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Age-related difficulty in post-intubation tracheal stenosis reconstruction: a comparative analysis of CO2-laser, resection and anastomosis, and costal cartilage grafting techniques

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Abstract

Background: Costal cartilage graft (CCG) sustains primary donor material for laryngotracheal reconstruction in patients with post-intubation tracheal stenosis (PITS). But, the elasticity and viability of CCG decrease elderly. This study was aimed to examine the age factor in PITS cases according to the treatment groups, especially in the tracheal reconstruction surgery with CCG group.

Methods: This retrospective study was designed. Patients with a diagnosis of PITS were enrolled. The hazard ratio was calculated with the Cox regression model to define independent risk factors for failure among the variables.

Results: Eighty-five patients diagnosed with post-intubation tracheal stenosis (PITS) were enrolled in the study. Restenosis developed in 19 (22.4%) patients. The failure rate in patients aged 40 years and older was 7.5 times higher on average compared to patients under 40 years of age ($p = 0.004$, 95% *CI*: 1.6–35.2). Additionally, age group ≥ 40 and CCG treatment group were a significant risk factors for surgical failure ($p = 0.012$, $HR = 0.0003$, 95% CI for $HR = 0.0000006–0.173$, and $p < 0.001$, $HR = 0.001$, 95%CI for $HR = 0.000025–0.047$, respectively).

Conclusions: Age and CCG group were detected as independent risk factors for surgical failure, possibly due viability of costal cartilage.

Keywords: Costal cartilage, Tracheal stenosis, CO_2 laser, Laryngotracheal reconstruction, Decannulation failure

Introduction

Post-intubation tracheal stenosis (PITS) or laryngotracheal stenosis (LTS) is a challenging issue to manage and often requires a sequential, series of repetitive interventions [1–3]. The vast majority of acquired PITS or LTS in adults originated from endotracheal intubation [1–4]. Treatment options of PITS or LTS include tracheostomies, resection and anastomosis techniques, balloon dilation, laser treatment, T tubes, stents, and reconstruction with autologous cartilage grafts [2, 3, 5–9].

Successful postoperative decannulation was reported 80% and above with laser excision treatment [2, 7]. Success rates with resection and anastomosis techniques have been reported to vary between 40 and 96% [2, 10, 11]. This rate varies according to the length and level of the stenotic segment, the presence of previous interventions, and the characteristics of the patient [2, 11, 12]. The open surgical techniques for augmentation and reconstruction of the airway are another successful

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method for LTS. Autogenous cartilage graft from the rib, thyroid, auricle, and epiglottis has been used to reshape and keep permanent the airway [3, 9, 13–15]. Decannulation success of 90% and above with open surgical resection techniques have been reported in large series in the literature [2, 6, 10]. However, despite these successful results, in almost half of the patients, some additional procedures are required in addition to the primary treatment for a patent airway and decannulation success [1, 2, 16]. Laryngotracheal grafting techniques are relatively preferred in high airway stenosis (close to the glottis), in cases where resection and anastomosis are not suitable, in patients with neck defects, and in the pediatric population [15, 17, 18].

Due to the vitality of the transferred cartilage, airway reconstruction with graft techniques is highly effective in the pediatric population and is the primary recommended treatment method [9, 15, 19]. Therefore, age becomes an important risk factor in laryngotracheal reconstruction with cartilage graft, although it is not found to be significant in other treatment modalities in adults [2, 11]. Furthermore, it was shown that there is a considerable age effect on the elastic material properties of the costal cartilage and that no significant sex effect [20, 21]. Especially over 40 age, a significant calcification was detected compared to the < 40 age group [21]. This study was aimed to examine the age factor in PITS cases according to the treatment groups, especially in the tracheal reconstruction surgery with the costal cartilage graft (CCG) group.

Materials and methods
This retrospective study was designed. The study was conducted at a tertiary referential university hospital. Patients older than 18 years with a diagnosis of post-intubation tracheal stenosis (PITS) were enrolled in the study between April 2008 and June 2021. Other causes of PITS such as trauma or direct injury or external compression due to neoplastic process, or related prior surgery, were defined exclusion criteria for participants. Also, patients with malignancy, radiation therapy to the neck region, or with a diagnosis of connective tissue disease were eliminated. Patients who underwent urgent tracheostomy or any additional procedures to provide a patent airway during the perioperative period were not included in the study.

Age, gender, treatment for the PITS, the presence of prior interventions for stenosis, Cotton-Myer [22] and McCaffrey [23] grade of the stenosis, rate of the restenosis (decannulation failure) duration to the diagnosis

of restenosis, and total follow-up period were identified. Patients were grouped according to treatment as carbon dioxide laser treatment (CO_2 laser) or tracheal resection with primary anastomosis (TRPA) and costal cartilage graft (CCG).

Surgical procedure for laryngotracheal reconstruction with costal cartilage graft
General anesthesia, airway approach, neck incision, and anterior laryngeal split were performed as previously described [24]. The anterior cricoid arch was resected bilaterally, and cricothyroid joints were preserved. Stenotic segment of trachea and scar tissue was resected. The trachea was mobilized with a subperichondrial plane dissection. The patient was ventilated through an orotracheal tube inserted in the distal tracheotomy. The posterior cricoid lamina was split in the midline. Costal cartilage was harvested and prepared according to surgical steps defined by Grillo et al. [24]. One of the grafts was placed in the posterior groove and attached

Table 1 Summary of the findings

	n	%
Gender		
Female	40	47.1
Male	45	52.9
Treatment		
CO_2 laser	21	24.7
TRPA	54	63.5
CCG	10	11.8
Revision		
Primary	66	77.6
Revision	19	22.4
Result		
Success	66	77.6
Failure	19	22.4
Cotton-Myer grade		
G1	0	0.0
G2	8	9.4
G3	58	68.2
G4	19	22.4
McCaffrey grade		
G1	4	4.7
G2	28	32.9
G3	41	48.2
G4	12	14.1
	m	SD
Age	41.2	9.6
Duration to restenosis (*m*)	3.1	2.6
Follow-up (day)	66.2	37.7

TRPA tracheal resection with primary anastomosis, *CCG* costal cartilage graft, *m* months

to the cricoid with PDS 4-0 sutures. Posterior cartilage graft was covered by anastomosis superior and inferior mucosal flaps. The anterior defect was covered with the other costal cartilage graft fixed to between thyroid cartilage and healthy lower trachea with 4-0 PDS sutures. A T-tube stent was positioned in reconstructed segment and tracheotomy tract. In the follow-up, fiber endoscopic laryngoscopy/bronchoscopy was performed at monthly controls, and T-tubes were removed between 3 and 6 months.

Age, gender, revision status, Cotton-Myer grade, and treatment groups were compared with chi-square test according to surgical results (successful or failure). The hazard ratio was calculated with the Cox regression model to define independent risk factors for failure among the variables.

SPSS 22.0 program (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The study was carried out in accordance with the 1964 Helsinki Declaration and subsequent amendments. The institutional review board was approved by the ethic committee of affiliated university for the study (0157-24/03/2022, Izmir Katip Çelebi University).

Results

Eighty-five patients diagnosed with post-intubation tracheal stenosis (PITS) were enrolled in the study. The duration of intubation period was 13.4 ± 4.2 days (range, 1 h–25 days). Forty (% 47.1) of the patients were female, and 45 (%52.9) were male. The mean age of the patients was 41.2 ± 9.6 (min: 19, max: 65). The rate of tracheotomy-dependent patients was 94.1% ($n = 80$). Nineteen patients (22.4%) had undergone between one and 16 previous surgical interventions including a tracheotomy, dilatation, and T-tube stenting, laser resection, and TRPA. Restenosis developed in 19 (22.4%) patients during a mean follow-up period of 66.2 ± 37.2 months (min: 6, max: 155). Restenosis was diagnosed after a mean of 3.1 ± 2.6 months (min: 1, max: 11, median: 1.8 months) and days in all patients. There were 10 (11.8%) patients in the costal cartilage graft (CCG) group, 21 (24.7%) patients in the CO_2 laser group, and 54 (63.5%) patients in the TRPA group. A summary of the findings is given in Table 1. Restenosis rate was 33.3% ($n = 7$) in the CO_2 laser group, 14.8% ($n = 8$) in the TRPA group, and 40.0% ($n = 4$) in the CCG group ($p = 0.081$, χ^2 test). Gender distribution and mean age were similar in the treatment groups. The

Table 2 Distribution of findings according to treatment groups

	Treatment						p
	CO_2 laser ($n = 21$)		TRPA ($n = 54$)		CCG ($n = 10$)		
	n	%	n	%	n	%	
Gender							
Female	9	42.9	26	48.1	5	50.0	0.901
Male	12	57.1	28	51.9	5	50.0	
Revision							
Primary	15.0	71.4	50.0	92.6	1.0	10.0	0.017
Revision	6.0	28.6	4.0	7.4	9.0	90.0	
Result							
Success	14	66.7	46	85.2	6	60.0	0.081
Failure	7	33.3	8	14.8	4	40.0	
Cotton-Myer grade							
G1	0	0.0	0	0.0	0	0	-
G2	6	28.6	2	3.7	0	0	
G3	15	71.4	37	68.5	6	60.0	
G4	0	0	15	27.8	4	40.0	
McCaffrey grade							
G1	4	19.0	0	0	0	0.0	-
G2	14	66.7	13	24.1	1	10.0	
G3	3	14.3	32	59.3	6	60.0	
G4	0	0	9	16.7	3	30.0	
	m	SD	m	SD	m	SD	
Age	41.5	9.7	41.0	9.6	41.9	10.4	0.955
Duration to restenosis	1.43	0.53	3.25	1.91	5.75	4.11	0.022
Follow-up (day)	63.14	38.79	68.15	39.29	62.90	28.07	0.839

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distribution of findings according to treatment groups was given in Table 2.

Gender or Cotton-Myer grade of the PITS or surgery was not found to be risk factors for the development of stenosis (Table 3). The failure rate was found to be significantly higher in revision surgeries (revision vs. primary, $p = 0.001$, odds ratio: $OR = 7.0$ 95% CI: 2.2–22.0). In addition, the age of the patients whose PITS treatment failed was significantly higher than the successful group ($p = 0.018$, MD: 5.2, 95% CI: 9.5–0.9, t-test). The failure rate in patients aged 40 years and older was 7.5 times higher on average compared to patients under 40 years of age ($p = 0.004$, 95% CI: 1.6–35.2).

According to Cox regression analysis age, gender, and the presence of prior surgeries (revision), none of the Cotton-Myer or McCaffrey groups was not an independent risk factors for treatment failure. However, age groups (≥ 40) and CCG treatment group were found to be significant risk factors for surgical failure ($p = 0.012$, $HR = 0.0003$, 95% CI for HR = 0.0000006–0.173, and $p < 0.001$, $HR = 0.001$, 95% CI for HR = 0.000025–0.047, respectively). In addition, when the treatment groups were analyzed separately, the mean age of patients with surgical failure was found to be significantly higher in both groups (Table 4).

In the CO_2 laser group, 2 of 7 patients who developed restenosis underwent re-laser treatment and 5 of them TRPA surgery. While additional laser treatment was performed in 3 patients in the TRPA group, revision tracheal resection surgery was performed in one patient, and the other four patients underwent tracheal reconstruction with CCG. For the patients with a failed surgery in the CCG group, two patients decided to continue with a tracheostomy cannula, and the other two patients had planned a second grafting with CCG.

Table 3 Distribution of patients according to surgical results

	Result				p
	Success ($n = 66$)		Failure ($n = 19$)		
	n	%	n	%	
Gender					
Female	31	47.0	9	47.4	0.976
Male	35	53.0	10	52.6	
Age group					
< 40 years	31.0	47.0	2.0	10.5	0.004
≥ 40 years	35.0	53.0	17.0	89.5	
Revision					
Primary	57.0	86.4	9.0	47.4	0.001
Revision	9.0	13.6	10.0	52.6	
Treatment					
CO_2 laser	14	21.2	7	36.8	0.081
TRPA	46	69.7	8	42.1	
CCG	6	9.1	4	21.1	
Cotton-Myer grade					
G1	0	0.0	0	0.0	0.558
G2	5	7.6	3	15.8	
G3	46	69.7	12	63.2	
G4	15	22.7	4	21.1	
McCaffrey grade					
G1	4	6.1	0	0	0.073
G2	23	34.8	5	26.3	
G3	33	50.0	8	42.1	
G4	6	9.1	6	31.6	

TRPA tracheal resection with primary anastomosis, *CCG* costal cartilage graft

Discussion

The mean age of patients with surgical failure was significantly higher in the CCG group; also, age and CCG treatment group were detected as an independent risk factor for decannulation failure. The ossification of the costal cartilage with advancing age is a predictable finding. It

Table 4 *T*-test statistics of age variable according to treatment groups and results

Treatment groups		n	m	SD	p	Mean difference	95% CI of difference	
							Lower	Upper
CO_2 laser	Success	14	37.64	8.345	0.006	−11.7	−19.7	−3.8
	Failure	7	49.43	7.786				
TRPA	Success	46	39.39	8.686	0.002	−11.1	−17.952	−4.266
	Failure	8	50.50	10.184				
CCG	Success	6	34.50	4.324	0.011*	−18.50	−24.978	−12.022
	Failure	4	53.00	4.397				

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* *p*-value obtained from the Mann-Whitney *U*-test

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can be predicted that cartilage with reduced elasticity and loss of chondrocytes will have a poor prognosis after being transferred to the recipient tissue. The end of the 4th decade has been mentioned before as an age threshold at which costal cartilage ossification occurred and flexibility lost [20, 21, 25]. Although ossification can be detected in previous years, it does not because a problem is clinically related to its transfer to other tissues (cartilage graft). Although it is an expected outcome that the success of the CCG graft will decrease in PITS or LTR surgery at an advanced age (> 50), these patients have not benefited from other priority treatments (e.g., TRPA) or are unsuitable for them (e.g., short neck). Therefore, in addition to recommending other donor sites, such as the use of auricular or nasal septum cartilage in elderly patients, dissection of the central parts of the costal cartilage away from the perichondrium may be considered.

Ossification, which is an important age-related obstacle to obtaining a useful CCG, can begin in the adolescent period and from the 1st costal cartilage. Ultimately, it results in complete fusion of the xiphisternal joint over the age of 35 in men and 40 in women [26]. In addition to age-related changes in costal cartilage ossification, gender-related patterns of calcification show differences. Rejtarova et al. [27] suggested that the peripheral ossification pattern can be considered male specific, while the central lingual ossification pattern determines female sex. Also, they showed that central globular ossifications could be found in both sexes [27].

Gustafson et al. [19] found a 29% reintubation rate after single-stage laryngotracheal reconstruction in patients with pediatric congenital and acquired laryngotracheal stenosis. In this study, a significant negative correlation was found between age and reintubation rates in univariate and multivariate analysis. In this study, which included 200 children between the ages of 2 months and 19 years, the success rate was found to be significantly lower in patients aged 4 years and younger [19]. The results of this presented study are completely opposite to the reference study, but the study group and sample size are completely different. In addition, as can be expected, the airway that continues to develop during early childhood is the most important challenging factor, while the viability of CCG transferred at older ages is more important. In similar studies by Younis et al. [17] ($n = 46$) and Koltai et al. [18] ($n = 54$) including children who underwent laryngotracheal reconstruction using CCG, the age was not analyzed as a factor for failure. In these studies, success rates were reported as 89% and 83%, respectively.

Terra et al. [15] reported an 80% success rate after tracheal reconstruction performed with CCG in adult Cotton-Myer grade 3 and 4 PITS patients ($n = 20$).

The mean age of patients was reported as 36.1 (min: 18 — max: 54) in this study. In addition, the authors routinely applied solid endolaryngeal stent with T-tube to all patients postoperatively [15]. Liu et al. [9] reported a successful decannulation rate of 74.1 % ($n = 46$) in a total of 62 patients aged between 2 and 68 years (average 28). They included patients with all causes of LTS even anterior neck defect. A successful decannulation was obtained in the referenced study between 10 days and 12 months postoperatively (average: 6 months) after removing the tracheal T-tube. Risk factors for surgical failure were not discussed in this study [9].

In this presented study, only PITS patients were included, and the sample size was lower than reference studies. According to the literature, the low success rate may be affected by the chosen etiology and sample size. In addition, the size of the stenosis, the patient's underlying health status (blood sugar, obesity), previous interventions, and the experience of the surgical team may all be effective factors. In this study, the changing structure of the cartilage framework with respect to age was referred to. The small sample size may question the validity of significant results, despite the appropriate statistical method. The TRPA procedure is the gold standard treatment for PITS or LTS in adult and eligible patients [2, 3]. However, if the need for cartilage graft arises, which is inevitable in some cases, it should be taken into account that the age factor may affect the results in rib cartilage harvesting. Of course, this result does not prevent CCG collection, and other cartilage donors are not as abundant as costal cartilage (e.g., ear, septum). However, if needed, nasal septum cartilage with or without mucosa graft, auricular cartilage may be required to harvest in addition to CCG.

The small sample size, with the lack of a homogeneous and adequate number of patients undergoing CCG alone, is an important limitation for evaluating this negative prognostic feature attributed to cartilage grafting. In addition, surgical failure associated with ossified cartilage tissue due to advanced age can only be validated by performing a histopathological examination in this study. This issue is another main limitation of the study. Nevertheless, the detection of cartilage tissue that has lost viability properties during cartilage transfer should encourage surgeons to turn to other cartilage donors.

Conclusion

The viability of costal cartilage deteriorates with age, and the failure rate increases independently. In these cases, other donor sites can be evaluated for harvesting viable cartilage grafts, or different dissection techniques of the costal cartilage can be performed according to different ossification patterns.

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Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available due to ethical reasons but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (0157-24/03/2022, İzmir Katip Çelebi University) and with the Helsinki Declaration of 1975, as revised in 2008. Consent to participate is not applicable as it is a retrospective study.

Consent for publication
N/A

Competing interests
The authors declare that they have no competing interests.

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