Unilateral Vocal Fold Paralysis After Congenital Cardiotoracic Surgery: A Meta-analysis

abstract

BACKGROUND AND OBJECTIVE: There is variation in the literature in regard to the occurrence of unilateral vocal fold paralysis (UVFP) after congenital cardiothoracic surgery. The objective of this study was to identify and appraise the evidence for the occurrence of UVFP after congenital cardiothoracic surgery in a meta-analysis.

METHOD: A comprehensive search strategy in Medline, Embase, and the Cochrane Library was conducted, limited to English publications. Two independent reviewers screened studies for eligibility criteria. Of the 162 identified studies, 32 (20%) met the inclusion criteria. Using the Oxford Centre for Evidence-Based Medicine guidelines, 2 reviewers appraised the level of evidence, extracted data, and resolved discrepancies by consensus. Weighted pooled proportion and 95% confidence intervals (CIs) are reported.

RESULTS: Thirty-two studies (n = 5625 patients) were included. Levels of evidence varied from level 3 to 4. Among all studies, the weighted pooled proportion of UVFP was 9.3% (95% CI, 6.6% to 12.5%), and among 11 studies (n = 584 patients) that postoperatively evaluated patients with flexible nasopharyngolaryngoscopy to document presence of UVFP, the weighted pooled proportion of UVFP was 29.8% (95% CI, 18.5% to 42.5%). Twenty-one studies (n = 2748 patients) evaluated patients undergoing patent ductus arteriosus ligation surgery, and the weighted pooled proportion of UVFP was 8.7% (95% CI, 5.4% to 12.6%). Six of these (n = 274 patients) assessed all patients postoperatively, and the weighted pooled proportion of UVFP was 39% (95% CI, 18% to 63%). Pooled analyses of risk factors and comorbidities are reported. Heterogeneity and publication bias were detected.

CONCLUSIONS: UVFP is a demonstrated risk of congenital cardiothoracic surgery. Routine postoperative nasopharyngolaryngoscopy for vocal fold assessment by an otolaryngologist is suggested.

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KEY WORDS unilateral vocal fold paralysis, cardiothoracic surgery, patent ductus arteriosus

ABBREVIATIONS
CI—confidence interval
G-tube—gastrostomy tube
OCEBM—Oxford Centre for Evidence-Based Medicine
PDA—patent ductus arteriosus
UVFP—unilateral vocal fold paralysis

This article was presented as a podium presentation at the Annual Meeting of the American Society of Pediatric Otolaryngology in Arlington, Virginia, on April 26, 2013.

Accepted for publication Mar 4, 2014

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.
Unilateral vocal fold paralysis (UVFP) secondary to left recurrent laryngeal nerve injury during cardiothoracic surgery is a known risk. The path of the nerve, which loops around the arch of the aorta, makes it susceptible to injury. This is especially true in patent ductus arteriosus (PDA) ligation surgery, given the nerve’s proximity to the PDA. Sequelae of UVFP may include stridor, absent or weak cry, aspiration, or feeding and swallowing difficulties. Therefore, adequate and timely diagnosis can help guide appropriate management. Although some patients are asymptomatic, this does not preclude proper assessment. Flexible nasopharyngolaryngoscopy is a short and well-tolerated procedure performed without sedation by otolaryngologists that allows direct visualization of the larynx and subsequent diagnosis of UVFP.

There is variation in the literature in regard to the occurrence of UVFP after congenital cardiothoracic surgery. This may result from the lack of routine postoperative vocal fold function assessment. To date, there has been no systematic review of the evidence for the occurrence of UVFP after cardiothoracic surgery in infants and children.

The primary objective of this study was to identify and appraise the evidence for the occurrence of UVFP after congenital cardiothoracic surgery (all types of surgery and PDA ligation surgery only) in infants and young children. We also sought to determine the occurrence of UVFP in patients who underwent postoperative assessment by flexible nasopharyngolaryngoscopy. Other outcomes investigated included UVFP-associated risk factors and comorbidities.

METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline.

Literature Search Strategy

The literature was searched using Ovid Medline (1946 to October 2012), Embase (1980 to 2012 Week 41), and the Cochrane Library (Cochrane Database of Systematic Reviews, 2012, Issue 3). The electronic database search combined intervention-specific terms (cardiothoracic surgery, cardiac surgery, heart surgery, cardiopulmonary bypass, patent ductus arteriosus, PDA ligation, closure) and outcome-specific terms (vocal fold, vocal cord, recurrent laryngeal nerve, immobility, mobility, paralysis, paresis, injury). To ensure that all relevant published articles were captured, the search was not limited by publication date or study design. Relevant articles and abstracts were selected and reviewed. Reference lists from these sources and recent review articles were searched for additional publications.

Study Selection Criteria

Articles were assessed for eligibility independently by 2 review authors (J.E.S. and G.R.) and were included if they were prospective or retrospective fully published studies that reported occurrence of UVFP after congenital cardiothoracic surgery in infants and young children. Secondary outcomes included type of surgery (PDA ligation or other), postoperative assessment of vocal cord function by flexible nasopharyngolaryngoscopy, patient demographics, respiratory and swallowing outcomes, and comorbidities. Non-English publications were excluded.

Assessment of Quality

Methodological quality of identified studies was appraised using the Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 Levels of Evidence:

- Level 1: Systematic review of randomized trials, systematic review of nested case–control studies, n-of-1 trials
- Level 2: Individual randomized trials or (exceptionally) observational studies with dramatic effect
- Level 3: Nonrandomized controlled cohort/follow-up studies provided there are sufficient numbers to rule out a common harm
- Level 4: Case series, case–control, or historically controlled studies
- Level 5: Mechanism-based reasoning

Data Analysis

Relevant data were extracted from fully published reports by 2 independent review authors (J.E.S. and G.R.) following prescribed tables developed a priori. Disagreement was resolved by consensus. Descriptive statistics were extracted or calculated for occurrence of UVFP. Cases of bilateral vocal fold paralysis were excluded. A qualitative synthesis of results was performed when applicable. Meta-analysis was performed by calculating pooled proportion of the weighted occurrence for UVFP using DerSimonian–Laird weights for the random effects model. Subgroup analyses developed a priori for postoperative assessment for UVFP and PDA ligation surgery only were conducted. Inverse variance measuring mean difference for the random effects model was used for the analysis of continuous variables. Heterogeneity between studies was tested using the Q statistic with the I² approach. Publication bias was analyzed by visual inspection of the funnel plot and Egger’s test. StatsDirect software 1.7.8 (StatsDirect Limited, Cheshire, UK) and Review Manager 5.1.7 (The Nordic Cochrane Centre, The Cochrane Collaboration, Oxford, UK) were used.

RESULTS

One hundred sixty-two studies were identified through the literature search. Titles and abstracts of these studies...
were screened for the inclusion and exclusion criteria. The search strategy did not include a limit for study design; therefore, many of the studies excluded were comments, editorials, or reviews. A resultant 50 full-text articles were further screened. Thirty-two studies that satisfied the inclusion criteria were included in the analysis (Fig 1).6–37 OCEBM levels of evidence varied from level 3 (9 studies)9–11,14–16,20,23,26 to level 4 (23 studies)6–8,12,13,17–19,21,22,24,25,27–37 (Table 1). Occurrence of UVFP, type of surgery, patient demographics, and vocal fold assessment are reported in Table 1.

Analysis by Type of Surgery

Thirty-two studies involving 5625 patients reported the occurrence of UVFP after any type of cardiothoracic surgery.6–37 The weighted pooled proportion for UVFP was 9.3% (95% CI, 6.6% to 12.5%) (Fig 2). Heterogeneity analysis measured an $I^2$ (inconsistency) of 91.4% (95% CI, 89.3% to 92.9%). This is the percentage of variation across studies that is due to heterogeneity rather than chance. Funnel plot analysis revealed a possible publication bias; Egger’s test showed the presence of bias (bias = 2.5; 95% CI, 1.8 to 3.2; P < .0001).

Twenty-one studies involving 2748 patients reported the occurrence of UVFP after PDA ligation only.7,8,10–15,17,20,21,24,27–31,34–37 The weighted pooled proportion was 8.7% (95% CI, 5.4% to 12.6%) (Fig 3). Heterogeneity analysis measured an $I^2$ of 81.6% (95% CI, 65.0% to 88.4%). Funnel plot analysis and Egger’s test showed the presence of publication bias (bias = 3.3; 95% CI, 2.2 to 4.4; P < .0001).

Analysis for Postoperative Assessment of Vocal Fold Function

Only 10% of patients underwent postoperative vocal fold function assessment. Among patients undergoing any type of cardiothoracic surgery procedure, 11 studies involving 584 patients postoperatively evaluated every patient with flexible nasopharyngolaryngoscopy.6,9–11,14–17,20,22,25 The weighted pooled proportion for UVFP was 29.8% (95% CI, 18.5% to 42.5%) (Fig 4). Heterogeneity analysis measured an $I^2$ of 90.4% (95% CI, 85.2% to 93.1%). Both funnel plot and Egger’s test analyses showed publication bias among the studies (bias = 7.0; 95% CI, 2.3 to 11.7; P = .0079).
<table>
<thead>
<tr>
<th>Author, Year (Country), Years of Study</th>
<th>Type of Surgery</th>
<th>Patient Demographics</th>
<th>Occurrence of UVFP (Cases/Total) (%)</th>
<th>Assessment for Vocal Cord Function</th>
<th>Level of Evidence</th>
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</thead>
<tbody>
<tr>
<td>Dewan et al, 2012 (USA), May 2007–May 2008</td>
<td>All cardiothoracic surgery</td>
<td>+VCP: SA 8.86 ± 5.99 d SW 2.99 ± 0.54 kg − VCP: SA 10.36 ± 6.73 d SW 5.11 ± 0.90 kg</td>
<td>15/76 (19.7%)</td>
<td>Flexible NPL after extubation, swallowing evaluation</td>
<td>4</td>
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<tr>
<td>Rukholm et al, 2012 (Canada), Jul 2003–Jul 2010</td>
<td>PDA ligation</td>
<td>+VCP: GA 25.4 wk (24.9–26.0) BW 745.8 g (685.4–822.1) SA 28.9 wk (28.0–30.0) SW 945.8 g (785.5–1255.2) − VCP: GA 26.7 wk (26.0–27.5) BW 890.0 g (835.4–1121.5) SA 34.0 wk (29.5–38.5) SW 1404.6 g (966.3–1843.3)</td>
<td>19/111 (17.1%)</td>
<td>27.9% NPL postoperative 0.9% NPL preoperative</td>
<td>4</td>
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<tr>
<td>Carpes et al, 2011 (Canada), Nov 2008–Aug 2009</td>
<td>All cardiothoracic surgery</td>
<td>+VCP: SA 0.7 m (0.1–14.2) SW 3.7 kg (3.2–9.2) − VCP: SA 7.8 m (4.1–15.7) SW 7.5 kg (4.9–15.7)</td>
<td>8/100 (8%)</td>
<td>Flexible NPL immediately preoperatively and within 72 h of extubation</td>
<td>3</td>
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<tr>
<td>Benjamin, 2010 (USA), Jan 2004–Dec 2006</td>
<td>PDA ligation</td>
<td>Extremely low BW +VCP: GA 24.5 ± 1.1 wk BW 722 ± 122 g SA 17 ± 8.7 d SW 722 ± 140 g − VCP: GA 24.8 ± 1.3 wk BW 728 ± 152 g SA 22 ± 14.5 d SW 798 ± 219 g</td>
<td>22/55 (40%)</td>
<td>Flexible NPL if suspected VCP</td>
<td>3</td>
</tr>
<tr>
<td>Roksund, 2010 (Norway), 1982–1985 (surgery), 2008–2009 (study)</td>
<td>PDA ligation</td>
<td>GA &lt;28 wk or BW &lt;1000 g +VCP: GA 12 d (4–29) BW 874 ± 138 g SA 12 d (4–29) − VCP: GA 27.1 ± 1.5 wk BW 928 ± 283 g</td>
<td>7/11 (64%)</td>
<td>Flexible NPL and continuous laryngoscopy during maximal treadmill exercise</td>
<td>3</td>
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<tr>
<td>Author, Year (Country), Years of Study</td>
<td>Type of Surgery</td>
<td>Patient Demographics</td>
<td>Occurrence of UVFP (Cases/Total) (%)</td>
<td>Assessment for Vocal Cord Function</td>
<td>Level of Evidence</td>
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<tr>
<td>Sørensen, 2010 (Denmark), 1998–2007</td>
<td>PDA ligation</td>
<td>GA &lt;37 wk GA 26 ± 6.5 wk (23 ± 3 to 34) BW 843.5 g (335–1793) SA 29 ± 4.7 wk (25 ± 6 to 40 ± 4)</td>
<td>3/46 (7%) NR</td>
<td></td>
<td>4</td>
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<tr>
<td>Mandhan, 2009 (New Zealand), Jan 1987–Dec 2005</td>
<td>PDA ligation</td>
<td>SW 1104 g (525–2520) GA 25.5 ± 2.3 wk BW 837 ± 277 2 g SA 14.1 ± 1.8 d SW 881.3 ± 338.1 g</td>
<td>1/145 (0.7%) NR</td>
<td></td>
<td>4</td>
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<tr>
<td>Smith, 2009 (USA), Apr 2004–Oct 2007</td>
<td>PDA ligation</td>
<td>Premature infants: GA 26.6 ± 2.5 wk BW 1000 ± 394 g SA 17 ± 12 d SW &lt;1 kg Flexible NPL</td>
<td>14/86 (16%) Postextubation flexible NPL</td>
<td></td>
<td>3</td>
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<tr>
<td>Spanos, 2009 (USA), 1995–2005</td>
<td>PDA ligation (suture ligature or clip)</td>
<td>Suture ligature: GA 25 ± 2.0 wk BW 740 ± 288 g SW 1054 ± 626 g Clip: GA 24.7 ± 1.3 wk BW 651 ± 169 g SW 762 ± 210 g</td>
<td>15/88 (19%) Flexible NPL after extubation</td>
<td></td>
<td>3</td>
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<tr>
<td>Srinivasan, 2009 (USA)</td>
<td>Norwood procedure</td>
<td>Group 1: SA 10 d (3–218) SW 3.2 kg (2.0–5.7)</td>
<td>4/40 (10%) Flexible NPL all patients in Group 2</td>
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<td>3</td>
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<td>Group 1, 2001–2004</td>
<td></td>
<td></td>
<td>18/40 (45%) (all scoped)</td>
<td></td>
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<td>Group 2, 2005–2007 (standardized management)</td>
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<td>Clement, 2008 (Canada), Oct 2003–May 2004</td>
<td>PDA ligation</td>
<td>SA 6 d (2–64) SW 3.3 kg (2.3–4.3) +VCP: GA 24.8 wk (24–36) BW 7.25 g (5.80–8.87) SA 14.5 d (6–31) –VCP: GA 27.0 wk (25–31) BW 1040 g (700–1540) SW 13.8 d (4–53) Video fluoroscopic swallow study</td>
<td>12/23 (52%) Flexible NPL, 20 pts</td>
<td></td>
<td>4</td>
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<td>Davis, 2008 (USA)</td>
<td>Hypoplastic left heart syndrome, TGA</td>
<td>SA 6.1 ± 3.8 d BW 3.33 ± 0.65 kg SA 0.2 ± 0.0 d</td>
<td>5/27 (18.5%) NR</td>
<td></td>
<td>4</td>
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<tr>
<td>Author, Year&lt;sup&gt;19&lt;/sup&gt; (Country), Years of Study</td>
<td>Type of Surgery</td>
<td>Patient Demographics</td>
<td>Occurrence of UVFP (Cases/Total) (%)</td>
<td>Assessment for Vocal Cord Function</td>
<td>Level of Evidence</td>
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<td>Sachdeva, 2007&lt;sup&gt;19&lt;/sup&gt; (USA), Jan 2000–Jan 2006</td>
<td>All cardiothoracic surgery</td>
<td>SA 13.5 d (1–1604) SW 3.45 kg (0.9–14.5)</td>
<td>38/2255 (1.7%)</td>
<td>NR if all scoped</td>
<td>4</td>
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<tr>
<td>Pereira, 2006&lt;sup&gt;20&lt;/sup&gt; (USA), Mar 2001–Feb 2004</td>
<td>PDA ligation</td>
<td>GA 25 wk BW 740 g SA 23 d SW 914 g</td>
<td>7/81 (11.5%)</td>
<td>Flexible NPL postextubation</td>
<td>3</td>
</tr>
<tr>
<td>Villa, 2006&lt;sup&gt;21&lt;/sup&gt; (France), Sep 1991–Feb 2004</td>
<td>PDA ligation</td>
<td>Low BW infants, 24 pts Low BW infants: 2.1 ± 0.4 kg</td>
<td></td>
<td>NR</td>
<td>4</td>
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<tr>
<td>Khariwala, 2005&lt;sup&gt;22&lt;/sup&gt; (USA), 4 y period</td>
<td>All cardiothoracic surgery</td>
<td>Pediatric</td>
<td>11/48 (23%) UVFP 3/48 (6%) Bilateral VCP</td>
<td></td>
<td>4</td>
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<tr>
<td>Skinner, 2005&lt;sup&gt;23&lt;/sup&gt; (USA), Apr 2003–Dec 2004</td>
<td>Norwood procedure Aortic arch reconstruction</td>
<td>SA 6 d (2–19) SW 3.1 kg (1.9–4.2) SA 9 d (4–33) SW 3.1 (2.0–3.7)</td>
<td>3/33 (9%)</td>
<td>Inpatient ORL consultation Flexible NPL (median 10 d postoperative) Modified barium swallow</td>
<td>3</td>
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<tr>
<td>Vida, 2004&lt;sup&gt;24&lt;/sup&gt; (Italy), Jun 1994–Dec 2002</td>
<td>PDA ligation</td>
<td>SA 45 m (3–161) SW 18 kg (42–70)</td>
<td>1/150 (0.7%)</td>
<td>NR</td>
<td>4</td>
</tr>
<tr>
<td>Einarson, 2003&lt;sup&gt;25&lt;/sup&gt; (Canada), Jan 1998–Dec 1999</td>
<td>All cardiothoracic surgery</td>
<td>Neonates &lt;28 d: SA 7.9 ± 5.6 d (1–25) SW 3.22 ± 0.62 kg (1.5–4.8)</td>
<td>8/101 (8%)</td>
<td>ORL assessment not specified</td>
<td>4</td>
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<tr>
<td>Kohr, 2003&lt;sup&gt;26&lt;/sup&gt; (USA), Mar 1999–Sep 1998</td>
<td>All cardiothoracic surgery</td>
<td>SA 4.8 ± 5.2 y (1 d–16.7 y) SW 19.6 ± 7.1 kg (3.1–72.5) Premature infants excluded</td>
<td>4/50 (8%)</td>
<td>ORL if recommended by speech–language pathologist</td>
<td>3</td>
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<tr>
<td>Liang, 2003&lt;sup&gt;27&lt;/sup&gt; (Taiwan), Mar 1998–May 2001</td>
<td>PDA ligation Subgroup &lt;1 y +VCP: SW 9.0 kg (8.9–9.1) −VCP: SW 10.3 kg (6.2–11.5)</td>
<td>3/18 (16.7%)</td>
<td>Bronchoscopy if hoarseness, inspiratory stridor, or weak cry</td>
<td></td>
<td>4</td>
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<tr>
<td>Niinikoski, 2001&lt;sup&gt;28&lt;/sup&gt; (Finland), 1988–1998</td>
<td>PDA ligation Very low BW infants &lt;1500 g GA 27.2 wk BW 863 ± 339 g SA 12 ± 8 d SW 969 ± 231 g</td>
<td>1/101 (1%)</td>
<td>NR</td>
<td>4</td>
<td></td>
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<tr>
<td>LeBlanc, 2000&lt;sup&gt;29&lt;/sup&gt; (Canada), Jan 1985–Dec 1998</td>
<td>PDA ligation Nonpremature infants Premature infants: GA 26 wk (23–35) BW 847.5 g (400–2300) SA 21 d (4–60) SW 982.5 (475–2740)</td>
<td>3/261 (1.1%)</td>
<td>NR</td>
<td>4</td>
<td></td>
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<tr>
<td>Russell, 1998&lt;sup&gt;30&lt;/sup&gt; (Canada), Jan 1985–Dec 1997</td>
<td>PDA ligation</td>
<td></td>
<td>3/176 (1.7%)</td>
<td>NR</td>
<td>4</td>
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<tr>
<td>Author, Year(^{27}) (Country), Years of Study</td>
<td>Type of Surgery</td>
<td>Patient Demographics</td>
<td>Occurrence of UVFP (Cases/Total) (%)</td>
<td>Assessment for Vocal Cord Function</td>
<td>Level of Evidence</td>
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<tr>
<td>Hawkins, 1996(^{31}) (USA), Jul 1994–Mar 1996</td>
<td>PDA ligation (coil occlusion or surgical closure)</td>
<td>Coil occlusion: SA 4.1 ± 4.9 y (6 m–15 y) SW 18 ± 16 kg Surgical closure: SA 3 ± 3.9 y (4 m–10 y) SW 12 ± 7 kg</td>
<td>0/20 (0%) 1/20 (5%)</td>
<td>NR</td>
<td>4</td>
</tr>
<tr>
<td>Lavoie, 1996(^{32}) (USA), Dates NR</td>
<td>VATS for various procedures</td>
<td>SA 2.65 y (1 d–14.1 y) SW 11.78 kg (580 g–45.9 kg)</td>
<td>1/45 (2.2%)</td>
<td>NR</td>
<td>4</td>
</tr>
<tr>
<td>Rajasinghe, 1996(^{33}) (USA), Jul 1992–Jan 1995</td>
<td>Aortic coarctation and tubular hypoplasia repair</td>
<td>SA 13 d (3–34) and 69 d (61–78) SW 2.9 kg (1.3–5)</td>
<td>1/23 (4.3%)</td>
<td>NR</td>
<td>4</td>
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<tr>
<td>Zbar, 1996(^{34}) (USA), Jan 1991–Jan 1994</td>
<td>PDA ligation</td>
<td>&lt;12 m + VCP: GA 26.3 wk BW 0.9 kg SA 31.9 d SW 1.1 kg VCP: GA 33.8 wk BW 2.3 kg SA 88.4 d SW 5.4 kg</td>
<td>6/98 (6.2%) 22.7% for extremely low BW (&lt;1 kg)</td>
<td>ORL assessment only if symptomatic</td>
<td>4</td>
</tr>
<tr>
<td>Laborde, 1995(^{25}) (USA), Sep 1991–Mar 1995</td>
<td>PDA ligation</td>
<td>&lt;6 m, 70 pts (30%) 6–48 m, 125 pts (54%) &gt;48 m, 37 pts (18%) SW 12.8 kg (1.2–65)</td>
<td>6/230 (2.6%)</td>
<td>Postoperative laryngoscopy</td>
<td>4</td>
</tr>
<tr>
<td>Fan, 1989(^{36}) (USA), Dates NR</td>
<td>PDA ligation</td>
<td>&lt;1300 g</td>
<td>7/167 (4.2%)</td>
<td>Fiberoptic laryngoscopy</td>
<td>4</td>
</tr>
<tr>
<td>Davis, 1988(^{37}) (USA), Jun 1980–Jul 1987</td>
<td>PDA ligation</td>
<td>Premature infants</td>
<td>3/106 (2.8%)</td>
<td>NR</td>
<td>4</td>
</tr>
</tbody>
</table>

BW, birth weight; GA, gestational age; NPL, nasopharyngolaryngoscopy; NR, not reported; ORL, otorhinolaryngology; pts, patients; SA, age at surgery; SW, weight at surgery; TGA, transposition of the great arteries; VATS, video-assisted thoracoscopic surgery; VCP, vocal cord paralysis.
Six studies involving 274 patients postoperatively evaluated every patient with flexible nasopharyngolaryngoscopy after PDA ligation.\textsuperscript{10,11,14,15,17,20} The weighted pooled proportion for UVFP was 39% (95% CI, 18% to 63%) (Fig 5).

Heterogeneity analysis measured an $I^2$ of 93.2% (95% CI, 88.5% to 95.4%). Analysis of the funnel plot by visual

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**FIGURE 2**

UVFP after all types of cardiothoracic surgery (32 studies). Weighted pooled proportion for UVFP was 9.3% (95% CI, 6.6% to 12.5%).
inspection did not suggest publication bias; Egger’s test confirmed its absence (bias = 7.6, 95% CI, −3.4 to 18.5; P = .13).

**Analysis for Demographics**

Five studies involving 354 patients reported birth weights for patients with and without UVFP after surgery.8,10,11,14,17,34 For patients with and without UVFP, birth weights ranged from 725 to 900 g and 728 to 2300 g, respectively. The weighted pooled mean difference between patients with and without UVFP was −201 g (95% CI, −372 g to −30 g) (P = .02) (Fig 6); patients with UVFP were 201 g smaller than those without. Heterogeneity analysis measured an \( I^2 \) of 79%.

Weight at the time of surgery was reported among 6 studies (373 patients) as a comparison for patients with and without UVFP.8,9,27,34 Surgical weight ranged from 846 g to 9000 g among patients with UVFP and 1404 g to 10 300 g for those without. The weighted pooled mean difference was −2820 g (95% CI, −2156 g to −346 g) (P < .0001), showing patients with UVFP to have significantly smaller weights at the time of surgery (Fig 7). Heterogeneity analysis measured an \( I^2 \) of 71%.

Gestational age of patients with and without UVFP was reported among 6 studies involving 399 patients.8,10,11,14,17,34 Among patients with and without UVFP, gestational ages ranged from 24.5 to 27.1 weeks and 24.8 to 33.8 weeks, respectively. The weighted pooled mean difference was −1.1 weeks (95% CI, −1.7 to −0.46 weeks, P = .0007), statistically significantly correlating younger gestational ages with a higher incidence of UVFP (Fig 8). There was low heterogeneity among the studies (\( I^2 = 28\% \)).

Five studies involving 378 patients reported age at the time of surgery for...
FIGURE 4
UVFP after all cardiothoracic surgery in patients who underwent postoperative vocal fold assessment (11 studies). Weighted pooled proportion for UVFP was 29.8% (95% CI, 18.5% to 42.5%).

FIGURE 5
UVFP after PDA ligation only and postoperative vocal fold assessment (6 studies). Weighted pooled proportion for UVFP was 39% (95% CI, 18% to 63%).
patients with and without UVFP.\cite{6,8,9,17,34} Surgical ages ranged from 8.9 to 31.9 days and 10.4 to 237 days, respectively. The weighted pooled mean difference between patients with and without UVFP was $-17.8$ days (95% CI, $-41.8$ to $-6.3$ days, $P = .15$) and not statistically significant (Fig 9). Heterogeneity analysis measured an $I^2$ of 62%.

**Analysis for Duration of Ventilation**

Five studies, comprising 226 patients, reported a comparison of duration of ventilation for patients with and without UVFP.\cite{6,10,11,17,20} The weighted pooled mean difference was not statistically significant (6.88 days; 95% CI, $-22.1$ to $15.9$ days; $P = .13$) (Fig 10). $I^2$ was 51%.

**Analysis for Gastrostomy Tube Use**

A comparison of gastrostomy tube (G-tube) use in patients with and without UVFP was reported among 283 patients in 5 studies.\cite{8,10,17,20,23} The pooled odds ratio was 7.3 (95% CI, 1.6 to 32.8, $P = .010$), suggesting a correlation of G-tube use among patients without UVFP (Fig 11). $I^2$ was 49%.

**Other Analyses**

Additional pooling of data were not possible because of the nonuniform reporting of data among studies included or too few studies that reported the same outcome. Length of stay in hospital was reported in 2 studies.\cite{8,17} Mean length of stay was statistically significantly longer among patients with UVFP in both studies. Dewan et al\cite{6} reported on patients who underwent median sternotomy for cardiac surgery (34.9 ± 29.5 days vs 22.9 ± 14.6 days, $P = .02$), and Clement et al\cite{17} investigated extremely low birth weight infants undergoing PDA ligation (148.2 vs 96.8 days, $P < .001$). Two studies did not report any recovery of vocal fold function at follow-up points.

**FIGURE 6**

Birth weight (6 studies). Weighted pooled mean difference between patients with and without UVFP was $-201$ g (95% CI, $-372$ g to $-30$ g) ($P = .02$).

**FIGURE 7**

Weight at time of surgery (5 studies). Weighted pooled mean difference was $-820$ g (95% CI, $-1564$ g to $-76$ g) ($P = .03$).

**FIGURE 8**

Gestational age (6 studies). Weighted pooled mean difference was $-1.1$ weeks (95% CI, $-1.7$ to $-0.46$ weeks) ($P = .0007$).
Khariwala et al reported a recovery of 11 patients (82%). Carpes et al reported recovery of vocal fold movement in 3 of 7 patients at 3 months' follow-up. Furthermore, Spanos et al reported long-term follow-up (range 1–18 months) for 6 patients with UVFP. Only 2 patients were found to have full recovery. Sachdeva et al reported follow-up in 9 patients with UVFP and found full recovery of function in 3 patients, partial recovery in 4 patients, and no signs of recovery in 2 patients; however, no time frame for follow-up was reported.

**FIGURE 9**

Age at time of surgery (5 studies). Weighted pooled mean difference between patients with and without UVFP was −17.8 days (95% CI, −41.8 to 6.3 days) (P = .15).

**FIGURE 10**

Duration of ventilation (5 studies). Weighted pooled mean difference was 6.88 days (95% CI, −2.1 to 15.9 days), P = .13.

**FIGURE 11**

G-tube use (5 studies). Pooled odds ratio was 7.3 (95% CI, 1.6 to 32.8) (P = .010).

**DISCUSSION**

To our knowledge, this is the first systematic review and meta-analysis to report the pooled occurrence of UVFP after cardiothoracic surgery in infants and children. Among 32 studies, involving 5625 patients, the weighted pooled proportion of UVFP was 9.3%. For those undergoing only PDA ligation, the pooled proportion was 8.7%. However, it is important to consider the occurrence of UVFP in the population of patients who underwent routine postoperative vocal cord function assessment by flexible nasopharyngolaryngoscopy. Only 10% of patients after any type of cardiothoracic surgery or PDA ligation surgery underwent postoperative vocal fold function assessment. The weighted pooled proportion of patients with UVFP in this population was 30% for patients undergoing all types of cardiothoracic surgery and 39% for those undergoing PDA ligation.

These data suggest that the occurrence of UVFP among patients who were postoperatively assessed for vocal fold function is significant. Ninety percent of patients included in our analysis of 32
Methods of Vocal Fold Assessment

Methods of vocal fold assessment generally included assessment with flexible nasopharyngolaryngoscopy, a well-tolerated bedside examination that does not require sedation. Ten studies performed the assessment after extubation.8–11,14–17,20,23 One study did not specify whether patients underwent flexible nasopharyngolaryngoscopy; however, an otorhinolaryngologist assessed all the patients, and therefore we assumed that those needing additional assessment would have undergone the diagnostic laryngoscopy.22 Carpes et al9 also performed the assessment immediately preoperatively. Roksum et al11 assessed patients approximately 25 years after PDA ligation by performing flexible nasopharyngolaryngoscopy and continuous laryngoscopy during maximal treadmill exercise. Three studies also included swallowing assessments.6,7,23

Preoperative assessment of vocal fold function merits discussion. The inherent benefit is the avoidance of attributing the occurrence of UVFP to iatrogenic injury if it is noted preoperatively. However, patients may have associated heart failure, pulmonary failure, and poor respiratory reserve secondary to their cardiac anomaly, which may preclude adequate preoperative evaluation. Preoperative assessment of vocal fold function was reported only in the study from BC Children’s Hospital.8 The authors performed flexible laryngoscopy immediately before surgery in the operating room and within 72 hours after extubation. Twenty-four (15%) patients could not undergo preoperative assessment because of endotracheal intubation, and 4 (2.5%) were found to have UVFP preoperatively and were excluded from their study. Additional techniques for vocal fold function assessment may include extubation followed by direct laryngoscopy and rigid bronchoscopy, laryngeal electromyography, or laryngeal ultrasound. The authors reported this technique to be a safe, operator-friendly method for determining the likelihood of function return in a variety of patients, including those who had undergone PDA ligation. The mean patient age was 21.4 months. Wang et al40 reported the usefulness of laryngeal ultrasound for vocal fold assessment. They showed maximum glottic angle and vocal fold–arytenoid angle to be quantitative ultrasonographic indicators of vocal fold immobility among 45 children of median age 4 years and 6 months (range 9 months–13 years). However, the efficacy of laryngeal electromyography or ultrasound has not been described in neonates or infants, nor has it been used in the intubated patient.

Risk Factors

UVFP was shown to be statistically significantly associated with younger gestational age, lower birth weight, and lower surgical weight among the limited number of studies that reported these outcomes. Age at time of surgery was not a significant risk factor for UVFP. Length of mechanical ventilation was not significantly different between groups. G-tube use was statistically significantly higher among patients without UVFP. These analyses are based on limited patient numbers because of the small number of studies that reported these outcomes by presence or absence of UVFP.

Patients who need congenital cardiac surgery often have multiple comorbidities. Two studies8,11 reported associations between bronchopulmonary dysplasia and UVFP after PDA ligation. Roksum et al11 reported outcomes for 11 patients; bronchopulmonary dysplasia was present in 86% of patients with UVFP and 50% of those without UVFP (P < .001). Among 111 patients, Rukholm et al8 reported 74% of patients with UVFP to have bronchopulmonary dysplasia, compared with 47% of those without UVFP (P = .043); however, given the Bonferroni method of statistical analysis for multiple comparisons, only P < .006 was considered significant. This retrospective study from our center at McMaster University showed only gastroesophageal reflux disease to be statistically significantly associated with UVFP after PDA ligation, and not G-tube feeding, sepsis, pneumonia, retinopathy of prematurity, or anemia of prematurity.8 Benjamin et al10 compared neurodevelopmental outcomes between patients with and without UVFP after PDA ligation and found no significant difference between groups.

Surgical technique for PDA ligation and its correlation with occurrence of UVFP has also been investigated. Spanos et al15 compared rates of paralysis between vascular clip and suture ligation procedures in a prospective study and found similar incidence of UVFP in both groups (19% vs 20%). All cases of UVFP were in infants who weighed < 1 kg at birth. Zbar et al34 showed iatrogenic UVFP to be associated only with the use of surgical clips and not suture; however, the authors determined that it was not possible to establish a plausible correlation because clips were
used in 91% of premature infants who needed PDA ligation. Carpes et al reported the use of cautery in 8 (100%) patients with UVFP, compared with 60 (65%) patients without UVFP. Additional inquiry in regard to surgical technique and perhaps operator learning curve may be warranted.

**Study Weaknesses**

The inherent weakness of our study is due to the heterogeneity that is introduced when data are pooled from studies with nonuniform patient populations and methods. Variability in the type of surgery (PDA ligation versus other cardiothoracic surgery), vocal fold assessment, and patient demographics contributes to this weakness. The random effects model for statistical analysis and a priori subgroup analyses were undertaken to account for some of these limitations.

Case series were the most common type of study. This study type satisfied the criteria for level 4 evidence according to the OCEBM; future studies should be aimed toward higher levels of evidence. Significant publication bias was detected for all analyses (type of surgery and postoperative vocal fold assessment) except for the subgroup of 6 studies that included patients who underwent PDA ligation only and routine postoperative assessment.

**Recovery of Vocal Fold Function**

Recovery of vocal fold function warrants discussion. From the studies included in this analysis, 2 studies reported no recovery at follow-up points of 6 and 5 to 19 months, respectively. The population of patients with vocal fold paralysis in these studies was 6 and 7 patients, respectively. Zbar et al hypothesized that their high rate of nonrecovery resulted from the surgical clipping technique. Conversely, Khariwala et al reported a recovery rate of 82% (9 of 11 patients) among their single-center retrospective review of patients undergoing surgical repair of congenital cardiac defects, attributing the rate of recovery to stretching of the recurrent laryngeal nerve and subsequent return of full function. The time frame for this recovery ranged from 8 weeks to 10 months. Carpes et al also reported recovery of vocal fold movement in 3 of 7 patients at 3 months’ follow-up. Spanos et al reported long-term follow-up of 6 patients with UVFP. Follow-up ranged from 1 to 18 months, and of the 6 patients, only 2 were found to have full recovery. Sachdeva et al reported follow-up in 9 patients with UVFP and found recovery of function in 3 patients, partial recovery in 4 patients, and no signs of recovery in 2 patients. Although excluded from our current analysis because their study population included only patients with UVFP, Truong et al reported a retrospective case series to determine the rate of recovery of pediatric vocal fold paralysis after cardiac surgery. They reported that 28 (35%) patients recovered function, with a median time from diagnosis to recovery of 6.6 months, and that 52 (65%) of patients had persistent paralysis, with a median follow-up time of 16.4 months. Furthermore, the authors reported that premature patients were significantly less likely to recover vocal fold function. Given the wide variation of results, additional investigation is needed to adequately determine recovery of vocal fold function after cardiac surgery. However, it should be noted that recovery of UVFP has been reported as late as 11 years after the initial surgery; therefore, the results showing poor recovery may simply reflect follow-up time that is too short.

**Surgical Management of UVFP**

Early identification of UVFP would allow subsequent surgical interventions such as medialization laryngoplasty (injection or surgical) or laryngeal reinnervation if appropriate. Injection medialization laryngoplasty was reviewed in 13 patients (27 injections) with a variety of injectable materials (Gelfoam, Radiesse Voice Gel). Cohen et al demonstrated the procedure to be a safe and effective treatment for carefully selected patients. Subjective or objective symptom improvement was experienced in 24 of 27 months. Zur reported her recent success with recurrent laryngeal nerve reinnervation using the ansa cervicalis for unilateral vocal fold immobility in children. Among 10 children (9 of whom had previous PDA ligation), 7 demonstrated physiologic frequency range improvement at 6 months’ follow-up. Median time from injury to repair was 64.5 months. Paniello et al reported the results of a multicenter randomized controlled trial comparing medialization laryngoplasty with laryngeal reinnervation and showed older patients to be better suited for laryngoplasty, whereas reinnervation was better suited for younger patients. Given these possible surgical interventions, adequate postoperative assessment of vocal fold function is warranted to identify patients who may benefit from these procedures. However, conservative management including voice therapy should always be considered before surgical intervention.

**CONCLUSIONS**

UVFP is a demonstrated risk of cardiothoracic surgery among infants and children. Pooled analysis suggests that it may be associated with a younger gestational age and lower birth weight and weight at time of surgery. Routine postoperative nasopharyngolaryngoscopy for vocal cord assessment by an otolaryngologist is suggested.
REFERENCES


Unilateral Vocal Fold Paralysis After Congenital Cardiothoracic Surgery: A Meta-analysis
Julie E. Strychowsky, Gavin Rukholm, Michael K. Gupta and Diane Reid
*Pediatrics* 2014;133:e1708; originally published online May 19, 2014; DOI: 10.1542/peds.2013-3939

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