recommended for invasive treatments.

In two former studies completed by our research group, the tubomanometry test (TMM), a relatively new test for evaluating the eustachian tube (ET) patency, had been proved to be useful in predicting the outcomes of medication treatment [5, 6]. However, whether this result could still be applied to patients who received combined treatments, including medication and ETA, is unclear. This study was performed to explore the relationship between several pre-treatment factors, including TMM and the treatment outcomes in patients who received combined conservative treatments or medication treatment alone. The results might also be useful in proving the advantages of combined treatments and guiding patient selection for conservative treatments.

MATERIALS AND METHODS

Study Population
This study retrospectively reviewed a total of 107 adult patients who were diagnosed with OME in the outpatient department of our hospital between January 2015 and June 2016. All patients were treated by the same medical group. The inclusion criteria were as follows: (1) age ≥18 years; (2) main complaints of ear fullness and (or) hearing loss for more than 3 weeks but less than 3 months, with no signs of alleviation; (3) no tympanic membrane perforation; (4) no upper respiratory tract infections during treatment; (5) the mean air-bone gap (ABG, calculated as the average air-bone gap value of 500, 1000, 2000, 4000Hz) of more than 10 dB; (6) type B or C tympanometry results. Patients who declined the treatment and patients who presented with nasopharyngeal neoplasms or adenoidal hyperplasia according to the results of fibreoptic nasopharyngeal endoscopy were excluded. Before treatment initiation, all patients took the TMM (Spiggle and Theis, Overath, Germany) test to evaluate the ET functions. This study was performed following the principles of the Declaration of Helsinki and the protocol was approved by the ethics committee of Peking University First Hospital.

Tubomanometry
All the TMM tests were performed according to previous literature at three pressures (30, 40, and 50 mbar) [5, 7]. The functional state of the ET was evaluated using the sum of the opening latency index (R value) at the three pressures; R value was calculated as $R = (P1−C1)/(C2−C1)$. P1 indicates the start of the movement of the eardrum after pressure application, C1 indicates the start of the pressure increase in the nasopharynx, and C2 represents the reach of the maximum pressure increase in the nasopharynx. P1–C1 represents the latency of

---

MAIN POINTS

- Conservative treatments including medication and eustachian tube auto-inflation (ETA) are usually the preferred choices for newly diagnosed otitis media with effusion (OME) patients.

- Currently, there are no standard criteria for patient selection for conservative treatments.

- For adult patients with OME who received conservative treatments, younger age, small mean air-bone gap, high tubomanometry value, and the combined treatment of medication and ETA are considered as good predictors of treatment success.

---

tubal opening, and C2–C1 represents the time of increased pressure in the nasopharynx. The R value quantifies the ET patency: an R value ≤1 indicates satisfactory ET function and is weighted as 2 points, indicating that the tube opening occurs before C2; an R value >1 suggests a delayed opening or restricted ET function and is weighted as 1 point, indicating that the tube opening occurs after C2; while a non-measurable R value indicates that the ET has not opened or is occluded and is weighted as 0. The TMM value is calculated as the sum of all points at 30, 40, and 50 mbar, and therefore, its theoretical range is 0-6. A higher TMM score indicates a better ET function.

Treatments
The medication treatments for this group of patients consisted of oral Myrtol Standardized Enteric capsules (300 mg, 3 times/day) (Gelomyrtol, Pohl-Boskamp GmbH & Co. KG, Schleswig–Holstein, Germany), nasal steroids (2 times/day) [Budesonide nasal spraying (Rhinocort, AstraZeneca AB, Sodertalje, Sweden) or Fluticasone propionate nasal spray (Flixonase, Glaxo Wellcome SA, Burgos, Spain)], and oral loratadine (10 mg, 1 time/night) (Clarityne, Bayer SA-NV, Diegem, Belgium). The medication treatment course was two weeks.

The ETA procedures in this study were performed using a modified Politzer device (Streamsys, Zhuo Zhi Technology Co. Ltd, Hefei, China). The mechanism of this device is similar to that of the one introduced by Arick in his study, [8] which could help complete the politzerization by the patients themselves or their family members in the home setting. This device could emit a controlled air pressure and sufficient volume velocity, but is not considered harmful. The device has two settings: setting 1 delivers an air pressure of 20 kPa at a volume velocity of 1267 mL/min, setting 2 delivers an air pressure of 36 kPa at a volume velocity of 1986 mL/min.

The patients who received the ETA treatment had their own "Streamsys" devices to administer the treatment twice daily, in the morning and evening. During each session, the treatment was administered to the affected side of the nostril in patients with one affected ear, or to one nostril and then to the other in patients with both affected ears. The procedure was repeated 10 minutes later. To deliver the therapy, the tip of the device was inserted into the nostril while compressing the other nostril with a finger. The patient should then hold a small amount of water in their mouth without swallowing it. Then the device was turned on, which allows the air flow into the nasal cavity at a constant volume velocity. After 1-2 seconds of air flow, they could swallow the water. In this study, all patients used setting 2 mode at the beginning of the treatment, and patients who felt uncomfortable with this setting at the beginning or during the treatment course could change to setting 1.

Evaluation of Clinical Efficacy
In this study, the evaluations of clinical efficacy were done immediately after two weeks of treatment. An ear was defined as a responder if one or more of following conditions happened: (1) symptoms were significantly relieved or disappeared; (2) the ABG decrease was within 10 dB, or the mean air conduction hearing threshold decreased by more than 10 dB; (3) the tympanometry converted to type A or from type B to C. While a non-responder ear was defined when no significant alterations happened in symptoms or hearing tests. Patients with non-responder ears after two weeks of conservative treatments were suggested additional invasive treatments, such as tympanocentesis or myringotomy tube insertion. Therefore, the treatment outcomes that related to conservative methods were all evaluated at this time.

Statistical Analysis

Statistical analyses were performed using the statistical software Statistical Package for the Social Sciences (SPSS) 20.0 (IBM Corp., Armonk, NY, USA). All continuous data were displayed as mean±standard deviation. The unpaired student's t test was used to compare the quantitative variables among different groups. Pearson's Chisquare test was used to compare the categorical variables among different groups. The Receiver Operating Characteristic (ROC) curve test was used to determine the best cutoff value of independent variables. Multiple logistic regression analysis was used to evaluate the significance of independent variables of treatment efficacy. $p<0.05$ was considered to be statistically significant.

RESULTS

The cohort included 50 men (46.7%) and 57 women (53.3%), with a mean age of 55.7±17.0 years and range 20 to 85 years. Before treatment, the number of patients with only one and both ears affected were 79 and 28 (73.8% and 26.2%), respectively. Therefore, a total of 135 affected ears were included. Among these ears, 75 were classified as responders (55.6%), while the other 60 were classified as nonresponders (44.4%). The baseline characteristics according to the treatment outcomes (Table 1) demonstrated a significantly higher ratio of positive subjective Valsalva result in responders than in nonresponders ($p<0.05$). However, no significant differences were found between these two groups with respect to age, sex, affected side, and the condition of the contra-lateral ear ($p>0.05$). The results of hearing tests and treatment plan according to the treatment outcomes are shown in Table 2. The results demonstrated significant differences between responders and nonresponders for ABG, TMM value, and the treatment plan received ($p<0.05$), while no significant difference was observed in the tympanometry test ($p>0.05$).

All the variables listed in Table 1 and 2 were analyzed using logistic regression to identify the factors that could predict the treatment outcomes. The results are shown in Table 3, suggesting that younger age, smaller ABG, higher TMM value, and the combined treatment plan were significantly related to the treatment success ($p<0.05$).

The ROC analysis of age, ABG, and TMM value for treatment outcomes suggested that the area under the curve (AUC) could reach 0.582, 0.622, and 0.646, respectively. The optimal cutoff values as determined by the Youden Index were 50.5 years for age, 16.9 dB for ABG, and 1.5 for TMM value. In this study, the affected ears were placed into different groups according to the integers that were close to these optimal cutoff values (shown in Table 4), suggesting that the affected ears of age ≤50 years, ABG <17 dB, and TMM values of 2-6 were more likely to benefit from the treatments ($p<0.05$).

Table 1. Baseline characteristics of all affected ears according to treatment outcomes

	Responders (n=75)	Nonresponders (n=60)	T or Chi-square value	p
Age (years)	53.7±17.2	58.8±16.6	1.745	0.083
Sex			1.614	0.204
Male	33	33		
Female	42	27		
Affected side			0.786	0.375
Left	42	29		
Right	33	31		
Contra-lateral ear			0.006	0.938
Affected	32	26		
Normal	43	34		
Subjective Valsalva			6.896	0.009
Positive	42	20		
Negative	33	40		

Table 2. Hearing tests and treatment plans of all affected ears according to treatment outcomes

	Responders (n=75)	Nonresponders (n=60)	T or Chi-square value	p
ABG (dB)	16.3±8.6	19.9±8.5	2.420	0.017
Tympanometry			2.954	0.086
B type	39	40		
C type	36	20		
TMM value	2.7±2.3	1.6±2.2	−2.919	0.004
Treatment plan			9.763	0.002
Medication	31	41		
Medication+ETA	44	19		

ABG: air-bone gap; TMM: tubomanometry; ETA: eustachian tube auto-inflation.

Table 3. Logistic predictor to treatment outcomes

	Odds ratio value	95% CI	p
Age (years)	0.970	0.946-0.994	0.017
ABG (dB)	0.928	0.883-0.976	0.004
TMM value	1.433	1.174-1.750	<0.001
Treatment plan	3.784	1.677-8.536	0.001

ABG: air-bone gap; TMM: tubomanometry; CI: confidence interval.

Table 4. Treatment outcomes according to different age, ABG value and TMM value

	Responders (n=75)	Nonresponders (n=60)	Chi-square Value	p
Age (years)			4.981	0.026
≤50	34	16		
>50	41	44		
ABG (dB)			6.695	0.010
<17	48	25		
≥17	27	35		
TMM value			12.540	<0.001
0-1	27	40		
2-6	48	20		

ABG: air-bone gap; TMM: tubomanometry.

DISCUSSION

The ETA maneuver completed by the Politzer method was initially introduced by Shea in 1971 [4]. This method is hard to standardize when compared with medication in the absence of air-pressure and air-flow volume control that might cause ineffective or harmful air pressures in the middle ear. Arick et al. [8, 9] introduced a simple device that could be used in completing the controlled Polizter maneuvers and further proved the clinical values of such devices in treating OME. Theoretically, the combined treatments including medication and ETA might be more effective than treatment alone. In this study, a similar device was used for ETA to prove this, and we further explored the possible factors that are related to the treatment outcomes. These results might also be useful in selecting the candidates for such treatment.

Factors such as age, ABG, TMM value, and treatment plan are considered as independent predictors of treatment outcomes. Such results confidently suggest the clinical value of the combined treatment. The other three factors could not be changed in clinical work. As a result, the use of ETA, if tolerated, on the basis of medications was the only way to increase the scores as well as the potential treatment success rate related to it.

The TMM test, a semi-objective method for evaluating ET patency, is now the most accurate method to describe ET function. The ET dysfunction is thought to be closely related to OME occurrence: [10] in addition to mechanical obstruction, it could induce a negative pressure in the middle ear, which could provoke a middle ear mucosal inflammation, capillary disruption, and transduction of fluid from the local vessels to the middle ear [11]. Therefore, the ET dysfunction could also be viewed as a poor predictor of treatment success. Our team has proved this conclusion in OME patients who received medication therapy alone, [5] while the results of this study suggested that this conclusion was still applicable for OME patients who received combination treatment including medication and ETA.

Few studies have explored the relationship of age with treatment outcomes in adults with OME. It is unclear as to whether younger patients are more likely to benefit from therapy. This might be due to decreasing ET mucosal cilium function with increasing age. The affected ears with smaller ABG are more likely to be observed in responders, and the actual mechanism involved is still unclear. However, there are some studies proposed that a higher ABG, which means that a greater decrease in the function of sound transmission is related to the presence of a more viscous fluid in the middle ear, [12, 13] and it is hard to expelit through the ET via conservative therapy.

In addition, it should be noted that the tympanometry results were not related to the treatment outcomes, although the type C tympanograms always go hand in hand with lower conductive hearing loss (smaller ABG). However, the affected ears with type C tympanograms showed a higher response rate (64.3%, 36/56) than the affected ears with type B results (49.4%, 39/79), but the difference was not statistically significant (p=0.086). Therefore, a different and a more comprehensive result might be arrived at by increasing the patient sample size in our future study. On the other hand, in a regression analysis, only the most significant factor can usually be included among several other factors that have similar predictive abilities. This might be the reason as to why ABG was included, but not the tympanometry results.

However, there are some limitations should be acknowledged in this study. First, all the data were retrospectively collected from a single center, which may decrease the scientific power of the conclusion. However, this was the first study that concerned the results of different conservative treatments and their predictors, and, the study design then seemed proper. Second, smoking history, including the patients' smoking history and the exposure to second-hand smoke, were missing and were not analyzed in this study. Such information will be added to the future study of our group, which may be useful in exploring the relationship between smoking history and the prognosis of OME. Finally, the study had no control group that included untreated OME patients. Because OME has a certain probability of natural spontaneous resolution, a multicenter, prospective, randomized, longitudinal control trial which includes at least four randomized control groups is required to tease out the natural history of spontaneous resolution and to evaluate actual therapeutic results, including patients with the following four treatment arms: no treatment, medical treatment alone, medical treatment with ETA, and ETA alone.

CONCLUSION

In summary, for adult patients with OME who received conservative treatments, younger age, small ABG, high TMM value, and the combined treatment of medication and ETA are considered as good predictors of treatment success. The results could be useful in identifying the affected ears with different probabilities of treatment success, and then could be valuable in guiding the treatment options in such patients.

REFERENCES

1. Paksoy M, Altin G, Eken M, Hardal U. Effectiveness of intratympanic dexamethasone in otitis media with effusion resistant to conventional therapy. Indian J Otolaryngol Head Neck Surg 2013; 65: 461-7. [Crossref]

2.   Perera R, Glasziou PP, Heneghan CJ, McLellan J, Williamson I. Autoinflation for hearing loss associated with otitis media with effusion. Cochrane Database Syst Rev 2013; 5: CD006285. [Crossref]

3.   Schilder AG, Marom T, Bhutta MF, Casselbrant ML, Coates H, Gisselsson-Solén M, et al. Panel 7: Otitis Media: Treatment and Complications. Otolaryngol Head Neck Surg 2017; 156: S88-S105. [Crossref]

4.   Atkinson H, Wallis S, Coatesworth AP. Otitis media with effusion. Postgrad Med 2015; 127: 381-5. [Crossref]

5.   Zhang J, Zhong Z, Xiao S, Liu Y, Zhen Z, Ren L, et al. Tubomanometry value as an associated factor for medication outcomes in adult acute otitis media with effusion. Eur Arch Otorhinolaryngol 2018; 275: 53-7. [Crossref]

6.   Zhong Z, Liu Y, Xiao S, Zhang J, Zhang X. The function of tubomanometry in forcasting the progonosis of acute otitis media with effusion. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2015; 29: 429-32.

7.   Schröder S, Lehmann M, Sauzet O, Ebmeyer J, Sudhoff H. A novel diagnostic tool for chronic obstructive eustachian tube dysfunction—the eustachian tube score. Laryngoscope 2015; 125: 703-708. [Crossref]

8.   Arick DS, Silman S. Nonsurgical home treatment of middle ear effusion and associated hearing loss in children. Part I: clinical trial. Ear Nose Throat J 2005; 84: 567-8, 570-4, 576 passim. [Crossref]

9.   Arick DS, Silman S. Treatment of otitis media with effusion based on politzerization with an automated device. Ear Nose Throat J 2000; 79: 290-2, 294, 296 passim. [Crossref]

10. Mills R, Hathorn I. Aetiology and pathology of otitis media with effusion in adult life. J Laryngol Otol 2016; 130: 418-24. [Crossref]

11. Buchman CA, Stool SE. Functional-anatomic correlation of eustachian tube obstruction related to the adenoid in a patient with otitis media with effusion: a case report. Ear Nose Throat J 1994; 73: 835-8. [Crossref]

12. Sichel JY, Priner Y, Weiss S, Levi H, Barshtein G, Eliashar R, et al. Characteristics of the type B tympanogram can predict the magnitude of the air-bone gap in otitis media with effusion. Ann Otol Rhinol Laryngol 2003; 112: 450-4. [Crossref]

13. Forquer BD, Linthicum FH. Middle ear effusion: relationship of tympanometry and air-bone gap to viscosity. Ear Hear 1980; 2: 87-90. [Crossref]