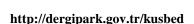
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A COMPARATIVE CLINICOPATHOLOGIC ANALYSIS OF TONSILLECTOMY AND ADENOIDECTOMY CASES: A RETROSPECTIVE STUDY

TONSİLLEKTOMİ VE ADENOİDEKTOMİ YAPILAN OLGULARIN RETROSPEKTİF İNCELENMESİ VE KARŞILAŞTIRMALI KLİNİKOPATOLOJİK ANALİZİ



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Abstract

Objective: In this retrospective study, we aimed to determine the rate of malignancy detected in patients who underwent tonsillectomy, adenoidectomy or adenotonsillectomy in our clinic, and to correlate the clinical findings of adults and children by giving their histopathological analysis.

Methods: Histopathological specimens of 288 adenoidectomy, tonsillectomy and adenotonsillectomy cases operated in our clinic between years of 2017-2019 were collected retrospectively and re-evaluated with clinical data.

Results: Malignancy was suspected clinically in 12.8% (n=37) of all cases, and most of them (n=33) were in tonsillectomy group. Although reactive lymphoid hyperplasia was a common diagnosis among all cases (92.7%), 11 (3.8%) patients were diagnosed as a benign/malign neoplasm. The malignancy rate among all cases was found to be 2.1% (6/288), among tonsillectomy cases was 8.8% (6/68). All malignancies were detected among tonsillectomy cases in adults.

Conclusion: This retrospective analysis of adenotonsillar surgeries correlated with histopathological findings showed that the incidence of tonsil neoplasm in adult patients is higher than the previously published data. In the tonsillar tissues presenting with a surgical indication of clinical suspicion for malignancy such as ulceration and necrosis, and of enlargement of tonsils, a histopathological evaluation are obviously warranted. These results are in agreement with that a routine histopathological examination is needed to be regardless of the clinically presence of high malignancy suspicion prior to tonsillectomy in adults.

Keywords: Adenoidectomy, neoplasm, pathology, tonsillectomy

Öz

Amaç: Bu retrospektif çalışmayla, kliniğimizde tonsillektomi, adenoidektomi veya adenotonsillektomi uygulanan hastalarda malignite oranını saptamayı, yetişkinlerin ve çocukların histopatolojik analizlerini yaparak klinik bulgularıyla ilişkilendirmeyi amaçladık.

Yöntem: 2017-2019 yılları arasında kliniğimizde opere edilen 288 adenoidektomi, tonsillektomi ve adenotonsillektomi olgusunun histopatolojik örnekleri, retrospektif olarak toplandı ve klinik verilerle tekrar değerlendirildi.

Bulgular: Tüm olguların %12,8'inde (n=37) malignite şüphesi vardı ve bunların çoğu (n=33) tonsillektomi grubunda idi. Reaktif lenfoid hiperplazi, tüm olgularda (%92,7) en sık tanı olmasına rağmen, 11 (%3,8) olguya benign / malign neoplazm tanısı konuldu. Tüm olgularda malignite oranı %2,1 (6/288) iken, tonsillektomi yapılan olgularda %8,8 (6/68) bulundu. Tüm maligniteler, sadece yetişkinlerde, tonsillektomi yapılan olgularda saptandı. **Sonuç:** Adenotonsiller ameliyatların histopatolojik raporlarla korelasyonu yapılan bu retrospektif analiz, erişkin hastalarda, tonsil neoplazm insidansının daha önce yayınlanan yerilerden daha yüksek olduğunu göstermiştir. Ülserasyon nekroz tonsiller büyüme gibiklinik malignite süpheli

insidansının, daha önce yayınlanan verilerden daha yüksek olduğunu göstermiştir. Ülserasyon, nekroz, tonsiller büyüme gibiklinik malignite şüpheli, cerrahi endikasyonu olan tonsil dokularında, histopatolojik değerlendirme yapılması gerekliliği açıkça görülmektedir. Bu sonuçlar, yetişkinlerde, tonsillektomi öncesi, klinik olarak yüksek malignite şüphesi olmasına bakılmaksızın, rutin bir histopatolojik incelemeye ihtiyaç duyulduğu gerçeğiyle uyumludur.

Anahtar Kelimeler: Adenoidektomi, neoplazm, patoloji, tonsillektomi.





Introduction

In an ideal system, it is useful to carry out a pathological examination of the resected tonsils and adenoids, as well as all other surgically removed samples. However, institutions are increasingly limiting or eliminating routine microscopic examination of tonsils / adenoids as a cost-effective precaution. In addition to losing the opportunity to determine unexpected findings, another disadvantage of this tendency is that pathologists are deprived of valuable experience and diagnostic skills in tonsil / adenoid pathology. 1,2

The common indications of tonsillectomy with or without adenoidectomy are recurrent or chronic infections of throat and sleep-related respiratory disorders.³ Absolute clinical indications for removal of tonsils are nasopharyngeal or oropharyngeal airways obstruction, swallowing problems, clinical suspicion for malignancy and uncontrollable bleeding from tonsillary blood vessels.⁴ The most common neoplasm of the tonsil is squamous cell carcinoma (SCC) which involves three-quarters of tonsillar malignancies although there are other pathologies including malignant lymphoma.⁵

There is no clear consensus on whether all tonsil and adenoid specimens should be examined histopathologically. Considering the cost of these pathological procedures and the loss of labor power in the laboratory, the clinical evaluation for the need to perform histological examination in which cases in tonsillectomy and/or adenoidectomy is gaining more importance.6 Although some study in the literature argue that malignancy rates are low, therefore histopathological examination may not be necessary; In our experience, especially in adult patients, histopathological examination should be performed considering all patients with or without clinical suspicion of malignancy.⁷ Pathological examinations of tonsils and adenoids frequently represents a non-reactive specific process, such as follicular lymphoid hyperplasia, therefore, a routine microscopic examination can sometimes provide important clues for local or systemic conditions that may have been unnoticed in some way.⁸ In practice, pathologists need to be aware of common or rare diseases that may be observed in tonsils or adenoids. In this retrospective study, we aimed to determine the rate of malignancy detected in patients who tonsillectomy, adenoidectomy adenotonsillectomy in our institute, and to analyse the clinical findings of adults and children by giving their histopathological analysis.

Methods

Patients

This retrospective study collected the data obtained from medical records of 288 patients who had undergone a tonsillectomy or adenoidectomy or both in the period from January 2017 to December 2019. History of allergic rhinitis, concha hypertrophy, recurrent otitis media, lymphadenopathy, septum deviation, sinusitis, hypertrophy/enlargement of tonsil or adenoid were considered to be selected for clinical assessment. Clinical

grading of tonsils and adenoids were classified according to the scores between 0-4 determined by a protocol proposed by literature. Paro indicates the tonsils inside the tonsillar fossa with no air obstruction. Whereas, 1-4 indicate the tonsils slightly out of the tonsillar fossa presenting 25%, 25-50%, 50-75% and 75% of air obstruction.

To calculate the size of the adenoids, the patients were examined with fibre endoscopy in the sitting position. The sizes of adenoids were classified into four categories according to the literature and tonsil scores which are explained above. ¹⁰

All procedures performed in studies involving human participants were in accordance with the principles of Declaration of Helsinki. Ethical approval was obtained from the Local Clinical Research Ethics Committee (GOKAEK-2020/2.04 2020/8). A written informed consent was obtained from all individual participants included in the study.

Histopathological examination

All tonsil and adenoid tissues were fixed in 10% neutralised formaldehyde. The resected tissues were cut into 3-mm thick slices to view the nodules. Materials were totally embedded in paraffin, cut into 5-µm sections then stained with haematoxylin and eosin (H&E) examined under a light microscope. Lastly, the clinical results were compared with age, histopathology and type of operations.

Statistical analysis

GraphPad version 3.06 2003 software was used for statistical analyses. The nonparametric Mann-Whitney test was used to compare quantitative variables, while the Chisquare test or Chi-square test for independence were used to compare dependent or independent qualitative data. *P* value that is less than 0.05 was considered significant.

Results

Among 288 patients, 129 were male and 159 were female. Most of the patients were younger than 18 years (mean age 12.55 ± 15.87 [1-17]) and most of these patients have undergone an adenotonsillectomy. The mean age of adult patients was 38.79 ± 18.68 [18-89]. Most of adults have undergone a tonsillectomy. Totally, 101 adenoidectomy, 68 tonsillectomy and 119 adenotonsillectomy were performed. Common clinical symptoms were snoring and apnea among all patients. Before the surgeries, prophylactic antibiotics treatment were given to all patients as well. (Table 1).

Among adenoidectomies and adenotonsillectomy (Table 2), the most common clinical findings among the patients younger than 18 years was allergic rhinitis and sinusitis (2.1%) which were significantly higher than the findings in tonsillectomy (p=0.017 and 0.032, respectively). The second most common clinical finding was lymphadenopathy which was significantly higher among tonsillectomy cases than other surgeries (p=0.005) (Table 2).

Among adenotonsillectomies, grading scores of both right and left tonsils were considerably higher than other operations (p<0.0001) while grading score of adenoids were

significantly higher in adenoidectomies than other operations (p<0.0001) (Table 2). Surgical indications were mainly due to enlargement of nasal airway among adenoidectomy and adenotonsillectomy cases (61.4% and 63.0%, respectively). The second most indication of adenoidectomy cases was serous otitis media (SOM) and of adenotonsillectomy cases was recurrent infection. The most common indication of tonsillectomy was suspicion of malignancy and the second one was recurrent infection (Table 2).

Regarding the histopathological examinations of adenoids following the adenoidectomies, 100 patients presented reactive lymphoid hyperplasia (RLH) and most of these patients were younger than 18 years (p=0.0006) (Table 3). Among tonsillectomy cases, 48 patients had RLH, and 5 had squamous papilloma as benign diagnosis. Six of tonsillectomy cases were diagnosed as a malignancy (SCC, DLBCL and Burkitt lymphoma), all of whom were older

than 18 years. No cases of malignancy were verified among young patients (<18 years) (Table 3). All of adenotonsillectomies were diagnosed as RLH.

Totally, there were 37 patients who were detected with a clinical suspicion for malignancy (Table 4). Among these patients, 5 were younger than 18 years, 80% of them were diagnosed as RLH but none of them showed a malignancy. Histopathologically, 10 adult patients were diagnosed as a neoplasm following a tonsillectomy, 4 of them were squamous papilloma, which was a benign neoplasm. The rest of these patients were diagnosed as malignant neoplasm, 2 of them were SCC, 3 were DLBCL and 1 was Burkitt lymphoma (Table 4). There was no statistically significance in the distribution of the malignancies according to ages. However, total distribution of cases with a clinical suspicion for malignancy showed a significant difference among the type of operations (p<0.0001). Malignancy was detected mostly in tonsillectomy specimens with a clinical suspicion for malignancy (p<0.0001) (Table 5).

Table 1. Demographic features and preoperative symptoms of tonsillectomy and adenoidectomy cases

Characteristics	Adenoidectomy	Tonsillectomy	Adenotonsillectomy	Total	
Number (%)	101 (35.1)	68 (23.6)	119 (41.3)	288	
<18 years	93 (40.4)	20 (8.7)	117 (50.9)	230	
≥ 18 years	8 (13.8)	48 (82.8)	2 (3.4)	58	
Age (Mean \pm SD)	7.45 ± 8.3	31.44 ± 21.8	6.16 ± 3.7	12.58 ± 15.9	
[Min-Max]	[1-63]	[3-89]	[1-26]	[1-89]	
Gender	N (%)	N (%)	N (%)	N (%)	
Male	61 (60.4)	31 (45.6)	67 (56.3)	159 (55.2)	
Female	40 (39.6)	37 (54.4)	52 (43.7)	129 (44.8)	
Clinical symptoms	N (%)	N (%)	N (%)	N (%)	
Recurrent infection	19 (18.8)	28 (41.2)	83 (69.7)	130 (45.1)	
Apnea	60 (59.4)	8 (11.8)	79 (66.4)	147 (51.0)	
Halitosis	1 (0.99)	2 (2.9)	0 (0)	3 (1.0)	
Sore throat	1 (0.99)	31 (45.6)	1 (0.8)	33 (11.5)	
Snoring	77 (76.2)	14 (20.6)	107 (89.9)	198 (68.8)	
Hearing loss	36 (35.6)	1 (1.5)	5 (4.2)	42 (14.6)	
Pre-medication	N (%)	N (%)	N (%)	N (%)	
Nasal steroid	24 (23.8)	2 (2.9)	26 (21.8)	40 (13.9)	
Antihistamines	10 (9.9)	3 (4.4)	13 (10.9)	18 (6.3)	
Antibiotics	8 (7.9)	14 (20.6)	22 (18.5)	58 (20.1)	

Table 2. Clinical findings of tonsillectomy and adenoidectomy cases

Characteristics	Adenoidectomy	Tonsillectomy N = 68	Adenotonsillectomy	D l	TOTAL
	N = 101		N = 119	P value	N = 288
Allergic rhinitis	N (%)	N (%)	N (%)		N (%)
<18 years	19 (18.8)	2 (2.9)	16 (13.4)	0.017	37 (12.8)
≥ 18 years	1 (0.99)	2 (2.9)	1 (0.8)	0.017	4 (1.4)
Recurrent Acute	N (%)	N (%)	N (%)		N (%)
Otitis Media					
<18 years	2 (1.98)	0 (0)	0 (0)	NA	2 (0.69)
≥ 18 years	0 (0)	0 (0)	0 (0)		0 (0)
Concha hypertrophy	N (%)	N (%)	N (%)		N (%)
<18 years	14 (12 0)		- (1 a)		24.7.0
≥ 18 years	14 (13.9)	2 (2.9)	5 (4.2)	0.137	21 (7.3)
	3 (2.97)	3 (4.4)	1 (0.8)		7 (2.4)
Sinusitis	N (%)	N (%)	N (%)		N (%)
<18 years	3 (2.97)	0 (0)	3 (2.5)	0.032	6 (2.1)
≥ 18 years	1 (0.99)	3 (4.4)	0 (0)		4 (1.4)
Septum deviation	N (%)	N (%)	N (%)		N (%)
<18 years	5 (4.95)	2 (2.9)	4 (3.4)	0.403	11 (3.8)
≥ 18 years	5 (4.95)	3 (4.4)	1 (0.8)		9 (3.1)
Lymphadenopathy	2 (1.98)	8 (11.8)	3 (2.5)	0.005	13 (4.5)
Grading Score	N (%)	N (%)	N (%)		N (%)
Right tonsil					
0	0 (0)	2 (2.9)	0 (0)		2 (0.7)
1	64 (63.4)	25 (36.8)	3 (2.5)		92 (31.9)
2	24 (23.8)	14 (20.6)	18 (15.1)		56 (19.4)
3	8 (7.9)	19 (27.9)	49 (41.2)	< 0.0001	76 (26.4)
4	5 (4.95)	8 (11.8)	49 (41.2)		62 (21.5)
Left tonsil					
0	0 (0)	0 (0)	0 (0)		0 (0)
1	65 (64.4)	29 (42.6)	3 (2.5)		97 (33.7)
2	23 (22.8)	16 (23.5)	18 (15.1)		57 (19.8)
3	8 (7.9)	14 (20.6)	46 (38.7)	< 0.0001	68 (23.6)
4	5 (4.95)	9 (13.2)	52 (43.7)		66 (22.9)
Adenoid					
0	0 (0)	52 (76.5)	6 (5.0)		58 (20.1)
1	3 (2.97)	10 (14.7)	1 (0.8)		14 (4.9)
2	24 (23.8)	3 (4.4)	23 (19.3)	<0.0001	50 (17.4)
3	37 (36.6)	3 (4.4)	67 (56.3)		107 (37.2)
4	37 (36.6)	0 (0)	22 (18.5)		59 (20.5)
Surgical Indications					
Enlargement	62 (61.4)	9 (13.2)	75 (63.0)		146 (50.7)
Recurrent infection	7 (6.9)	24 (35.3)	41 (34.5)		72 (25)
Halitosis	0 (0)	1 (1.5)	0 (0)		1 (0.3)
SOM	30 (29.7)	1 (1.5)	1 (0.8)	<0.0001	32 (11.1)
Malignity suspicion	2 (2.0)	33 (48.5)	2 (1.7)		37 (12.8)

Chi-squared Test for Independence

SOM: Serosis Otitis Media

Table 3. Comparison of histopathological findings of tonsillectomy and adenoidectomy cases according to the age groups

Surgery	Findings		years 230		3 years = 58	<i>P</i> value		otal 288
		N	%	N	%		N	%
Adenoidectomy $(N = 101)$	RLH* Actinomyces	93 0	40.4 0	7 1	12.1 1.7	0.0006	100 1	34.7 3.5
Tonsillectomy $(N = 68)$	Benign lesions Malign lesions	20 0	8.7 0	52 6	89.7 3.4	0.312	72 6	25 2.1
Adenotonsillectomy (N = 119)	RLH	117	50.9	2	3.4	-	119	41.3

^{*}RLH: reactive lymphoid hyperplasia

Table 4. Comparison of histopathological findings of tonsillectomy and adenoidectomy cases with a clinical suspicion for malignancy (n=37) according to the age groups

Surgery	Histopathology Findings	<18 years N = 5	≥ 18 years N = 32	P value	Total N (%)
	rindings				14 (/0)
		N	(%)		
Adenoidectomy	RLH*	0 (0)	1 (3.1)		1 (50)
(N=2)	Actinomyces	0 (0)	1 (3.1)	-	1 (50)
	RLH	2 (40)	14 (43.8)		16 (48.5)
	Actinomyces	0 (0)	2 (6.3)		2 (6.1)
	Ulcer, necrosis	1 (20)	0 (0)		1 (3.0)
	PEH**	0 (0)	1 (3.1)		1 (3.0)
T 11 (Epithelial cyst	0 (0)	1 (3.1)		1 (3.0)
Tonsillectomy (N = 32)	Inclusion cyst	0 (0)	1 (3.1)	0.297	1 (3.0)
(N=33)	Fibroepithelial polyp	0 (0)	1 (3.1)		1 (3.0)
	Squamous papilloma	0 (0)	4 (12.5)		4 (12.1)
	SCC [^]	0 (0)	2 (6.3)		2 (6.1)
	DLBCL^^	0 (0)	3 (9.4)		3 (9.1)
	Burkitt lymphoma	0 (0)	1 (3.1)		1 (3.0)
Adenotonsillectomy $(N = 2)$	RLH	2 (40)	0 (0)	-	2 (100)

^{*}RLH: reactive lymphoid hyperplasia, **PEH: pseudoepitheliomatous hyperplasia, ^SCC: squamous cell carcinoma, ^^DLBCL: diffuse large B-cell lymphoma

Table 5. Comparison of histopathological findings of tonsillectomy and adenoidectomy cases with a clinical suspicion for malignancy (n=37)

Histopathology	Adenoidectomy	Tonsillectomy	Adenotonsillectomy	P value	
N (%)	(N=2)	(N = 33)	(N=2)	r value	
RLH	1 (50)	16 (48.5)	2 (100)	0.367	
Actinomyces	1 (50)	2 (6.1)	0 (0)	0.079	
Ulcer, necrosis	0 (0)	1 (3.0)	0 (0)	0.940	
Epithelial cyst	0 (0)	1 (3.0)	0 (0)	0.940	
PEH	0 (0)	1 (3.0)	0 (0)	0.940	
Inclusion cyst	0 (0)	1 (3.0)	0 (0)	0.940	
Fibroepithelial polyp	0 (0)	1 (3.0)	0 (0)	0.940	
Squamous papilloma	0 (0)	4 (12.1)	0 (0)	0.762	
SCC	0 (0)	2 (6.1)	0 (0)	0.880	
DLBCL	0 (0)	3 (9.1)	0 (0)	0.821	
Burkitt lymphoma	0 (0)	1 (3.0)	0 (0)	0.940	
TOTAL $(N = 37)$	2 (5.4)	33 (89.2)	2 (5.4)	<0.0001	

Chi-squared Test for Independence

RLH: reactive lymphoid hyperplasia, PEH: pseudoepitheliomatous hyperplasia, SCC: squamous cell carcinoma, DLBCL: diffuse large B-cell lymphoma

Discussion

Recently, the malignancy rates especially in the tonsils have increased in adults, deducing the necessity of routine histopathological examination of tonsils. However, there is still a debate about whether or in which cases histopathological examination is necessary. 11 In this retrospective study including one center's experience, it was found that malignancy was suspected clinically in 12.8% of all adenoidectomy, tonsillectomy adenotonsillectomy cases, and most of these cases (n=33) were in the tonsillectomy group. Although RLH was the most common diagnosis determined histopathologically among all cases (92.7%), a total of 11 (3.8%) patients were diagnosed as a neoplasm by histopathological examination. According to the literature, the incidence of malignant pathologies following tonsillectomies in adults ranges from 2% to 11.8%. 12,13 In our study, the malignancy rate among all cases was found 2.1% (6 out of 288 cases) and among tonsillectomy cases it was 8.8% (6 out of 68 tonsillectomies). All malignancies were detected among tonsillectomy cases in adults. In a study by Younis et al. 12 although no malignancy was detected in pediatric tonsillectomy cases, malignancy rate was 11.8% (40 out of 339 adult tonsillectomies) and most of them had SCC. In the study by Faramarzi et al., 14 the malignancy was detected in 26 out of 5058 tonsillar specimens, most of which had non-Hodgkin's lymphoma. In another study by Aksakal et al. 11

of 1356 patients who underwent tonsillectomy, only two adults were diagnosed as malignancy (Mantle cell lymphoma, and DLBCL). They noticed that both of these patients had clinical findings suspicious for malignancy such as tonsillar asymmetry, tonsillar discoloration, and weight loss. While unexpected malignancy was not detected in these studies, risk factors, such as tonsillar asymmetry, history of head and neck cancers, and atypical tonsillar lesions, were observed before surgery in patients with malignancy. In our study we also found the tonsillar enlargement, as well as ulceration on tonsils and lymphadenopathy among adults diagnosed as a malignancy in histopathological examination and none of these malignancies were unexpected before surgery.

The studies with larger series have reported that the rate of malignancy is very low in adenoidectomies or tonsillectomies. Some of these studies evaluated the incidence of malignancies among tonsillar neoplasms to clarify the consequences of not performing routine histological examination on the tonsillectomy samples. A published cohort of pediatric adenotonsillar surgeries correlated with histopathological reports reported a total of 10 malignancies among 152,352 cases. However, we did not find any neoplasm among the patients under 18 years, although the overall features of tonsillar neoplasm such as type of lymphoma were found to be in line with those in the literature. Lifshitz et al. considered all tonsillar neoplasms

presenting with a pre-operative high index of suspicion as "absolute" indication for operation. We also support this idea by suggesting an excisional biopsy of the tonsils of cases carrying a clinical suspicion for malignancy.

Large-scale studies with pediatrics revealed rates of malignancy up to 0.17%. ^{12, 17-19} In the study of Williams et al. ¹⁷ preoperative risk factors, such as necrotic tonsil, tonsillar asymmetry, and lymphadenopathy, were found in all three of the cases with tonsillar malignancy. In our study, similar preoperative risk factors such as tonsillar hypertrophy and lymphadenopathy were found in cases of tonsillar malignancy. These findings suggest that a detailed preoperative risk assessment is also crucial in adults with a lymphadenopathy.

In a study by Aksakal et al. 11 of 1574 pediatric patients, three had an epidermal cyst, and one had a lymphangiomatous polyp, and there were well-defined, benign lesions on preoperative evaluation, and the pathological results were consistent with the clinical findings. On the contrary, among our cases with a clinical suspicion for malignancy, papillomatous or vegetative appearance were observed in the polyp and cysts, suggesting that the cases which are clinically suspected for malignancy may not always present a malignancy in histopathology.

The tonsillectomy is one of the most common operations performed in children due to the indications of recurrent tonsillitis, obstructive sleep apnea, suspicion of malignancy and SOM. In many institutions, the tonsils and adenoids of these patients are routinely sent for pathological examination, as well as in our center. The correlation between the early incidental diagnosis of a lymphoma in tonsils and adenoids to a better prognosis of the disease still remains unknown, therefore, the adenoids and tonsils are suggested to be sent to pathology departments for histopathological examination.

In this study we reported a retrospective analysis of adenotonsillar surgeries correlated with histopathological findings in both adults and children. We reported that the incidence of tonsillar neoplasm in adult patients is significantly higher than the previously published data. A histopathological evaluation is obviously warranted for the tonsillar tissues presenting with a surgical indication of clinical suspicion for malignancy such as ulceration and necrosis, and with the enlargement of tonsils. These considerations are in agreement with the fact that a routine histopathological examination is needed even if the clinically confirmed case has a high malignancy suspicion or not, prior to tonsillectomy in adults.

Limitations

This study had several limitations. CRP and WBC levels were studied in a time interval, and the estimations were therefore expressed as time intervals. Measurements were limited with the following 5 days of the procedure, thus the return of CRP levels to baseline values could not be demonstrated. There are several methods to estimate CRP levels, and the results may change depending on the method used. However, we used 4 repeated measurements of CRP with the same method to demonstrate the progression of CRP, and the progression curve would not change if a different method was used. Hence, our results can be used in daily clinical practice, regardless of the method used to estimate CRP levels. In our study cohort, we observed pocket infection in two patients, and this inadequate number limited us to validate our results only in uninfected patients.

Conclusion

The course of CRP levels indicate a progression curve early after CIED implantation. Age and procedure duration longer than 1 hour lead to higher post-procedural CRP levels. Occurrence of hematoma is not predictive for high levels of post procedural CRP and WBC. Post- implantation level of WBC does not indicate such a trend and no any factor predict high post procedure levels of that biomarker.

Conflict of Interest

The authors declare that they have no conflict of interest.

Compliance with Ethical Statement

Ethical approval was obtained from the Clinical Research Ethics Committee of the XXX

Author Contributions

BYB: Design; BYB, FM: Project development; BYB, FM: Data collection; BYB: Analysis; BYB: Literature search; BYB, FM: Manuscript writing.

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