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Clinical prognostic index for tympanoplasty (PRIT) in Pediatric patients

Introduction

Factors commonly associated with otologic surgery outcome in the pediatric patient are directly related to cranial dimensions of the child and adequate function of the middle ear [1,2], which directly depends on the eustachian tube (ET) and is even further compromised if the patient has any craniofacial malformation such as cleft lip and palate (CLP) [3], or syndromic disorders such as trisomy 21 [4], just to mention some examples [5].

Assessment of the eustachian tube in a perforated ear can be difficult [6] and we can therefore resort to the contralateral ear function to assess both tubes function and their relationship with the nasopharynx [7,8].

Myringoplasty success in children ranges from 35% to 92% [9] and these results are generally attributed to different patient selection criteria [10] and/or surgical success definition by the author [11]. Some define myringoplasty success solely as integration of the tympanic membrane graft [12]. A more complete definition of success is: 1) Tympanic membrane or graft without evidence of perforation at the last clinic visit. 2) Hearing improvement of at least 20 dB or no auditory threshold decrease, and 3) aerated middle ear space, expressed by a tympanic membrane in anatomic position without atelectasis, retraction or lateralization [13,14]. For the purposes of this study, the latter will be the definition of success.

In 2012, Boronat et al. reported a retrospective cohort of 44 patients with 53.6% of tympanoplasty success, and associated seven logistic regression–obtained variables that intervene in surgical outcome; [15] they proposed these variables as a prognostic model for surgical outcome, but the results were not entirely conclusive owing to the sample size. Dornhoffer [16], analyzed a retrospective cohort of 1000 patients, out of which 129 were pediatric patients, and found discouraging differences between myringoplasty success and patient age at...
the moment of surgery [17]. Manning found that ET adequate function was a predictive factor for good surgical outcome [18]. Other factors such as perforation type and size, presence of otorrhea, the surgeon, the surgical technique, etc. have been studied as risk factors for surgical outcomes, but the reports are heterogeneous.

There is no clinical preoperative assessment method that allows for tympanoplasty outcome to be predicted in pediatric patients. We believe that having a tool such as the proposed index, the Prognostic Index for Pediatric Tympanoplasty (PRIT), will be useful for the otorhinolaryngologist, since it is a practical instrument.

**Material and Methods**

This was an ambispective cohort study carried out at the otorhinolaryngology department of a pediatric tertiary care hospital from January 2005 to May 2017.

**Sample size**

The calculation is based on events per variable for multivariate analyses, with at least 10 patients per variable in the logistic regression.

**Criteria for sample selection**

All patients with tympanic membrane perforation for any cause who underwent type I tympanoplasty or myringoplasty were included.

**Inclusion criteria**

Patients aged 5-16 years, with or without craniofacial alterations, with or without otorrhea, with or without contralateral ear altered status, with or without adenoidectomy, with lateral or medial technique, preoperatively assessed with tonal audiometry or brainstem auditory evoked potentials with latency-intensity curve, with hypoacusis of up to 40 dB were included. Participants also had to have 6-month postoperative audiometric evaluations available, in addition to complete medical records.

**Statistical analysis**

One hundred and sixty-one patients were included. Descriptive statistics were used for baseline dichotomous variables (gender, time of evolution, perforation size, perforation type, surgeon, cause of perforation, previous adenoidectomy, history of craniofacial malformation and status of contralateral ear), with values expressed as simple frequencies and percentages, and for quantitative variables (age in years), medians and IQR were reported owing to their free distribution.

**Bivariate analysis**

The gender, perforation site, contralateral ear status, cause of perforation, craniofacial malformation, otorrhea, mucosal status, etc. variables were analyzed using the $^2$ test or Fisher’s exact test contrasted with anatomo-functional success. In

the cases where the variable was quantitative or ordinal (age, degree of perforation, pre- and postsurgical auditory threshold), receiver operating characteristics (ROC) curves were constructed to look for cutoff points and make them dichotomous. In all cases, the clinical relevance measure was weighted using the odds-ratio (OR) with the corresponding 95% confidence interval (CI).

**Multivariate analysis**

Logistic regression was used, with anatomo-functional success as the dependent variable. In this model, those variables that achieved statistical significance in the bivariate analysis were included and variables that in clinical practice constituted a risk factor, such as age and perforation type or size, were added.

**Prognostic index model**

Possible risk factors were weighed, and those with the highest statistical relevance were assigned a value. Adjustment was made for age, since craniofacial development is regarded by many authors as an important factor for prognosis [19] and a ROC curve was constructed with the purpose to find an optimal cutoff point for the PRIT scale.

The PRIT significance was analyzed using the $^2$, test, contrasting the resulting cutoff point vs. failure. In all cases, a $p$-value < 0.01 was considered to be significant. The analyses were carried out using the SPSS 21.0 software.

According to the 2008 Declaration of Helsinki and its subsequent amendments for biomedical research studies involving human subjects [2021], as well as to local regulations on health research [22], this work is classified as minimal risk research.

**Results**

**General characteristics of the population**

The cohort included 161 patients of 5 to 16 years and 11 months of age, with tympanic membrane perforation for any cause and superficial hypoacusis, who were programmed for myringoplasty or type I tympanoplasty between January 2005 and March 2017. Thirteen patients were excluded due to some extension of the surgical technique.

To construct the PRIT index, 148 patients were analyzed, out of which 2 (1.42%) were lost to followup at six months. Of the remaining 146 patients, 65.9 (45.20%) were females, the most common cause of perforation was otitis media (75.34%), 47.8% had inferior localization, in 49.3%, the perforation size was 25-50 %, and most perforations (89%) were of the central type. No craniofacial malformations were observed in 91.1% of the population and the remaining 8.9% had CLP sequel; adenoidectomy prior to tympanoplasty had only been performed in 50 patients (34.2%).

Fourteen patients with otorrhea were intervened, which accounted for 9.8%, and approximately half of intervened
patients (75, 52.36%) had some type of contralateral ear abnormality, generally tympanic membrane perforation or serous otitis media (Table 1).

### Anatomofunctional success

Anatomofunctional success was obtained in 59.6% of cases. For the bivariate analysis of all qualitative variables [2], was calculated, and surgical outcome was observed to be directly affected by otorrhea (p < 0.0001), as well as by contralateral ear abnormal status (p < 0.024), with no other variable being significant for surgical outcome. For quantitative variables (mean auditory threshold and age), ROC curves were constructed in order to establish cutoff points. Once the cutoff point was available, quantitative variables were analyzed similarly to the other variables, and were not significant when contrasted with the surgical outcome; however, the age variable remained for the rest of the analysis owing to its biological importance (Table 2).

### Factors related to failure

For the multivariate analysis, the selected variables were those that have been commonly reported by other authors as probable factors for failure, including the work that was previously carried out in our department by Boronat et al. in 2012. All variables were analyzed, contrasting them with anatomofunctional success (success of all 3 variables), with the OR being calculated with the corresponding 95% CI (Figure 1).

According to data shown in Table 2, failure occurs 2.4 fold more frequently in patients with otorrhea than in those without it (95% CI: 1.76–3.29); patients whose contralateral ear has inflammatory pathology, such as chronic suppurative otitis media or serous otitis media have 1.59 fold more failure than patients with a healthy contralateral ear (95% CI: 1.05–2.41) (Figure 1).

Marginal perforation shows that patients with this type of perforation have 1.27 fold higher risk for experiencing failure than those with central perforation (95% CI: 0.75–2.18); patients whose contralateral ear is tympanic membrane perforation or serous otitis media have 1.59 fold more failure than patients with a healthy contralateral ear (95% CI: 1.05–2.41) (Figure 1).

### Integration of variables to the index model

All variables introduced to the regression satisfy the minimum sample size (n > 10), and are therefore considered to have statistical power. According to Table 3 results, gender, with an OR of 1.570 (95% CI: 0.754 –3.266), perforation size > 50%, with an OR of 0.834 (95% CI: 0.373–1.861) and the age < 7.5 years variable, with an OR of 0.512 (95% CI: 0.196–1.337), are no risk factors for surgery failure (Figure 2). Although dichotomous age has been shown not to be a risk factor, the PRIT index model was adjusted for the age in years.

### Elaboration of the PRIT index

With logistic regression–associated values and clinical variables, a PRIT model is proposed. This model weighs
potentially predictive variables according to the ORs significance and, in this case, otorrhea was assigned a value of 6 (OR: 11.59; 95% CI: 2.441–57.626), 3 points were assigned to the contralateral ear abnormal status variable (OR: 2.484; 95% CI: 1.181–5.223) and 1 point to marginal perforation (OR: 2.717; 95% CI: 0.857–8.611) (Table 3), with a possible score of 0 to 10 points resulting when added up, according to the assessed clinical characteristics. For the creation of the index, this value was adjusted for the age in years, that is, total score was multiplied by the patient’s age in years (Table 4).

The PRIT score was calculated for each patient and subsequently, by means of a ROC curve, 30 points was established as the cutoff point, with a sensitivity of 80% and specificity of 80%.

Clinical use of the PRIT index is hypothetically exemplified above; on both examples, a 5-year-old patient is assessed.

**Risk associated to the PRIT value**

Age-adjusted clinical significance of the proposed PRIT (< 30 and > 30 points) was analyzed against the failure outcome variable using Pearson’s [2], test with a p-value < 0.001.

The values expressed in table 5 clearly show that patients who obtained a PRIT score > 30 points have a 2.3-fold higher risk for experiencing failure than those with < 30 points.

**Discussion**

There are numerous articles [23] that try to reach a consensus on the risk factors tympanoplasty failure might be attributed to in the pediatric population [24]. Surgical success obtained in the present analysis is 59.6%, which is similar to that reported by Boronat et al. in 2012, but with regard to risk factors that produce failure there is considerable controversy or lack of homogeneous evidence.

One of the most controversial factors is patient age. The cutoff point in our study was 7.5 years, similar to that reported by Splete [25], where the age to consider surgery is suggested to be above 7 years. By itself, age had no statistical significance, as opposed to findings in a meta-analysis reported in 2015 [26], but when interacting with other variables such as otorrhea, contralateral ear status and type of perforation or marginal perforation [27] (the PRIT model), age was able to significantly predict failure (p < 0.001).
Otorrhea has no statistical significance in multiple reports [28], such as the one by Onal in 2005; however, in our study, otorrhea was significant since the beginning of the analysis (p < 0.001), and at risk estimation, it was shown to be an important factor for failure (RR: 2.41; 95% CI: 1.76 – 3.29) [29]. Otorrhea was mentioned as a factor that can directly affect surgical outcome by Lin et al. in 2008, but many other studies report having practiced this type of surgeries in patients with otorrhea with good results being obtained. In the multivariate analysis [30], otorrhea was clearly the most relevant variable in the outcome of failure with an OR of 11.859 (95% CI: 2.441 – 67.104), followed by the contralateral ear abnormal status variable (OR: 2.484; 95% CI: 1.181–5.223).

Craniofacial postnatal development apparently should be taken into account when programming any ear surgery since, at younger ages, the ET function is not fully adequate and, in addition, at pediatric age, its anatomical situation seems to put the patient in disadvantage prior to 7.5 years of age, which is consistent with Boston pediatric hospital experience, where only the age younger than 8 years was reported to be significant for failure [31]. In contrast, other authors claim that age has nothing to do with tympanoplasty outcomes in children [32,33]. On the other hand, Hassman concluded that contralateral ear abnormal status must be taken into account, since it is an indicator of nasopharyngeal pathology that might affect ET correct functioning [34].

The type of perforation is also important. In some textbooks of the specialty, marginal perforations [35] have been referred to as dangerous or insecure perforations, since the remnant eardrum in the tympanic perforation acts as a barrier that prevents squamous epithelium of the duct from migrating to the middle ear [35]. In the logistic regression carried out in this study, the marginal perforation type was found to be the third most relevant variable, in spite of the CI crossing the null hypothesis value of 1, with an OR of 2.717 (95% CI: .857–8.611). This type of perforations have also been associated with failure by Scharff and by Mendes R [35].

### Conclusions

Tympanoplasty success was obtained in 59.6% of pediatric patients. The construction of the PRIT model for clinical use in tympanoplasty planning for pediatric patients was achieved (p < 0.001). Tympanoplasty failed in 40.4% of patients, and the variables that influenced on the outcome were otorrhea and contralateral ear status. All results correspond to a 6 months follow-up period.

### Perspective

Validation of this index is necessary making sure there is a balance, especially in the sample of groups by age, in order to assess if age really represents a risk for surgical outcomes.

### References


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