• Review Article •

Interventions in functional epiphora–a systematic review

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Received: 2024-08-09 Accepted: 2024-12-24

Abstract

● **AIM:** To review the success rates and complications of interventions for functional epiphora in adults.

● **METHODS:** A systematic review of English-language articles from the electronic databases PubMed, SCOPUS, and Google Scholar. The primary outcome was subjective resolution or improvement of epiphora symptoms. Secondary outcomes were treatment-related adverse events. Subjects above 18 years of age who underwent surgical or non-surgical treatment for functional epiphora (exhibited symptoms of epiphora with a patent lacrimal system) were included. Articles were excluded if they were 1) case reports; 2) abstract only studies; 3) published in a language other than English. Data extraction was performed independently by two authors. The Effective Public Health Practice Project checklist was used for quality assessment of the included studies.

● **RESULTS:** A total of 762 articles were identified; 28 met the study criteria. Most studies employed silicone tube intubation alone or as an adjuvant procedure to dacryocystorhinostomy (DCR). Other interventions included lacrimal probing, balloon dacryoplasty, lateral tarsal strip and botulinum toxin A. DCR had the highest success rate, as well as the longest mean follow-up time. Complications were minor, transient, and mostly stent-related.

● **CONCLUSION:** This updated systematic review on the success rates of interventions for functional epiphora in adults proposes the following management algorithm. Dacryocystography (DCG) should be performed in all patients with functional epiphora. If DCG is abnormal, we advocate DCR. If DCG is normal, proceed with dacryoscintigraphy (DSG). We perform DCR for post-sac delay on DSG and lateral tarsal strip for pre-sac delay. Botulinum toxin A is an off-label, short-term treatment option in those with normal DSG.

● **KEYWORDS:** epiphora; success; dacryocystorhinostomy; lacrimal duct obstruction; review

DOI:10.18240/ijo.2025.05.21

Citation: Tai ELM, Lee AL, Kueh YC, Abdullah B, Chang B. Interventions in functional epiphora–a systematic review. *Int J Ophthalmol* 2025;18(5):937-950

INTRODUCTION

Epiphora, defined as overflow of tears at the lid margin, has a significant effect on visual function, with an effect on vision-related activities comparable to that of a unilateral cataract[1]. The most common cause of epiphora is nasolacrimal duct obstruction (NLDO), which is characterised by a "hard stop" and non-patency to syringing[2]. Functional epiphora, a term used interchangeably with functional nasolacrimal duct obstruction (FNLDO), refers to epiphora in the presence of a patent lacrimal system[3]. It also implies exclusion of overt causes of epiphora such as punctal stenosis, lid malpositioning and reflex hypersecretion[4]. For ease of reference, we use the acronym FNLDO to refer to this subgroup of patients who have epiphora despite patency to syringing.

Although the severity of epiphora among patients with FNLDO is equivalent to that of those with complete NLDO, the treatment of structural or anatomical NLDO has hitherto received the majority of attention[5-6]. In contrast to complete NLDO, where dacryocystorhinostomy (DCR) is the gold standard of treatment, the evidence base for the treatment of FNLDO is less well established[7]. Successful surgery improves symptoms and psychological well-being in patients with

FNLDO[3], and the scarcity of literature on the management of this condition creates an opportunity to fill this research gap. To the best of our knowledge, there is no updated systematic review covering the current treatments available for functional epiphora. This systematic review seeks to provide insight into the success rates and complications of various interventions in the management of functional epiphora in adults.

MATERIALS AND METHODS

Search Strategy The search was carried out during a 5-month period (October 2022 to February 2023) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria and, where applicable, the Cochrane Handbook. We searched English-language articles from the electronic databases PubMed, Scopus, and Google Scholar. The following keywords were used either individually or in combination to aid in retrieving the articles: functional epiphora, FNLDO, patent epiphora, obstructive epiphora, partial, incomplete, nasolacrimal duct stenosis, nasolacrimal duct obstruction, lacrimal drainage, lacrimal pump failure, botulinum toxin, dacryocystoplasty, dacryoplasty, dacryocystorhinostomy, efficacy, management, surgical, surgery, silicone intubation, stent, stents, stenting, success, treatment, tarsal strip, tightening, canthopexy. To ensure that the information was as up to date as possible, the inclusion for the review was limited to the years 1981 to 2023.

Articles were included in the systematic review if they fulfilled the following eligibility criteria: 1) comparative prospective [*e.g.*, randomised and non-randomised controlled trials (RCT), cohort study] or retrospective group designs (*e.g.,* case-control, cross-sectional), non-comparative retrospective or prospective designs (*e.g.*, case series); 2) included participants were above 18 years of age; 3) included either surgical or non-surgical treatment for functional epiphora (exhibited symptoms of epiphora with a patent lacrimal system). Articles were excluded if they were 1) case reports; 2) abstract only studies; 3) published in a language other than English.

In order to refine our search, the exclusion criteria were as follows: anatomical nasal abnormalities; nasal or eyelid infection/inflammation; previous nasal, lacrimal or eyelid surgery, trauma or tumour; history of failed stenting or balloon dacryoplasty; congenital NLDO or stenosis; canalicular/punctal obstruction or stenosis; history of chemotherapy or radiotherapy; ocular surface disease; dry eye; eyelid malposition; medial canthal tendon laxity or lid laxity; granulomatous disease; facial palsy; and orbicularis muscle weakness. It is important to highlight that despite a rigorous exclusion criterion, it was still possible to compile a sizable quantity of data by carefully examining the results (including the tables or graphs) and extracting only the portion that fulfilled the selection criteria.

Study Outcomes The primary outcome was defined as the success of the intervention based on subjective resolution or improvement of the symptoms of epiphora. Secondary outcomes included the presence of treatment complications such as premature stent extrusion or loss, granulation formation, and rhinostomy scarring.

Screening and Data Extraction Study selection was performed according to the predetermined inclusion and exclusion criteria. Screening was performed by reading the abstracts and the full articles. A standardised data extraction form was used. The variables extracted from the studies included study location (country), number of patients, age, gender, diagnostic tests used, intervention, duration of follow up, timing of stent removal (if applicable), overall success rate, and post-operative complications. Data extraction from each of the included studies was performed independently by two authors. Any differences in the extracted data were discussed. When there were still disagreements, a third author was consulted.

Quality Assessment The Effective Public Health Practice Project (EPHPP) checklist was used for quality assessment of the included studies[8]. This checklist is widely used in systematic reviews[9-13] and consists of six components of assessment of study methodology; selection bias, study design, confounders, blinding, data collection methods, withdrawal and dropouts. The six components were scored as weak, moderate, or strong, while the overall quality rating for each included study was also scored likewise. An overall quality rating of “strong” was assigned when there were no weak ratings, “moderate” when there was one weak rating, and “weak” when there were two or more weak ratings on the EPHPP components. The quality assessment was conducted by two authors. Any discrepancy of scoring was discussed to reach a consensus. Components of EPHPP which were not relevant to the studies (blinding was not applicable for retrospective studies, non-comparative studies, case series, or studies with a single group) were labelled as non-applicable.

RESULTS

Literature Search The initial search yielded a total of 762 articles. Of these, 112 articles were duplicates and thus were removed. The 582 of remaining articles which did not meet the review criteria were excluded after screening the titles and abstracts. Data extraction was done by reading the full text for the remaining 68 articles, after which 42 full-text articles which met the exclusion criteria were excluded. This left a total of 28 studies fulfilling the selection criteria (Figure 1). From the included studies, 5 were RCTs, followed by 2 clinical controlled trials, and 3 retrospective studies with comparative groups. The 7 prospective non-comparative studies, and the 11 retrospective record reviews make up the remainder of the included studies in this review.

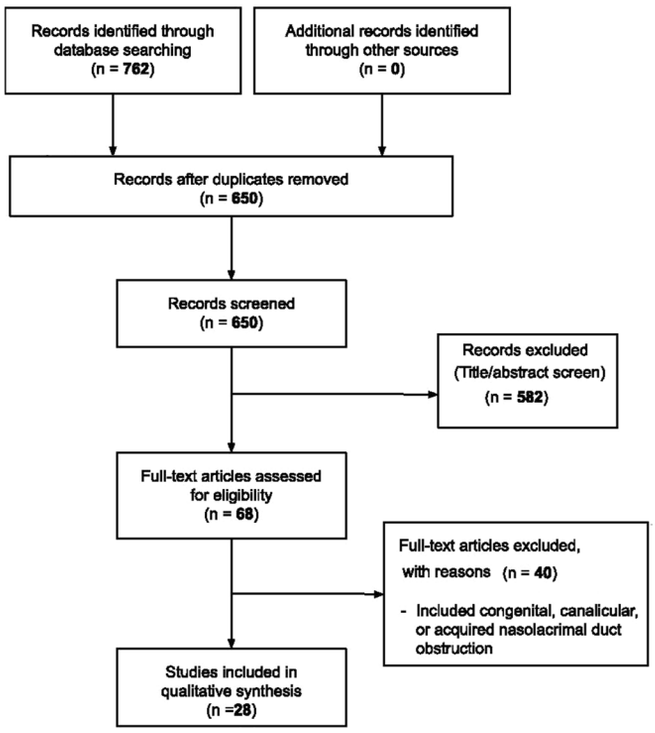

Figure 1 PRISMA flow chart.

Description of Studies A total of 1706 eyes were pooled. The total number of patients for each study ranged from 12 to 340, with a mean age ranging from 42.18 to 75 years old. The majority of studies evaluated multiple interventions for FNLDO. Interventions included silicone tube intubation (STI) alone (7 studies), external DCR (ExtDCR) with or without STI (6 studies), endoscopic DCR (EDCR) with or without STI (5 studies), balloon dacryoplasty with or without STI (4 studies), lateral tarsal strip procedure (LTS; 3 studies), lacrimal probing (2 studies) and medical-based therapies such as botulinum toxin injection and topical steroid application. In ten studies, STI was used in conjunction with other treatments. For those treatment options involving STI, the average duration of stent retention varied from 4wk to 6mo. Table 1 summarised the studies included in this systematic review.

Outcomes A Meta-analysis was not performed (due to the heterogeneity of all the included studies). Hence, meaningful interpretations of the study outcomes in the included studies required expert discussion and clinical judgement. The two primary outcomes, percentage of success and postoperative complications, were narratively described in Table 2. The overall success outcome of the studies' interventions ranged from 10.3% to 100%. Post-operative complications were reported in 15 studies, while four studies reported no complications. Nine studies did not report the complication rate.

Quality Assessment Based on the EPHPP global rating decision tool, two studies were assessed as being of strong quality, six of moderate quality, and 16 of weak quality (Table 3). The majority of the studies were considered weak due to their study design and lack of control for confounding factors. Given the relative rarity of this condition, all eligible participants in the included studies were from hospital-based samples. Based on the individual methodology component assessment for selection bias, studies that screened patients for FNLDO using both dacryocystography (DCG) and dacryoscintigraphy (DSG) were deemed most representative of their target population, as the combination of these diagnostic imaging tests can demonstrate the location of a relative obstruction along the lacrimal outflow pathway as well as quantify delayed tear passage. In terms of study design, only the three randomised controlled trials were rated as strong. Five studies were classified as strong in terms of confounders since age and underlying eye diseases were either balanced at baseline or controlled throughout the analysis. Data collection methods were considered strong for all studies, due to the use of standardized tests for evaluation of success, such as the fluorescein dye disappearance test and patency based on endoscopic evaluation of the lacrimal ostium.

DISCUSSION

In adults with persistent functional epiphora, our systematic review identified that DCR had the highest success rates. Complications were minor, transient, and stent-related, in the majority. Although STI may be an alternative to DCR in surgery-averse patients with abnormal DCG, its success rates appear to be inferior to DCR. The benefits and drawbacks of each intervention were highlighted in Table 4.

Silicone Tube Intubation STI was the most common intervention for FNLDO, whether singly or as an adjunct to other procedures[15-22]. When used as a stand-alone treatment to reinforce flow along the original lacrimal drainage pathway in FNLDO, we observed overall success rates of approximately 70%. Resistance within the lacrimal outflow system is distributed between the canaliculi and the nasolacrimal duct, with the former contributing more than 50% of the total resistance[23]. Based on Poiseuille's Law, which states that resistance to flow is inversely proportional to the fourth power of the radius, expansion of the canalicular portion of the lacrimal system, such as achieved by STI, would thus reduce resistance, resulting in improved flow. Although the success rates of monocanalicular and bicanalicular STI are similar, purported advantages of monocanalicular STI are the simplicity of tube insertion and removal[15]. On the flip side, the effect of STI on reduction in lacrimal system resistance may be greater with two stents than one[24]. Besides increasing flow volume *via* dilation of the soft tissue portion of the lacrimal outflow system, STI may act to straighten the kink in the common canaliculus insertion to the sac, facilitate flow *via* capillary action, and maintain the osteotomy post DCR[15,24-26].

Table 1 Characteristics of the studies reviewed

Study design	First author, y	Country	Interventions	Patients/ eyes	Mean age, y (SD or range)	Males, *n* (%)	Timing of stent removal (SD or range)	Mean follow-up[a] (min-max)
Randomised controlled trials	Andalib, 2014	Iran	Monocanalicular STI	NR/26	52.75 (NR)	NR	3mo	6mo
			STI	NR/26	49.06 (NR)	NR	3mo	
	Bleyen, 2007	Netherlands	Balloon dacryoplasty w/ STI (8 bar for 90s, deflated, and reinflated for 60s)	35/35	54 (11.8)	4 (11.4)	12.2 (5.5)wk	43.4 (9-76)mo
			STI	35/35	53 (13.1)	8 (22.9)	11.5 (5.6)wk	34.9 (14-68)mo
	Maroto Rodriguez, 2022	Spain	Botulinum toxin A (5U/0.05 mL to palpebral lobe)	12/21	61.5 (NR)	0	N/A	30 wk
			LTS	13/20	62.23 (NR)	3 (23.1)	N/A	
	Masoomian, 2021	Iran	Lacrimal probing	NR/35	45.94 (15.9)	14[+] (40.0)	N/A	11 (9-14)mo
			Lacrimal probing with MMC injection (0.5 mL of 0.2 mg/mL)	NR/38	42.18 (12.3)	13[+] (34.2)		
	Sadiq, 1998	UK	Irrigation w/ punctal dilation	NR/15	69.2 (30-89)	NR (37)	N/A	3mo
			Retropunctal cautery and one-snip punctoplasty	NR/15			N/A	3mo
Clinical controlled trials	Tong, 2016	China	STI	37/37	52.8 (9)	8 (21.6)	5.1 (3-6)mo	14.8 (8-25)mo after stent removal
	Zaidi, 2011	UK	EDCR w/ STI	21/21	62 (26-94)	21 (45.6)	3mo	6mo
			ExtDCR w/ STI	25/25			3mo	
Retrospective with comparative groups	Cho, 2013	Korea	STI	91/108	55.6 (9.8)	42 (46.2)	5.8 (1-31)mo	6mo
			EDCR w/ STI	29/32	54.3 (9.7)	7 (24.1)	3.7 (2-6)mo	
			ExtDCR w/ STI	13/13	57.6 (12.9)	5 (38.5)	3.1 (2-5)mo	
	Kashkouli, 2006	Iran & UK	STI (12 cases of monocanalicular STI)	33/39	60.93 (15.6)	9 (27.3)	7.55 (2.39)wk	14.60 (6-63)mo
			Balloon dacryoplasty w/ STI (8 atm for 90s, deflated, and reinflated to 9 atm for 60s)	22/23		4 (18.2)	7.39 (2.06)wk	
	Ozturker, 2022	Turkey	Transcanalicular DCR w/ STI	38/38	49.3 (19-77)	20 (52.6)	2.6 (1-5)mo	25.9 (8–85)mo
			Non-endoscopic endonasal DCR w/ STI	47/47	64.1 (37-89)	13 (27.7)	2.2 (0-6)mo	44.2 (11–72)mo
			ExtDCR w/ STI	50/50	56.5 (23-82)	16 (32)	2.3 (0-7)mo	45.9 (6–97)mo
Prospective with single group/non-comparative/ consecutive cases	Callejas, 2010	USA	EDCR w/ STI	NR/20	NR	NR	4wk	8mo
			EDCR w/o STI	NR/15	NR	NR	N/A	
	Dareshani, 2013	Pakistan	Lacrimal probing	340/340	NR (18-70)	117 (34.4)	NA	6mo
	Kim J, 2018	Korea	STI	36/36	61.4 (8.8)	8 (22.2)	NR	6mo
	Narasimha Naik, 2020	India	ExtDCR w/ STI	23/23	44.3 (NR)	9 (39.1)	16-24wk	6mo
	Simsek, 2015	Turkey	ExtDCR w/o STI	23/26	46.83 (28-73)	5 (21.7)	16 (11-30)wk	72.85 (47-88)wk
	Whittaker 2003	UK	Botulinum toxin A (2.5-5 U)	14/14	60 (41-84)	5 (35.7)	N/A	13wk
	Yang, 2019	Korea	Topical steroids	NR/41	NR	NR	N/A	6mo
Record review (retrospective case series)	Ali, 2014	India	Balloon dacryoplasty w/ STI (8 atm for 90s, deflated and reinflated to 8 atm for 60s)	12/21	58.2 (42-71)	4 (33.3)	12wk	6mo after stent removal
	Bleyen, 2008	Netherlands	STI	53/72	55.9 (13)	10 (18.5)	10.4 (5.1)wk	29.3 (6-66)mo
	Cannon, 2009	UK	LTS	18/25	69 (43-92)	NR	N/A	3mo (NR)
	Coumou, 2017	Netherlands	EDCR w/ STI	52/52	58 (18-91)	21 (40.4)	2-3mo	5.7 (3-21)mo
	Delaney, 2002	UK	ExtDCR w/ STI	49/50	62 (21-86)	13 (26.5)	3.6mo (3wk-9mo)	36 (11-69)mo
	Kim SH, 2018	Korea	STI	33/43	55.3 (19.5)	17 (39.5)	6mo	12mo
	Konuk, 2008	Turkey	Balloon dacryoplasty w/o STI (5min at 5 atm)	NR/46	NR	NR	N/A	NR (36-142mo)
	Moscato, 2012	USA	STI	30/44	57.4 (15.5)	8 (26.7)	4.0 (0.6-24)mo	2.6 (0.2-7.0)y
	Shapira, 2022	Australia	EDCR w/o STI	23/24	61.0 (17.07)	7 (30.4)	N/A	13 (1-84)mo
	Vick, 2004	USA	LTS	21/34	75 (NR)	11 (52.4)	N/A	7.6-11.2wk (NR)
	Yang, 2022	Korea	STI	48/81	60 (55-68)	28[+] (34.6)	3mo	6mo

NR: Not reported; N/A: Not applicable; w/: With; w/o: Without; STI: Silicone tube intubation; EDCR: Endoscopic dacryocystorhinostomy; extDCR: External dacryocystorhinostomy; LTS: Lateral tarsal strip procedure; atm: Atmospheres. [a]For studies which did not report follow-up duration, the last point at which outcomes were assessed is reported; STI implies bicanalicular silicone tube intubation.

Table 2 Outcomes of interventions for functional epiphora

First author, y	Ix	Intervention	Criteria for successful outcome	Overall successful outcome, (%)	Complications
Andalib, 2014	Irrigation, FDDT, DSG	Monocanalicular STI	Complete resolution of epiphora or intermittent epiphora with positive FDDT	19/25 (76)	Early stent loss (1 case)
		STI		16/21 (76.2)	Early stent loss (2 cases), peripunctal pyogenic granuloma (2 cases, resolved after tube removal)
Bleyen, 2007	Irrigation, FDDT, TMH, DCG	Balloon dacryoplasty w/ STI (inflated to 8 bar for 90s, deflated, and reinflated for 60s. Inflation procedure then repeated)	Complete: Munk score grade 0-1	18/35 (51.4)	Bloody nasal secretions (4 cases), inability to retrieve stent (2 cases), early stent removal due to allergic reaction (1 case)
			Partial: Munk score grade 2	2/35 (5.7)	
			Total: Complete and partial success	20/35 (57.1)	
		STI	Complete: Munk score grade 0-1	20/35 (57.1)	Slight nasal bleeding (3 cases), stent loss (2 cases), inability to retrieve stent (1 case), early stent removal due to slit-inferior punctum (1 case)
			Partial: Munk score grade 2	1/35 (2.9)	
			Total: Complete and partial success	21/35 (60)	
Maroto-Rodriguez, 2022	Irrigation	Botulinum toxin A (Xeomin 5 units/0.05 mL to palpebral lobe)	Epiphora improvement based on a quality of life questionnaire assessing the impact of epiphora on daily activities	14/21 (66.7)	Transient eyelid ptosis (3 cases), metamorphopsia (1 case), conjunctivitis (1 case)
		LTS		13/20 (65)	Surgical scar discomfort (3 cases), conjunctivitis (1 case)
Masoomian, 2021	Irrigation, DSG	Lacrimal probing	Complete: Complete resolution of epiphora	8/35 (22.9)	None
			Partial: At least 50% improvement in epiphora	6/35 (17.1)	
			Total: Complete and partial success	14/35 (40)	
		Lacrimal probing with 0.5 mL of mitomycin C 0.2 mg/mL	Complete: Complete resolution of epiphora	23/38 (60.5)	
			Partial: At least 50% improvement in epiphora	4/38 (10.5)	
			Total: Complete and partial success	27/38 (71.1)	
Sadiq, 1998	Irrigation	Irrigation w/ punctal dilation	Improvement in epiphora	6/15 (40)	NR
		Retropunctal cautery and one-snip punctoplasty		13/15 (86.7)	
Tong, 2016	Irrigation	Medication (a one-month taper of tobramycin and dexamethasone)	Complete: Complete absence of tearing or minimal epiphora, both indoors and outdoors	2/37 (5.4)	None
			Partial: Partial resolution or improvement of epiphora, with no further intervention required	3/37 (8.1)	
			Total: Complete and partial success	5/37 (13.5)	
		STI	Complete: Complete absence of tearing or minimal epiphora, both indoors and outdoors.	28/37 (75.7)	
			Partial: Partial resolution or improvement of epiphora, with no further intervention required	4/37 (10.8)	
			Total: Complete and partial success	32/37 (86.4)	
Zaidi, 2011	Irrigation, DCG or DSG	EDCR w/ STI	Objective: Positive FEDT and patency based on irrigation and endoscopic evaluation of the lacrimal ostium	17/21 (80.1)	
			Subjective complete: Complete resolution of epiphora	7/21 (33.3)	Peri-rhinostomy granuloma (2 cases), scarred rhinostomy (2 cases)
			Subjective partial: Improvement in epiphora	11/21 (52.4)	
			Subjective total: Subjective complete and subjective partial success	18/21 (85.7)	
		ExtDCR w/ STI	Objective: Positive FEDT and patency based on irrigation and endoscopic evaluation of the lacrimal ostium	25/25 (100)	None
			Subjective complete: Complete resolution of epiphora	16/25 (64.0)	
			Subjective partial: improvement in epiphora	9/25 (36.0)	
			Subjective total: Subjective complete and subjective partial success	21/21 (100)	

Int J Ophthalmol, Vol. 18, No. 5, May 18, 2025 www.ijo.cn
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Table 2 Outcomes of interventions for functional epiphora (continued)

First author, y	Ix	Intervention	Criteria for successful outcome	Overall successful outcome, (%)	Complications
Cho, 2013	Irrigation, DSG	STI	Complete: Complete resolution of epiphora	74/108 (68.5)	NR
			Partial: Improvement in epiphora	28/108 (25.9)	
			Total: Complete and partial success	102/108 (94.4)	
		EDCR w/ STI	Complete: Complete resolution of epiphora	26/32 (81.3)	
			Partial: Improvement in epiphora	6/32 (18.7)	
			Total: Complete and partial success	32/32 (100)	
			Complete: Complete resolution of epiphora	7/13 (53.9)	
		ExtDCR w/ STI	Partial: Improvement in epiphora	6/13 (46.2)	
			Total: Complete and partial success	13/13 (100)	
Kashkouli, 2006	Irrigation, FDDT	STI (12 cases of monocanalicular STI)	Complete resolution of epiphora	21/39 (53.8)	Slight nasal and canalicular bleeding (all patients), slit punctum (4 cases), stent loss (3 cases)
		Balloon dacryoplasty w/ STI (inflated to 8 atm for 90s, deflated, pulled back to proximal ring, and reinflated to 9 atm for 60s)	Complete resolution of epiphora	14/23 (60.9)	Slight nasal and canalicular bleeding (all patients)
Ozturker, 2022	Irrigation, FDDT or DSG	Transcanalicular DCR w/ STI		25/38 (65.8)	Slitting of canaliculi (1 case), stent prolapse (1 case), thermal damage to lacrimal/nasal mucosa (1 case)
		Non-endoscopic endonasal DCR w/ STI	Complete resolution of epiphora and positive FDDT	33/47 (70.2)	None
		ExtDCR w/ STI		42/50 (84)	Canaliculus stricture (1 case)
Callejas, 2010	Irrigation, DCG, DSG	EDCR w/ STI	Complete resolution of epiphora, positive FDDT and patency based on endoscopic evaluation of the lacrimal ostium	16/20 (80)	NR
		EDCR w/o STI		7/15 (46.7)	
Dareshani, 2013	Irrigation, FDDT, Jones 1,	Lacrimal probing	Complete resolution of epiphora	35/340 (10.3)	Bleeding (30 cases), acute inflammation (11 cases)
Kim J, 2018	Irrigation, FDDT, DCG	STI	Munk score grade 0-1 and decrease in TMH	25/36 (69.4)	None
Narasimha Naik, 2020	Irrigation, FDDT, Schirmer's test, and tear breakup time	ExtDCR w/ STI	Objective: Patency on irrigation and positive FDDT	20/23 (86.9)	Cosmetic blemish (4 cases), conjunctival erosion (4 cases), foreign body sensation (4 cases), stent extrusion (4 cases), corneal erosion (2 cases), nasal synechiae (2 cases), granuloma formation (1 case), stent loss (1 case), difficult stent removal (1 case)
			Subjective: Complete resolution of epiphora	17/23 (73.9)	
Simsek, 2015	Irrigation, DSG	ExtDCR w/ or w/o STI	Patency on irrigation and no or mild epiphora by subjective evaluation	20/26 (76.9)	None
Whittaker, 2003	Irrigation	Botulinum toxin A (Botox 5 units in 4 patients; dose reduced to 2.5 units in the remainder due to side effects of ptosis and diplopia)	Objective: Improvement in Schirmer's test	6/11 (54.5)	Transient eyelid ptosis (1 case), transient diplopia (1 case); Complications occurred only in the two patients who received 5 units per injection
			Subjective: Improvement in Munk Score	8/11 (72.7)	
Yang, 2019	Irrigation, FDDT, TMH, DCG	Topical steroids	Improvement in epiphora, FDDT grade 0 or 1 & TMH<250 μm on anterior segment optical coherence tomography	19/41 (46.3)	IOP elevation (5 cases)
Ali, 2014	Irrigation, dacryoendoscopy	Anterograde balloon dacryoplasty w/ STI (inflated to 8 atm for 90s, deflated and reinflated to 8 atm for 60s in the distal and proximal NLD)	Objective: Patency on irrigation; Subjective: Complete resolution of epiphora	15/21 (71.4)	Bloody nasal secretions in first week (all patients), STI-related discomfort (2 cases)
			Subjective: Complete resolution of epiphora	13/21 (61.9)	
Bleyen, 2008	Irrigation, TMH, Jones test, DCG	STI	Complete: Munk score 0-1	31/66 (46.97)	Bloody nasal secretions (4 cases), early stent loss (4 cases), inability to retrieve stent (6 cases), early stent removal due to slit inferior punctum (4 cases)
			Partial: Munk score 2	2/66 (3.0)	
			Total: Complete and partial success	33/66 (50)	
Cannon, 2009	Irrigation, FDDT	LTS	Improvement in epiphora	20/25 (80)	NR
Coumou, 2017	Irrigation, DSG	EDCR w/ STI	Improvement in epiphora for participants age 18-60	21/23 (91)	Cheese wiring of stent, fat prolapse, epistaxis; Numbers not reported
			Improvement in epiphora for participants age 60+	24/29 (84)	

Table 2 Outcomes of interventions for functional epiphora (continued)

First author, y	Ix	Intervention	Criteria for successful outcome	Overall successful outcome, (%)	Complications
Delaney, 2002	Irrigation, Jones 1 and 2 test, DSG	ExtDCR w/ STI	Short-term (3.6mo postop.): Patency on irrigation, positive FDDT, and improvement in epiphora	32/35 (91.4)	NR
			Long term (3y postop.): Improvement in epiphora	28/35 (80)	
Kim SH, 2018	Irrigation	STI	Patency on irrigation, improvement in epiphora (Munk score 0-1) and FDDT grade 0-1	31/43 (72.1)	NR
Konuk, 2008	Irrigation, Jones 1 and 2 test, DCG	Retrograde balloon dacryoplasty (5 atm for 5min in NLD)	Munk score 0-1 and patency on irrigation	31/46 (67.4)	NR
Moscato, 2012	Irrigation	STI	Complete: Complete resolution of epiphora	31/44 (70.5)	Stent prolapse (1 case), stent extrusion (1 case), cheese-wiring (1 case), complicated stent removal requiring endoscopic access (1 case)
			Partial: Improvement in epiphora	3/44 (6.8)	
			Total: Complete and partial success	34/44 (77.3)	
Shapira, 2022	Irrigation, DCG, DSG	EDCR w/o STI	Complete: Complete resolution of epiphora	10/24 (41.7)	Scarred rhinostomy (1 patient)
			Partial: Improvement in epiphora	7/24 (29.1)	
			Total: Complete and partial success	17/24 (70.8)	
Vick, 2004	Irrigation, FDDT, TMH	LTS	Complete: Complete resolution of epiphora	14/34 (41.2)	NR
			Partial: Improvement of epiphora	17/34 (50.0)	
			Total: Complete and partial success	31/34 (91.2)	
Yang, 2022	Irrigation, TMH, DCG	STI	Munk score 0-1 and TMH<300 μm on anterior segment optical coherence tomography	49/81 (60.5)	NR

NR: Not reported; w/: With; w/o: Without; STI: Silicone tube intubation; EDCR: Endoscopic dacryocystorhinostomy; extDCR: External dacryocystorhinostomy; LTS: Lateral tarsal strip procedure; DSG: Dacryoscintigraphy; DCG: Dacryocystography; FEDT: Functional endoscopic dye test; FDDT: Fluorescein dye disappearance test; NLDS: Nasolacrimal duct stenosis; NLD: Nasolacrimal duct; atm: Atmospheres; TMH: Tear meniscus height; STI implies bicanalicular silicone tube intubation.

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Table 3 EPHPP quality assessment tool rating for individual studies

First author, y	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdrawals and dropouts	Global rating
Andalib, 2014	M	S	M	W	S	S	M
Bleyen, 2007	M	S	S	W	S	S	M
Maroto Rodriguez, 2022	W	S	S	M	S	S	M
Masoomian, 2021	M	S	S	W	S	S	M
Sadiq, 1998	W	S	W	W	S	S	W
Tong, 2016	W	M	W	W	S	S	W
Zaidi, 2011	M	M	W	W	S	S	W
Cho, 2013	M	M	S	NA	S	S	S
Kashkouli, 2006	W	M	W	NA	S	S	W
Ozturker, 2022	M	M	M	NA	S	S	S
Callejas, 2010	S	W	S	NA	S	S	M
Dareshani, 2013	W	W	W	NA	S	S	W
Kim J, 2018	M	W	S	NA	S	S	M
Narasimha Naik, 2020	W	W	S	NA	S	S	W
Simsek, 2015	M	W	W	NA	S	S	W
Whittaker 2003	W	W	W	NA	S	M	W
Yang, 2019	M	W	M	NA	S	S	M
Ali, 2014	M	W	W	NA	S	S	W
Bleyen, 2008	M	W	W	NA	S	S	W
Cannon, 2009	W	W	W	NA	S	S	W
Coumou, 2017	M	W	W	NA	S	S	W
Delaney, 2002	M	W	W	NA	S	S	W
Kim SH, 2018	W	W	W	NA	S	S	W
Konuk, 2008	M	W	W	NA	S	S	W
Moscato, 2012	W	W	W	NA	S	S	W
Shapira, 2022	S	W	M	NA	S	M	M
Vick, 2004	W	W	W	NA	S	S	W
Yang, 2022	M	W	M	NA	S	S	M

EPHPP: Effective Public Health Practice Project; S: Strong; M: Medium; W: Weak; NA: Not applicable.

Callejas *et al*[19] showed that when used in combination with EDCR, success rates were higher in the STI group than in the group without STI. This is attributed to the mechanical effect of STI as a conduit for tear drainage, correlating with findings that epiphora recurs by 4mo after stent removal in approximately 50% of cases[27].

Unfortunately, long-term stent maintenance is problematic. Patient dissatisfaction with STI is related to the additional cost and complications of STI, including epistaxis, false passage, and canaliculitis[28-31]. Punctal slitting and granuloma formation may result in symptom recurrence[32]. Even in technically successful, uncomplicated STI, low-grade inflammation of the lacrimal sac may lead to intermittent lacrimal symptoms[33]. Over time, inflammatory overgrowth of granulation tissue through the stent lumen tends to cause re-obstruction in both anatomical NLDO and FNLDO[33], explaining the reported success rates of 40%-75% at approximately 2y post STI[34-35]. Stent-related inflammation not only has chronic effects on the lacrimal sac mucosa, as evidenced by a study of lacrimal sac biopsies performed during dacryocystorhinostomy[33], but may also induce negative changes in lacrimal configuration necessitating adjunctive treatment during future interventions[27,34]. In addition, long-term stent retention may complicate later stent removal due to its adherence to the lacrimal apparatus[35].

Probing and Balloon Dacryoplasty Balloon dacryoplasty (BD) involves probing and subsequent dilation of the NLD using an inflatable balloon. Although inferior to STI in FNLDO, its overall success rates are higher than that of NLD probing alone and similar to the outcomes achieved in probing with adjunctive mitomycin C[14,36-38]. BD aims to mechanically reverse the age-related stenosis and subsequent tear stasis and lacrimal outflow pathway inflammation which characterise patients with FNLDO[37]. Based on the few retrospective studies evaluating its efficacy in FNLDO, success rates range from 60%-70%[36-37]. The limited success of BD can likely be attributed to failure to reverse the underlying pathology in patients with an established vicious cycle of tear stasis,

Table 4 The benefits and drawbacks of interventions for functional epiphora

Treatment	Study, y	Success rates (%)	Pros	Cons
Silicone tube intubation	Andalib, 2014	35/46 (76.1)	Simple to insert and remove; short procedure; quick recovery; minimally invasive; low risk of bleeding; re-establishes normal anatomic pathway; inexpensive; avoids incision/osteotomy	Stent-related complications including stent loss, extrusion, corneal abrasion, and punctal slitting; punctal slitting may result in persistent epiphora; may be less effective and require more follow-up than rhinostomy-based methods as the condition progresses; long term stent maintenance may be complicated by lacrimal symptoms and prejudice outcomes of future stent-free surgery
	Bleyen, 2007	21/35 (60)		
	Tong, 2016	32/37 (81.1)		
	Cho, 2013	102/108 (94.4)		
	Kashkouli, 2006	21/39 (53.8)		
	Kim J, 2018	25/36 (69.4)		
	Bleyen, 2008	33/66 (50)		
	Kim SH, 2018	31/43 (72.1)		
	Moscato, 2012	34/44 (77.3)		
	Yang, 2022	49/81 (60.5)		
External dacryocysto-rhinostomy	Zaidi, 2011	25/25 (100)	Rapid symptom relief; minimal follow up	External skin incision with potential scarring; Surgical risks including bleeding and cerebrospinal fluid leak; longer procedure and recovery times
	Cho, 2013	13/13 (100)		
	Ozturker, 2022	42/50 (84)		
	Narasimha Naik, 2020	17/23 (73.9)		
	Simsek, 2015	20/26 (76.9)		
	Delaney, 2002	28/35 (80)		
Endoscopic dacryocysto-rhinostomy	Zaidi, 2011	18/21 (85.7)	Avoids incision-related scarring (especially relevant in young, keloid-prone patients with flat nasal bridges); may preserve lacrimal pump by avoiding trauma to the medial canthal tendon; allows simultaneous treatment of intranasal problems *e.g.* septal deviation	Endoscopic access may not always be straightforward
	Cho, 2013	32/32 (100)		
	Callejas, 2010	23/35 (65.7)		
	Coumou, 2017	48/52 (92.2)		
	Shapira, 2022	17/24 (70.8)		
Transcanali-cular diode laser-assisted dacryocysto-rhinostomy	Ozturker, 2022	25/38 (65.8)	Portable instrumentation	Causes thermal damage to residual tissue–the energy levels required to create the osteotomy may increase failure rates by promoting fibrosis
Non-endoscopic endonasal dacryocysto-rhinostomy	Ozturker, 2022	33/47 (70.2)	Simpler and more economical setup and instrumentation; larger working space	View may be suboptimal compared to endoscopic dacryocystorhinostomy
Balloon dacryoplasty	Bleyen, 2007	20/35 (57.1)	Minimally invasive; low risk of bleeding	May be technically impossible in severely narrowed nasolacrimal ducts; may precipitate periorbital or orbital cellulitis in active dacryocystitis
	Kashkouli, 2006	14/23 (60.9)		
	Ali, 2014	13/21 (61.9)		
	Konuk, 2008	31/46 (67.4)		
Lateral tarsal strip	Maroto Rodriguez, 2022	13/20 (65)	Less invasive than dacryocystorhinostomy, with lower risks	May have lateral canthal discomfort and dystopia
	Cannon, 2009	20/25 (80)		
	Vick, 2004	31/34 (91.2)		
Botulinum toxin A	Maroto Rodriguez, 2022	14/21 (66.7)	Simple; quick; minimally invasive	Variable, time-limited effects; need repeated injections; dose-related side effects like ptosis and diplopia
	Whittaker 2003	8/11 (72.7)		
Lacrimal probing	Masoomian, 2021	27/38 (71.1), with mitomycin C	Simple; quick; minimally invasive; economical; re-establishes normal anatomic pathway	Risk of iatrogenic trauma; high failure rate without adjuvant mitomycin C; potential toxicity of mitomycin C
	Masoomian, 2021	14/35 (40)		
	Masoomian, 2021[14]	14/35 (40)		
	Dareshani, 2013	35/340 (10.3)		
Retropunctal cautery and one-snip punctoplasty	Sadiq, 1998	13/15 (86.7)	Simple; quick; minimally invasive; economical	May not address natural history of disease if epiphora is related to nasolacrimal duct stenosis
Punctal dilation and irrigation	Sadiq, 1998	6/15 (40)	Simple; quick; minimally invasive; economical; performed as part of routine examination in epiphora	Low success rates
Topical steroids	Yang, 2019	19/41 (46.3)	Simple; quick; minimally invasive	Lower success rates than mechanical interventions; steroid complications like elevated intraocular pressure

inflammation-related mucosal thickening, dysfunction of the cavernous plexuses supporting the lacrimal pump and eventual fibrosis with luminal stenosis. This correlates with slightly better outcomes of BD observed in the absence of chronic dacryocystitis[39], as well as evidence that BD has significantly higher success rates in partial than complete NLDO, in which the pathology affecting the NLD has passed beyond the possibility of reversal[40]. For these reasons, we do not recommend BD as an intervention for FNLDO. The role of inflammation in the pathology of FNLDO may also explain why probing in NLDS has greater success when combined with anti-fibrotic agents than when used alone, with differences

being evident in patients with greater degrees of stenosis or longer disease duration[14]. More than 90% of FNLDO cases are characterised by chronic inflammation[41], and steroid-antibiotic combinations like those employed by Yang *et al*[42] may be useful in treating this condition. In their trial, which used a mixture of dexamethasone 0.1% and tobramycin 0.3% to treat newly diagnosed functional epiphora, it was observed that half of the patients who had topical steroid instillation avoided further invasive interventions[42]. The aminoglycoside was included to prevent steroid-related infections, but may also be beneficial to cover for Pseudomonas aeruginosa, the bacteria most commonly isolated in cases of failed FNLDO treatment[43].

Lid Tightening Short term outcomes of LTS for FNLDO appear promising, but there is a lack of long-term data on the efficacy of this intervention, with follow-up available only up to 30wk[44-46]. In patients with equivocal lower eyelid laxity, eyelid taping to mimic the effect of a LTS predicts the likelihood of improvement in epiphora after surgical lid tightening[44]. LTS acts to strengthen the lacrimal pump by addressing horizontal lower eyelid laxity. Its effect on eyelid tightening may recreate the drawstring effect of the orbicularis muscle on tear propulsion towards the punctum as well as increase the pressure differential in the lacrimal sac upon blinking[47]. As lacrimal excretory system failure is thought to be the primary cause of FNLDO, it is critical to recognise and address subtle pathology that may prevent tears from flowing into the lacrimal passages. Punctoplasty with retropunctal cautery may thus have a dual effect, improving flow through the punctum while strengthening the lacrimal pump via a mild effect on medial lid tightening[48].

Dacryocystorhinostomy A systematic review of DCR in adults showed comparable outcomes between ExtDCR and EDCR[49]. We observed similar results in our studies of DCR for FNLDO, with success rates averaging approximately 80%. Most of the studies involving DCR for FNLDO used adjunctive STI[17,28,50-51]. DCR addresses distal drainage system resistance by connecting the lacrimal sac to the nasal cavity, while STI may act to dilate the proximal system[46]. EDCR is a popular alternative to ExtDCR where scarring from a skin incision is a concern, particularly in those with flat nasal bridges or prone to keloids. Other potential advantages of EDCR are maintenance of the lacrimal pump by avoiding surgery to the medial canthal tendon, as well as improved cost efficiency in view of the higher number of operations performed as day cases[52-53]. Challenges in EDCR implementation include the need for general anaesthesia and the learning curve required, although studies have shown that the latter may be addressed with appropriate training[54-56]. In situations when endoscopic access is not feasible, ExtDCR is nevertheless frequently required. Overall, the reported rate of complications with DCR was low, with stent-related issues being most prevalent. Granulomas were the most often reported adverse outcomes in EDCR. These findings may be biased as ExtDCR patients usually do not undergo post-operative nasal endoscopy.

Botulinum Toxin A Injection A minority of patients may have epiphora despite a normal DCG and DSG. Likewise, some patients with FNLDO who have undergone one intervention may experience limited improvement and seek further redress for their symptoms. Although a systematic review of the management of failed DCR is beyond the scope of this article, subsequent options might include eyelid tightening or a Lester-Jones tube[57]. In all cases, it is essential to undertake a patient-centered discussion highlighting the gaps in our current knowledge and the pros and cons of the available treatment options. It may occasionally be appropriate to offer botulinum toxin-A (BTA) injection with the understanding that this is an off-label indication which may provide only temporary relief. A recent survey among members of the British Oculoplastic Surgery Society found that the main indications for its use were elderly patients and those with medical comorbidities[58]. BTA is a neurotoxin generated from Clostridium botulinum, induces reversible inhibition of acetylcholine release from parasympathetic nerves, sympathetic preganglionic nerves, and sympathetic postganglionic lacrimal fibres[59]. Its injection into the lacrimal gland inhibits parasympathetically-induced tear formation by acting on presynaptic cholinergic nerve fibres, as shown by lower Schirmer test results obtained after injection[45,60]. In patients who fail to improve with DCR, especially in the presence of a normal lacrimal drainage capacity, injection of BTA may address the high tear secretion postulated to be the cause of persistent symptoms[61]. Diplopia and ptosis are well documented complications of lacrimal injection, especially with higher doses[60,62], although they occur much less frequently than with facial injections of BTA[63]. BTA has been evaluated singly[60] as well as in comparison to LTS[45] for the treatment of FNLDO. Although the subjective success rates of BTA and LTS in FNLDO are comparable at 30wk, Maroto Rodriguez *et al*[45] observed that BTA reduces the Munk scoring more than LTS. Unfortunately, BTA's effect is variable and time-limited, requiring repeat injections[45,58]. The most common complication reported with BTA injection is transient eyelid ptosis, particularly with higher doses, so using the minimum required dose to treat epiphora is recommended[60].

Strengths and Limitations Functional epiphora has accurately been attributed to an imbalance between tear secretion, tear film evaporation, and lacrimal clearance[64]. Although most studies of FNLDO exclude patients with eyelid malposition or facial palsies, variables affecting the

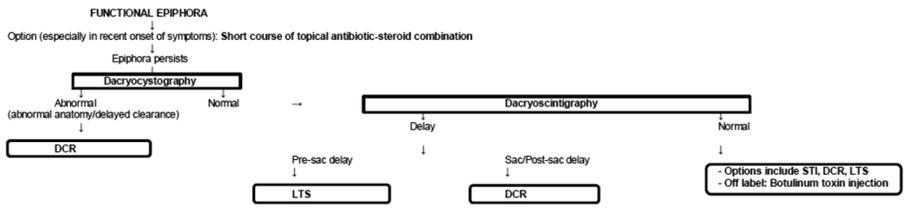

Figure 2 Algorithm of approach to functional epiphora DCR: Dacryocystorhinostomy; LTS: Lateral tarsal strip procedure; STI: Silicone tube intubation.

eyelids, palpebral aperture, blinking as well as Meibomian gland related issues may affect study outcomes[64-67]. Patients with FNLDO have lower eyelid pressure, independent of eyelid laxity[68]. This and other variations such as the degree of conjunctival redundancy may possibly have minor effects on success rates[69]. Additionally, due to their anti-inflammatory action, variations in the type, dosage, and duration of common antibiotic-steroid combinations provided after interventions may potentially have an impact on success rates. The length of follow-up, which ranged from about 8wk to 44mo, precludes direct comparisons of study outcomes, since success rates are expected to decline based on the natural history of nasolacrimal duct obstruction. Finally, a pertinent design weakness of all current studies evaluating treatments for FNLDO is a lack of objective, quantifiable evaluation of tear flows post-intervention. Although impractical in real world settings, for an ideal assessment of outcomes, in addition to evaluation for symptomatic improvement, DSG, or perhaps its less invasive counterpart imaging guided dacryocystography, performed both pre and post treatment for FNLDO would allow correlation of objective and subjective measures of success[70-73].

Patient-reported outcome measures are becoming increasingly important quality of care indicators[74-76]. As neither ostial patency nor a positive FDDT is a guarantee of intervention success[19], it is paramount to judge interventions by their effect on symptom relief. To the best of our knowledge, this is the first systematic review to evaluate the success of interventions for FNLDO in terms of their effect on subjective improvement of epiphora. The treatment options highlighted in this review are well known to its practitioners. Previous survey respondents to an American Society of Ophthalmic Plastic and Reconstructive Surgery survey of the management of FNLDO were divided between DCR, STI, lid tightening or a combination of these[4]. ExtDCR and EDCR were found to have the highest overall success rates in this systematic review, followed by STI. STI is likely to fail when either the inflammatory process blocks the stent or the disease's natural course leads to total NLDO following stent removal. This is reflected in the follow-up time of the included studies, in which studies involving DCRs had the longest mean follow-up duration of 3y or more, while the longest follow-up for STI was about 2 and a half years. For these reasons, we do not recommend STI for functional epiphora. Short term success rates of LTS appear encouraging, but the quality of the available evidence is weak. Although there are few long-term outcomes for BTA, it may provide temporary relief in refractory situations. In the absence of anti-inflammatory or anti-fibrotic agents, interventions that act to mechanically re-establish patency such as probing and BD may have a role only in carefully selected patients with a recent onset of epiphora who wish to delay definitive surgery for FNLDO.

Algorithm to Evaluation and Management of Functional Epiphora The term functional epiphora derives from the seminal work by Demorest[77], and refers to epiphora not directly attributable to a clinically evident anatomical outflow obstruction. Although our study is directed at identifying the most effective interventions for functional epiphora, at least an equal proportion of epiphora patients will have anatomical NLDO and will be helped by dacryocystorhinostomy, for which the evidence base for treatment is well established[78]. Among the remainder, epiphora may be due to a variety of causes including reflex tearing, lid malpositioning, or multifactorial, requiring more than one intervention to resolve symptoms[57,79-80]. It is thus paramount that the approach to functional epiphora be based on a logical process of sequentially evaluating for and addressing the most common causes of epiphora.

Patients with epiphora should undergo a detailed evaluation for mechanical issues impacting lacrimal drainage, such as eyelid, conjunctiva, and lacrimal outflow pathway anomalies. It is imperative to treat any co-existing reflex lacrimation. DCG and DSG can identify the precise location, type, and severity of NLD drainage impairment in patients with epiphora who have no visible aberrations[70-71,73,81]. An algorithmic approach to the treatment of functional epiphora guided by these investigations is presented in Figure 2. ExtDCR and EDCR may successfully address post-sac pathology, establishing permanent tear drainage in these compromised lacrimal systems[50,82]. STI is a less-invasive interim treatment, while LTS may have utility in pre-sac pathology. BTA may be required in the minority of patients who do not improve following conventional therapies, though the long-term safety and efficacy of repeated injections require further investigation. When all else fails, a lacrimal

bypass tube may be warranted, although even this procedure may not relieve symptoms in all cases[7,83-84]. Throughout the patient journey, it is prudent to bear in mind a principle we often overlook in our quest for surgical excellence, “primum non nocere” (first, do no harm). Despite a host of interventions at our fingertips, in rare cases, the patient may be better served by us doing nothing at all.

CONCLUSIONS

We present an updated systematic review on the success rates of interventions for functional epiphora in adults and an algorithm to the management of these patients. All patients with functional epiphora should have a DCG. If DCG is abnormal, we advocate DCR. If DCG is normal, proceed with DSG. We perform LTS for pre-sac delay and DCR for post-sac delay on DSG. BTA is an off-label, short-term treatment option in those with normal DSG or when surgery is not in the patient’s best interests.

ACKNOWLEDGEMENTS

Authors’ Contributions: Tai ELM: Conceptualization, Methodology, Investigation, Data Curation, Writing-Original Draft (Abstract, Introduction, Results, Discussion, Conclusion), Writing- Review & Editing, Visualization, Supervision; Lee AL: Investigation, Data Curation, Writing-Original Draft (Results), Writing-Review & Editing, Visualization; Kueh YC: Conceptualization, Methodology, Writing- Review & Editing; Abdullah B: Conceptualization, Methodology, Investigation, Data Curation, Writing-Review & Editing, Supervision; Chang B: Writing-Review & Editing, Supervision

Conflicts of Interest: Tai ELM, None; **Lee AL**, None; **Kueh YC**, None; **Abdullah B**, None; **Chang B**, None.

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