Association between tonsillectomy, adenoidectomy, and appendicitis

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ABSTRACT

Introduction: tonsillectomy, with or without adenoidectomy, is one of the most frequent surgical procedures generally performed, especially in young patients. Several studies suggest that there is a relationship between tonsillectomy and altered MALT immune system.

Objective: to examine the possible association between tonsillectomy or adenoidectomy and the risk of subsequent appendicitis.

Material and method: a cross-sectional study was performed in 650 patients admitted to the emergency department of a general hospital in Valencia, Spain. Previous history of tonsillectomy and/or adenoidectomy was related to a history of appendectomy. A descriptive study and an analysis of the relationship between previous operations and appendicitis was performed. A multivariable analysis controlled for age and sex was also performed, including the possible interaction of the gender variable. The independent effect of each of the procedures (tonsillectomy, adenoidectomy) was tested.

Results: the 25.5% of patients had undergone tonsillectomy and 11.5% adenoidectomy; 17.5% had had an appendectomy. On average, women were operated on more frequently than men. In the bivariate analysis, both tonsillectomy and adenoidectomy were significantly associated with subsequent appendectomy. In the multivariate analysis, this association was only maintained for tonsillectomy (OR: 3.23; 95% CI: 2.11-4.94). A stratified analysis controlling for sex showed a modification of this effect, with a higher association in women (OR: 5.20; 95% CI: 2.91-9.28) than in men (OR: 1.74; 95% CI: 0.90-3.39).

Conclusions: a clear association has been found, especially in women, between previous tonsillectomy and subsequent acute appendicitis. Due to a lack of data on acute appendicitis there should be further studies to explain the findings of this study, as this could be the first described risk factor of acute appendicitis.

Key words: Tonsillectomy. Adenoidectomy. Appendicitis. MALT system.

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INTRODUCTION

Tonsillectomy and adenoidectomy are two of the most frequently performed surgical procedures in general, and are very common in children and adolescents. Ogra observed that after tonsillectomy there was a reduced production of IgA against the oral antipolio vaccination in children (1).

Tonsillectomy has also been associated with Hodgkin's disease, especially in adolescents under 12 years of age (2). A study in Israel found an association only in mixed cellularity cases, not in other types (3). Other studies do not corroborate these findings (4). Mueller found a higher relative risk in older patients (5).

Some authors have not found changes in levels of immunoglobulins after tonsillectomy (6). Brandtzaeg described a lower level of secretory IgA after tonsillectomy and adenoidectomy (7). Ostergaard observed lower levels of IgA in children with atopic diseases and previous tonsillectomy (8). Cantani et al. also found low levels of IgA in children one month after tonsillectomy, and recommended their determination before and after surgery due to the possibility of subsequent disorders (9); another study confirmed these findings in salivary IgA levels (10). Friday et al. found low levels of IgG in children 30 months after tonsillectomy and/or adenoidectomy (11). An association has also been found between tonsillectomy and Crohn's disease, especially terminal-ileum Crohn's disease (12,13).

Based on all these findings, there seems to be some type of relationship between tonsillectomy and changes in the MALT system of the digestive tract. However,

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there does not seem to be any previous studies on the relationship between this procedure and another of the more frequent surgical removals of an organ included in the MALT system, the appendix. The appendix may substitute the loss of another MALT organ (tonsils) and become more frequently inflamed in infection. On the other hand, there are no clear risk factors described for acute appendicitis.

The purpose of this study was to examine the possible association between tonsillectomy or adenoidectomy and the risk of subsequent acute appendicitis.

PATIENTS AND METHODS

A cross-sectional study was performed including randomly selected patients admitted to the Emergency Department of Arnau de Vilanova Hospital, which serves a population of approximately 275,000 patients. A survey was performed, completed by the physician in front of the patient, to investigate previous tonsillectomy, adenoidectomy and appendectomy, and at what age they had been performed. The operation was confirmed by physical examination. Patients who were not sure of their responses were eliminated, as well as patients who could not respond. A total of 650 patients were selected.

The following variables were recorded: appendectomy (AP), age, sex, tonsillectomy (AM), age of tonsillectomy, adenoidectomy (AD), age of adenoidectomy, age of appendectomy, and interval between operations (age). Categorical variables included sex, AP, AM, AD; the rest were continuous variables.

Statistical analysis

All of the data were introduced in a database and analyzed using two statistical programs: SPSS v. 10 (14) and EPIINFO (15). For descriptive statistics, absolute and relative rates were used for categorical variables, and mean, median, standard deviation and range were used for continuous variables. Contingency tables were constructed to compare the frequency of surgical intervention on lymphatic organs in men and women, and the association of the sex variable; each of the operations was contrasted using a two- tailed Fischer's exact test.

Normal distribution was confirmed in continuous variables (age, age at which procedures occurred, and intervals between procedures) by sex using the Kolmogorov-Smirnov test with Killiefors correction. When a normal distribution was assumed, a Student's t-test was used to compare the means of continuous variables classified according to sex. If normality was not assumed, a non-parametric Mann-Whitney test was used.

To calculate the association measurements between variables, we considered appendectomy to be the response variable. Tonsillectomy and adenoidectomy were

considered explanatory variables. The sex and age of the patient were included in the models as control variables. The relative importance of each of these variables was calculated using multivariate models of logistic regression including variables that showed statistical significance ($p < 0.20$). The existence of differences in the effect of explanatory variables by sex was investigated by including the interaction terms within the models and then studying their statistical significance. If an interaction was found, a stratified analysis by sex was performed.

RESULTS

The prevalence of each of the surgical procedures in general and according to sex may be observed in table I. No significant differences were found. There is a difference of four years of age between surveyed men and women. There were no significant differences in frequency of operations, except for prevalence of appendectomy ($p = 0.06$); this was more frequent in women (20.4 vs. 14.7% in men). Table II shows the means and medians of the different ages at which surgeries were performed, as well as the intervals between tonsillectomy and/or adenoidectomy and appendectomy. Figure 1 shows the percentages of patients in which each operation was performed, following the distribution by age quartiles. Table III compares the average ages of appendectomy depending on the existence of a previous tonsillectomy or adenoidectomy. No significant differences were found. There were significant differences in the average age at

Table I. Age of the study population and procedures performed*

	Total (650)	Men (326)	Women (324)	Sig.
Age	45.62	43.73	47.52	0.012
Tonsillectomy	166 (25.5%)	78 (23.9%)	88 (27.9%)	0.369
Adenoidectomy	75 (11.5%)	39 (12%)	36 (11.1%)	0.806
Appendectomy	114 (17.5%)	48 (14.7%)	66 (20.4%)	0.064

*Number of operated patients (percentage).

Table II. Average age

	Age	Age AM	Age AD	Age AP	Interval between AM and/or AD and AP (years)
n	650	165	74	113	53
Minimum	9	2	1	6	1
Maximum	88	50	50	79	40
Average	45.62	9.92	8.64	22.01	12.38
Median	45	6	6	20.50	16.50
Stand. dev.	19.22	7.63	7.40	13.03	10.23

Fig. 1.- Percentage for each surgical procedure according to age. Distribution in quartiles.

Porcentaje de cada una de las intervenciones quirúrgicas a estudio según la edad. Distribución por cuartiles.

Table III. Average age (and 95% confidence interval) at appendectomy according to previous tonsillectomy (AM) or adenoidectomy (AD)

Procedure	Average age AP (years)	Sig.
AM	21.38 (18.41-24.35)	p = 0.640
No AM	22.54 (18.75-26.34)	
AD	25.27 (19.60-30.94)	p = 0.192
No AD	21.22 (18.50-23.93)	

appendectomy according to sex (Table IIIa) – the operation was performed earlier in women than in men (19.5 vs. 25.5 years in men).

The average time between tonsillectomy-adenoidectomy and appendicitis (Table IIIb) is 12.38 years (95% confidence interval: 9.56-15.20). If we compare time intervals according to sex, these are 16.87 years in men (95% CI: 9.71-24.03) and 10.61 years in women (95% CI: 7.81-13.40) (p = 0.099).

Tables IVa and IVb show the analysis of a simple association between tonsillectomy or adenoidectomy and subsequent appendectomy. Our results indicate a significant positive association; patients with a previous tonsillectomy exhibit 3.25 times more probabilities of being operated on subsequently for acute appendicitis: OR: 3.25 (95% CI: 2.13-4.96). The association between adenoidectomy and appendectomy was also significant: OR: 2.35 (95% CI: 1.37-4.03).

After stratifying according to sex, it may be observed that the association between tonsillectomy and appendectomy in men decreases, and statistical significance disappears: OR 1.74 (95% CI: 0.90-3.38), while in women the association is stronger: OR: 5.18 (95% CI: 2.92-9.20).

Table IIIa. Average age (and 95% confidence interval) at appendectomy according to sex

Sex	Average age AP	Sig.
Men	25.49 (20.63-30.35)	p = 0.029
Women	19.53 (17.28-21.78)	

Table IIIb. Average interval between procedures (and 95% confidence interval) in years between AM-AD and AP

		Sig.
Global	12.38 (9.56-15.20)	p = 0.099
Men	16.87 (9.71-24.03)	
Women	10.61 (7.81-13.40)	

Table IVa. Association between tonsillectomy (AM) and appendectomy (AP)

	AP	No AP	Total
AM	53 (31.9%)	113 (68.1%)	166
No AM	61 (12.6%)	423 (87.4%)	484
	114 (17.5%)	536 (82.5%)	650

p = < 0.0000001. OR: 3.25. ICOR 95%: 2.13 - 4.96

Table IVb. Association between adenoidectomy (AD) and appendectomy (AP)

	AP	No AP	Total
AD	23 (30.7%)	52 (69.3%)	75
No AD	91 (15.8%)	484 (84.2%)	575
	114 (17.5%)	536 (82.5%)	650

p = < 0.002. OR: 2.35. ICOR95%: 1.37 - 4.04

On the contrary, the association between adenoidectomy and appendectomy was stronger in men: OR: 3.10 (95% CI: 1.44-6.66) than in women: OR: 1.86 (95% CI: 0.86-4.02).

A multivariate analysis controlling for age and sex showed similar results. The odds ratio for the association between tonsillectomy and appendicitis was 3.23 (95% CI: 2.11-4.94), and between adenoidectomy and appendicitis 2.57 (95% CI: 1.48-4.46). However, after controlling the variable tonsillectomy, the association between appendicitis and adenoidectomy disappears (OR: 1.26; 95% CI 0.67-2.38); tonsillectomy remains significant and without major changes (OR: 2.97; 95% CI 1.82-4.82).

The study of possible interactions between variables showed a significant modification of effect (p = 0.013) between tonsillectomy and sex. A stratified analysis controlling for age showed a result similar to that of the simple analysis: OR 1.74 (95% CI 0.90-3.39) for men, and 5.20 (95% CI 2.91-9.28) for women; this has been presented previously (16).

DISCUSSION

More than a quarter of patients admitted to an Emergency Department within a General Hospital in Valencia have had a tonsillectomy, and over 11% have had an adenoidectomy; 17.5% had an appendectomy. There were no significant differences between sexes with respect to having had a previous tonsillectomy or appendectomy, but results suggest a higher prevalence of appendectomy in women. These prevalences in our sample do not differ from those previously estimated by the National Health Institute (INSALUD) or those described in a study performed in Madrid, with prevalences of 18, 17 and 20%, respectively (17). However, in our case the prevalence of tonsillectomy was lower than in other studies, the estimations of INSALUD (30%), and those of the study by López Ramos et al. in Madrid (17). In this study, the relation between MALTectomy and inflammatory bowel disease is analyzed. In the population-based control groups, the prevalence of tonsillectomy was 36 to 39%. The age of these control subjects was similar to that of ours (42 years old), which suggests that the performance of these procedures has been different in different areas of Spain.

On average, women are operated on for acute appendicitis at an earlier age than men are. We have also found differences in time between operations between men (16.9 years) and women (10.6), which seem logical and coincides with the fact that women are operated on at an earlier age than men.

A clear association was found between tonsillectomy and acute appendicitis. This association is not as evident (multivariate analysis) between adenoidectomy and appendicitis. There is also an important difference in the association between tonsillectomy and appendicitis in men and women. An explanation for these differences is not clear, but some studies indicate differences in the development of the immune system related to the X chromosome (18) or estrogens (19).

The study population is considered representative of the reference population. In the Valencian Community the health system is of universal coverage, and the number of persons with private insurance is around 10%. Furthermore, in acute cases, most people go to the Emergency Departments of public hospitals. Finally, the percentage of people presenting to Emergency Departments not in their reference area is low. In a previous study, only 3% of people seen in an Emergency Department in Valencia came from a different reference area (20).

The main limitation of the present study is its design; it is a cross-sectional study where information was obtained from data reported by patients. This fact could be biased by memory failure, especially in elderly patients or when surgery was performed many years before the study; we have tried to avoid this bias by eliminating patients who were not sure of their answers on inquiry. There is always a percentage of blank laparotomies,

which oscillates between 10 and 15% depending on the author (21), which is a bias that may be even higher in women (14-35%) (22-24) *versus* men; however, should it modify the results, which would not change the association.

The explanation of these findings opens a large possibility of different hypotheses to be corroborated in new studies. A first proposition would be that tonsillectomy produces an important deficiency in lymphoid tissue, which forces the remaining tissue (appendix) to make up for this deficiency in response to incoming pathogens, thus making it more likely to become inflamed or infected. Another possibility would be that there is a population with a higher predisposition (higher immune reactivity) to hypertrophy. This higher immune reactivity could even be abnormal, with a higher predisposition to diseases such as Crohn's and Hodgkin's diseases.

In younger age groups the frequency of tonsillectomy and appendectomy are similar. However, as age increases, there is a drastic fall in the amount of people reporting having had an adenoidectomy. This fact could reflect the evolution of the practice of these two procedures (in more recent years they have been performed simultaneously, but years ago this was not the case), or it could reflect forgetfulness of the procedure in surveyed patients. In our opinion, the first possibility explains the contradiction more strongly. In case that there had been a bias of misclassification in the diagnosis (persons who had had an adenoidectomy but said they had not), this bias may have affected the association between adenoidectomy and appendicitis.

Due to the aforementioned limitations and the possible explanations of these results, it would be interesting that more studies be performed to add information on the findings of this study; this could be one of the first risk factors described for acute appendicitis.

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