Review article

Does Frenotomy Improve Breastfeeding Difficulties in Infants with Ankyloglossia?

Running title: Frenotomy in Infants with Ankyloglossia

Footnote: This article is based on a study first reported in the Journal of the Japan Pediatric Society 2014; 118: 462-474, titled “Effectiveness of frenotomy in breastfeeding difficulties in infants with ankyloglossia: Systematic Review” (in Japanese).

Yasuo Ito, MD PhD

Department of Pediatrics and Pediatric Surgery, International University of Health and
Abstract

Background: The aim of this systematic review was to critically examine the existing literature regarding the effectiveness of tongue-tie division in infants with ankyloglossia by the new rating system of GRADE (Grades of Recommendations, Assessment, Development, and Evaluation).

Methods: A clinical question was structured according to PICO (Patient, Intervention, Comparison, and Outcome) as follows: In infants with poor breastfeeding and ankyloglossia (patient), does frenotomy (intervention) compared to lactation support alone (comparison) improve feeding (outcome)? An electronic literature search was systematically conducted from databases including PubMed, Japana Centra Revuo
Medicina (Igaku Chuo Zasshi), CINAHL, and Cochrane Library using the key words "ankyloglossia,” “tongue-tie,” “frenotomy,” and/or “breastfeeding” in English and equivalent terms in Japanese.

Results: The literature search yielded 4 randomized clinical trials, and 12 observational studies for analysis. The quality of the literature was rated in regard to the two most important outcomes (sucking/latching, and nipple pain) and five less important outcomes (milk supply/ milk production, continuation of breastfeeding, weight gain, adverse events, and dyad distress) in accordance with the GRADE system. Evidence levels of the most important outcomes were rated either A (strong evidence) or B (moderate evidence), and less important outcomes were rated C (weak evidence); every outcome consistently showed a favorable effect of a frenotomy on breastfeeding.

Conclusions: The literature review supported an overall moderate quality of evidence for the effectiveness of a frenotomy for the treatment of breastfeeding difficulties in infants with ankyloglossia. No major complications from a frenotomy were reported.

Key words: ankyloglossia, breastfeeding, frenotomy, GRADE, systematic review
Background

Ankyloglossia or tongue-tie is a congenital oral condition characterized by an abnormally short and thick lingual frenulum, which restricts tongue movement. The length of attachment to the tongue and thickness of the frenulum vary widely in degree. It is often classified into mild “partial ankyloglossia,” which is common, and severe as well as rare “complete ankyloglossia” where the tongue is fused to the floor of the mouth.\footnote{1} The diagnosis is primarily based on the appearance of the tongue and its functional disturbances caused by restricted tongue movement. However, at present, there is no agreement on the clinical criteria for diagnosis.

The effect of ankyloglossia on breastfeeding has been a subject of controversy for many years. However, ankyloglossia has become of increased clinical concern in the past two decades because of the resurgence of breastfeeding.\footnote{2} Many lactation consultants\footnote{3} believe that ankyloglossia can cause breastfeeding difficulties and that a frenotomy is the treatment of choice. Conversely, pediatricians\footnote{3} have been the most skeptical about its effect. The Japan Pediatric Society also takes the stand that ankyloglossia does not cause feeding difficulties; therefore, a frenotomy is not necessary in infancy.\footnote{4}
During the last decade, many high-quality studies including four randomized controlled trials (RCTs) \(^5\text{-}^8\) have demonstrated a favorable effect of frenotomy on breastfeeding problems related to ankyloglossia. The aim of this systematic review was to critically examine the existing literature regarding the effectiveness of tongue-tie division in infants with ankyloglossia by the new rating system of GRADE (Grading of Recommendations Assessment, Development, and Evaluation).\(^9\)

**Methods**

The review was performed by rating the level of evidence in accordance with the GRADE handbook.\(^10\)

**Structured clinical question**

A clinical question was structured according to PICO (Patient, Intervention, Comparison, and Outcome) as follows: In infants with poor breastfeeding and ankyloglossia (patient), does frenotomy (intervention), compared to lactation support alone (comparison), improve feeding (outcome)?

**Selection criteria of patients**

This article is protected by copyright. All rights reserved.
Literature focused on neonates and infants younger than 6 months of age who had breastfeeding problems and ankyloglossia was selected for analysis. Patients who suffered from other oral anomalies and disturbances of the central nervous system were excluded from the review.

*Primary outcome measures*

The primary outcome measures regarding breastfeeding problems associated with ankyloglossia and their relative importance are listed in Table 1. Sucking/latch and nipple pain were rated as the most important outcomes, because these two outcomes were considered to be the main reasons to abandon breastfeeding. Milk supply/ milk production, continuation of breastfeeding, weight gain, adverse events, and dyad distress were rated as relatively less important outcomes. The quality of the literature was assessed in regard to the two most important outcomes and the five important outcomes according to the GRADE system.

*Search strategy*

An electronic literature search was systematically performed using databases including PubMed (January 1966-April 2013), Japana Centra Revuo Medicina (Igaku Chuo Zasshi,
January 1983-April 2013), CINAHL, and Cochrane Library using the key words “ankyloglossia,” “tongue-tie,” frenotomy,” and/or “breastfeeding” in English and equivalent terms in Japanese. The search was limited to articles written in English and Japanese.

Selection criteria of literature

Selection criteria included RCTs and observational studies (cohort studies, case-controlled studies, and case series), which match the selection criteria of the patients. Case reports, case series with less than 10 subjects, opinion articles without patient data, literature reviews, Q&As, and letters to the editor were excluded.

Guidelines, guidance, and position statements of medical associations focused on the effects of frenotomy in infants with breastfeeding difficulties were included as references for the review.

Qualitative assessment of literature

The literature was divided into two groups: RCTs (high quality group) and observational studies (low quality group). In regard to the RCTs, downgrade factors of evidence level (risk of bias) such as blinding, ITT (intention-to-treat), incomplete outcome data,

This article is protected by copyright. All rights reserved.
selective reporting, and other bias were assessed. Conversely, for the observational studies, upgrade factors such as large effect, dose-dependent gradient, and plausible confounders were assessed as well as the risk of bias.

Statistical analysis

Meta-analysis was carried out using Review Manager (RevMan ver. 5.2) of the Cochrane Collaboration. Effect size was measured by risk ratio in dichotomous data and mean difference in continuous data with 95% confidence intervals (95% CI).

Results

Collected data

A total of 505 titles and abstracts were retrieved with the initial search terms of ankyloglossia or tongue-tie. Via the secondary search, relevant full-texts were obtained for 114 articles, using the search with terms of “frenotomy,” “frenuloplasty.” or “breastfeeding.” According to the exclusion criteria, case reports with less than 10 subjects, expert opinions, reviews, Q&As, and letters to the editor were eliminated.

After adding 4 articles by hand-searching, 4 RCTs, 12 observational studies, NICE guidance, a guideline of the Academy of Breastfeeding Medicine (ABM), and a...
position statement of the Canadian Paediatric Society\textsuperscript{26} met the criteria for the review (Figure 1).

\textit{Assessment of literature}

The results of qualitative assessment of literature for each outcome are as follows:

\textbf{Sucking/latch}

There were 4 RCTs, including one non-blinded,\textsuperscript{5} one single-blinded,\textsuperscript{7} and two double-blinded\textsuperscript{6,8} studies (Table 2). There was significant improvement in overall assessment of breastfeeding assessed by mothers in the frenotomy group, compared to the placebo group in the two studies.\textsuperscript{5,8} The mother’s subjective outcome measures included not only efficiency of the latch but also factors such as nipple pain and feeding cycle. The results of a double-blinded study by Berry et al.\textsuperscript{8} were less significant ($P < 0.02$), reflecting a placebo effect in comparison to those of a non-blinded study by Hogan et al.\textsuperscript{5} ($P < 0.001$). There was no significant difference between pre-frenotomy and post-frenotomy in LATCH (latch, audible swallowing, type of nipple, comfort, and hold) scores\textsuperscript{27} (minimal difficulties: 10 points; $P = 0.06$).\textsuperscript{6} However, significant improvement was demonstrated in the score of Infant Breast Feeding Assessment Tool (IBFAT; maximum score: 15 points)\textsuperscript{28} following tongue-tie division ($P = 0.029$).\textsuperscript{7} The

This article is protected by copyright. All rights reserved.
LATCH score includes nipple pain as an assessment item; however, the IBFAT score does not.

In observational studies, sucking/latch immediately improved in 57-92% after frenotomy, and in approximately 90% after 1-2 weeks. Assessment by LATCH score in two studies showed significant improvement post-treatment ($P < 0.0001$; $P < 0.05$).

Milk supply/milk production

There was only one observational study on milk intake and milk production (Table 3). Milk transfer (ml/min) was examined in 24 patients before and after frenotomy, and a significant increase was observed one week after frenotomy ($P < 0.01$). The 24-hour milk production (g) was measured in six mothers, and a significant increase was also observed in these women one week after frenotomy ($P = 0.035$).

Nipple pain

There were three blinded RCTs on maternal nipple pain (Table 4). Two were assessed by a standard visual analogue pain scale (maximum score: 10 points); one reported significant improvement following tongue-tie release ($P = 0.001$); however, no
significant difference between a frenotomy and a sham operation was noted in the other\textsuperscript{8} ($P = 0.13$). However, a study of nipple pain\textsuperscript{7} using the short-form McGill pain questionnaire (SF-MPQ,\textsuperscript{30} maximum score: 50 points) demonstrated marked improvement in the frenotomy group compared to the sham group, despite a placebo effect ($P < 0.001$).

Of five observational studies,\textsuperscript{13, 16, 17, 21, 22} significant improvement in the pain score was reported in three studies ($P < 0.0001$; $P < 0.05$; $P < 0.01$); one study\textsuperscript{16} also reported improvement in the Short-Form McGill Pain Questionnaire (SF-MPQ) after frenotomy ($P < 0.0001$).

Continuation of breastfeeding

There were eight reports\textsuperscript{5, 8, 12, 14, 16, 18, 19, 23} that discussed continuation of breastfeeding more than three months after frenotomy; however, they contained no controls. The continuation rate of breastfeeding ranged from 43\%\textsuperscript{19} to 78\%\textsuperscript{18} at the three-month follow-up, which was a rate of nearly twice the UK national average of 29\%\textsuperscript{8} at 4 months of age.
Weight gain

There was only one report\textsuperscript{21} that dealt with weight gain (Table 5). It noted that the neonates had gained significant weight by 15 centiles two weeks post-frenotomy ($P < 0.0001$).

Adverse events

A total of 1,795 patients from the included articles\textsuperscript{5-8, 12-23} underwent frenotomy without any major adverse events. Minor bleeding was usually readily controlled by applying gentle pressure to the site with a sponge. Among the collected articles, one article reported two cases of hemorrhagic shock following frenotomies in Nigeria; one was performed by a traditional birth attendant and the other was performed by an untrained community health worker.\textsuperscript{31}

Dyad distress

There were no reports that specifically discussed distress of the infant or the mother. Breastfeeding stress was included as a part of the overall assessment by the mother regarding sucking and latch.
Guidelines, guidance, and position statement

In 2004, the Academy of Breastfeeding Medicine (ABM) developed “Guidelines for the Evaluation and Management of Neonatal Ankyloglossia and its Complications in the Breastfeeding Dyad”\textsuperscript{25} based on observational studies up to 2002. They reported that, although conservative management of tongue-tie is usually sufficient, frenotomy may be considered appropriate for partial ankyloglossia, and if necessary, the procedure should be performed by an experienced physician or pedodontist.

In 2005, the National Institute for Clinical Excellence (NICE) of the UK issued an interventional procedure overview regarding division of ankyloglossia in infants with breastfeeding difficulties.\textsuperscript{24} They referenced data from an unpublished RCT report by Hogan et al.\textsuperscript{5} In the guidance, they noted that current evidence suggests that there are no major safety concerns about division of ankyloglossia, and the procedure can improve breastfeeding. However, they cautioned that to date the evidence was limited.

A position statement of the Canadian Paediatric Society\textsuperscript{26} was published in 2011, which referenced a RCT by Hogan et al.\textsuperscript{5} However, it did not reference a double-blinded RCT by Dollberg et al.\textsuperscript{6} in 2006. The position statement noted that frenotomy is not
commonly recommended; however, if an association between significant tongue-tie and major breastfeeding problems is clearly identified and surgical intervention is deemed necessary, frenotomy should be performed by a clinician experienced with the procedure. The American Academy of Pediatric Dentistry also expresses a similar position in its “Guideline on Pediatric Oral Surgery,” formulated in 2010. It notes that frenuloplasty or frenectomy may be a successful approach to facilitate breastfeeding when indicated. Subsequently, two more blinded RCTs were reported. However, to date, no guidelines based on this new evidence have been published.

Discussion

The quality of the literature was rated in regard to the two most important outcomes (sucking/latch and nipple pain) and five relatively less important outcomes (milk supply/milk production, continuation of breastfeeding, weight gain, adverse events, and dyad distress) according to the GRADE system.

Sucking or latch was difficult to assess independently from other outcomes because maternal subjective outcome measures included nipple pain, feeding time, infant satisfaction, and maternal distress. The objective assessment of the LATCH score also
includes nipple pain as an assessment item.

A RCT by Berry et al.\textsuperscript{8} and a RCT by Hogan et al.\textsuperscript{5} were both reported from the same institution, but on different subjects. The RCT by Berry et al.\textsuperscript{8} was double-blinded to supplement the weakness of the earlier non-blinded study.\textsuperscript{5} Meta-analysis of these two RCTs indicated strong evidence (risk ratio: 2.88; 95% CI: 1.82, 4.57) in favor of the frenotomy group compared to the placebo group (Figure 2a). Meta-analysis of two observational studies\textsuperscript{16,17} of LATCH scores also supported the effectiveness of frenotomy (mean difference: 2.07; 95% CI: 1.64, 2.49) (Figure 2b).

Geddes et al.\textsuperscript{17} researched tongue movement during breastfeeding using submental ultrasonography, and demonstrated that milk flowed into the infants mouth from the mother’s nipple by negative pressure created by up and down movements of the infant’s tongue. In tongue-tie babies, these actions were disturbed, and the nipple remained compressed by the baby’s tongue. Release of the tongue-tie reduced the nipple compression. The rate of milk transfer increased by almost two-fold and 24 hour-milk production also increased in a week.
Of three blinded RCTs6-8 evaluating nipple pain, one6 assessed by pain score and one assessed by SF-MPQ7, reported significant improvement of nipple pain immediately after frenotomy, compared with pre-operative pain or pain following a sham operation. Meta-analysis of three observational studies13,17,22 also demonstrated a marked decrease of nipple pain with a mean difference of -5.10 (95% CI: -5.60, -4.59) in the frenotomy group, compared to the placebo group (Figure 2c).

The continuation rate of breastfeeding three months after frenotomy12,14,16,18,19 was 2 times higher than that of the average rate of 4-month-old infants in the UK.14 Weight significantly increased after frenotomy by centile in two weeks.21 There were no major adverse events when the procedure was performed by an experienced healthcare professional. In addition, a frenotomy is an inexpensive procedure; thus, it has minimal impact on healthcare costs.

The results of this systematic review are summarized in the evidence profile (Table 6). The results of outcomes consistently showed the effectiveness of a frenotomy for breastfeeding difficulties. Evidence levels of the most important outcomes (sucking/latch and nipple pain), presented by RCTs and meta-analysis of observational

This article is protected by copyright. All rights reserved.
studies, were rated either A (strong evidence) or B (moderate evidence), the other four
important outcomes were rated C (weak evidence) because they were purely
observational studies, contained a small number of subjects, and/or lacked controls.

Further RCTs with long-term follow-up are indicated; however, this type of study is
always impacted by ethical problems. In addition, it is impossible to conceal a
frenotomy or sham operation from the mother for a long period of time.

Among existing guidelines, guidance statements, and position statements, NICE’s
guidance\textsuperscript{24} is the only one that was formulated by a systematic review; however, it is a
brief overview and not definitive. Despite limited evidence, NICE’s guidance
recommended frenotomy in infants with breastfeeding difficulties associated with
ankyloglossia. After the publication of the guidance, three more RCTs\textsuperscript{6-8} were
published; they strengthened the evidence level, which was lacking in NICE’s overview.

Our literature review found an overall moderate quality of evidence regarding the
effectiveness of tongue-tie division for the treatment of breastfeeding difficulties in
infants with ankyloglossia. There were no major complications from frenotomies, most
likely because they were performed by well-trained healthcare professionals.
To formulate more comprehensive guidelines, a group of professionals from all the relevant fields need to collaborate. The present study should offer the necessary means and information for a collaborative project.

Conclusions

A systematic review based on the GRADE system was conducted to examine the clinical question: Does a frenotomy improve breastfeeding difficulties in infants with ankyloglossia? In accordance with the exclusion and inclusion criteria, 4 randomized clinical trials and 12 observational studies were included in this review. The evidence levels of the two most important outcomes (sucking/latch and nipple pain) were rated either A (strong evidence) or B (moderate evidence); the other 4 less important outcomes were rated C (weak evidence), and every outcome consistently showed the effectiveness of a frenotomy for breastfeeding difficulties. No serious adverse events were reported. In conclusion, the answer to the clinical question is: Frenotomy does improve breastfeeding difficulties in infants with ankyloglossia. Further collaborative work is indicated to formulate more comprehensive guidelines.
Acknowledgements

The author is grateful to Hideki Kinugasa, Ph.D., Professor of Biostatistics and Clinical Epidemiology, University of Toyama Graduate School of Medicine and Pharmaceutical Sciences, for his statistical supports, and to Masahiro Yoshida, M.D. PhD., Chief of Medical Information Network Distribution Service of Japan Council for Quality Health Care, for his editorial advices on the GRADE system.

The author receives no financial support for this study and there are no conflicts of interest.
References


7 Buryk M, Bloom D, Shope T. Efficacy of neonatal release of ankyloglossia: a

8 Berry J, Griffiths M, Westcott C. A double-blind, randomized, controlled trial of
tongue-tie division and its immediate effect on breastfeeding. Breastfeed Med. 2012;
7: 189-193.

9 Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating

10 Schünemann H, Broek J, Oxman A (ed). GRADE Handbook for grading the quality
of evidence and the strength of recommendations. (Version 3.2, updated March,
2009) [Cited on 19 April 2013] Available from URL:
http://www.who.int/hiv/topics/mtct/grade_handbook.pdf

11 The Cochrane Collaboration. Cochrane Handbook for systematic review of
interventions (Version 5.1.0, 2011) . [Cited on 19 April 2013] Available from URL:
http://handbook.cochrane.org/

12 Masaitis NS, Kaempf JW. Developing a frenotomy policy at one medical center: a

13 Ballard JL, Auer CE, Khoury JC. Ankyloglossia: assessment, incidence, and effect


24 National Institute for Health and Care Excellence. Interventional procedure guidance 149. Division of ankyloglossia (tongue-tie) for breast feeding. [Cited on 19 April 2013] Available from URL:
http://publications.nice.org.uk/division-of-ankyloglossia-tongue-tie-for-breastfeeding-ipg149/the-procedure#indications

(http://www.bfmed.org/Media/Files/Protocols/ankyloglossia.pdf)


This article is protected by copyright. All rights reserved.


32 American Academy of Pediatric Dentistry. Guideline on pediatric oral surgery. [Cited on 7 May 2013] Available from URL:

http://www.aapd.org/search/?Keywords=Ankyloglossia
Legends to figures and tables

**Figure 1.** Flow diagram for selection of publications.

**Figure 2.** Meta-analysis of breastfeeding.

a: Overall improvement evaluated by mother; b: Latch evaluated by LATCH score; c: Nipple pain evaluated by pain score

**Table 1.** Outcomes of Evaluation and Relative Importance

**Table 2:** Sucking/Latch (Most Important Outcome): RCT

**Table 3:** Milk Supply/Milk Production (Important Outcome): Observational study

**Table 4:** Nipple Pain (Most Important Outcome): RCT

**Table 5:** Weight Gain (Important Outcome): Observational study

**Table 6:** Evidence Profile
Table 1. Outcomes for Evaluation and Relative Importance

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucking/latch</td>
<td>Most important</td>
</tr>
<tr>
<td>Milk supply/milk production</td>
<td>Important</td>
</tr>
<tr>
<td>Nipple pain</td>
<td>Most important</td>
</tr>
<tr>
<td>Continuation of breastfeeding</td>
<td>Important</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Important</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Important</td>
</tr>
<tr>
<td>Dyad distress</td>
<td>Important</td>
</tr>
</tbody>
</table>
Table 2. Sucking/Latch (Most Important Outcome): RCT

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Age</th>
<th>No. of participants</th>
<th>Follow up</th>
<th>Risk of Bias</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Participant</td>
<td>ITT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Provider</td>
<td>Data collector</td>
</tr>
<tr>
<td>Hogan 2005</td>
<td>3-70 d/o</td>
<td>frenotomy (n=20) placebo (n=20)</td>
<td>48 hours</td>
<td>⚫</td>
<td>⚫</td>
</tr>
<tr>
<td>Dollberg 2006</td>
<td>1-21 d/o</td>
<td>frenotomy (n=14) sham op (n=11)</td>
<td>immediate</td>
<td>☚</td>
<td>☚</td>
</tr>
<tr>
<td>Bury 2011</td>
<td>&lt;30 d/o</td>
<td>frenotomy (n=30) sham op (n=28)</td>
<td>immediate</td>
<td>☚</td>
<td>☚</td>
</tr>
<tr>
<td>Berry 2012</td>
<td>&lt;3m/o</td>
<td>frenotomy (n=27) sham (n=30)</td>
<td>immediate</td>
<td>☚</td>
<td>☚</td>
</tr>
</tbody>
</table>

ITT: Intention to treat; Risk of bias (downgrade factor) (⚪: high risk of bias; ⚫: low risk of bias);
LATCH score 27 (Latch, Audible swallowing, Type of nipple, Comfort (breast/nipple), Hold (positioning/help; minimal difficulty: 10 points);
IBFAT score 28 (Infant Breast Feeding Assessment Tool; maximum score: 15 points)
Table 3. Milk Supply/Milk production (Important Outcome): Observational Study

<table>
<thead>
<tr>
<th>Characteristics of Included Studies</th>
<th>Risk of Bias</th>
<th>Upgrade factor</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author/Year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geddes et al. 2008</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Age: Ave. 3d/0</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>No. of participants: 24</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Follow-up: &gt;1 week</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>ITT</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Selective reporting</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Other bias</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Large effect</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Dose-dependent gradient</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Plausible confounder</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Effects</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Results</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Frenotomy</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Control</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
<tr>
<td>Mean difference [95% CI]</td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
</tr>
</tbody>
</table>

| Milk transfer (ml/min) (n=24)       | ![Image](https://via.placeholder.com/150) | ![Image](https://via.placeholder.com/150) | ![Image](https://via.placeholder.com/150) |
| Mean difference [95% CI]            | ![Image](https://via.placeholder.com/150) | ![Image](https://via.placeholder.com/150) | ![Image](https://via.placeholder.com/150) |

Upgrade factor (L: large effect; N/A: not applicable). See Table 2 for other abbreviations.
Table 4. Nipple Pain (Most Important Outcome): RCT

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>No. of participants</th>
<th>Follow up</th>
<th>Blinding</th>
<th>ITT</th>
<th>Incomplete outcome data</th>
<th>Selective reporting</th>
<th>Other bias</th>
<th>mean ± SD</th>
<th>Effects</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dollberg</td>
<td>2006</td>
<td>1-21</td>
<td>d/o frenotomy (n=14)</td>
<td>immediate</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>5.3±2.2</td>
<td>7.1±1.9</td>
<td>1.80 [0.28,3.32]</td>
</tr>
<tr>
<td>Buryk</td>
<td>2011</td>
<td>&lt;30</td>
<td>d/o frenotomy (n=30)</td>
<td>immediate</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>4.9±1.46</td>
<td>16.77±1.88</td>
<td>-11.87 [-12.72, -11.02]</td>
</tr>
<tr>
<td>Berry</td>
<td>2012</td>
<td>&lt;=3</td>
<td>m/o frenotomy (n=14)</td>
<td>immediate</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>▲</td>
<td>-2.5±1.9</td>
<td>-1.3±1.5</td>
<td>-1.20 [-2.47, 0.07]</td>
</tr>
</tbody>
</table>

Pain score: standard visual analogue pain scale\(^{29}\) (maximum score 10 points); SF-MPQ: short-form McGill pain questionnaire\(^{30}\) (maximum score 50 points). See Table 2 for other abbreviations.
Table 5. Weight Gain (Important Outcome): Observational Study

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Age</th>
<th>No. of participants</th>
<th>Follow-up</th>
<th>Blinding</th>
<th>ITT</th>
<th>Incomplete outcome data</th>
<th>Selective reporting</th>
<th>Other bias</th>
<th>Risk of Bias</th>
<th>Upgrade Factor</th>
<th>Summary of Findings</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miranda 2010</td>
<td>12-36 d/o</td>
<td>62</td>
<td>2 weeks</td>
<td>⚫</td>
<td>⚫</td>
<td>⚫</td>
<td>⚫</td>
<td>⚫</td>
<td>⚫</td>
<td>VL</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Upgrade factor (VL: very large effect). See tables 2 and 3 for abbreviations.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Design, No.</th>
<th>Risk of Bias (RoB)</th>
<th>Bias across Studies</th>
<th>Overall Quality of Evidence</th>
<th>Summary of Findings (SoF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucking / latch</td>
<td>RCT, 4</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>Observational study, 12</td>
<td>×</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Milk supply/milk production</td>
<td>Observational study, 1</td>
<td>△</td>
<td>○</td>
<td>○</td>
<td>△</td>
</tr>
<tr>
<td>Nipple pain</td>
<td>RCT, 3</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>Observational study, 5</td>
<td>×</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Continuation of breastfeeding</td>
<td>Observational study, 8</td>
<td>×</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Observational study, 16</td>
<td>△</td>
<td>○</td>
<td>○</td>
<td>△</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Observational study, 16</td>
<td>△</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

Bias risk: ○ not serious, △ serious, × very serious, Strength of evidence: A strong, B moderate, C weak, D very weak

*See Figure 2a, † See Figure 2b, ‡ See Figure 2c
Figure 1. Flow diagram for selection of publications

Publications with the term “ankyloglossia” or “tongue-tie” in English and Japanese (n = 505)

Publications with the term “frenotomy,” “frenuloplasty,” or “breastfeeding” in English and Japanese (n = 114)

Added:
Observational studies (CINAHL)  n = 2
Guidance (NICE)                  n = 1
Guideline (hand search)          n = 1

Excluded:
Case report (<10 subjects),
expert opinion, review, Q&A,
letter to the editor (n=99)

RCT                              n = 4
Observation studies             n = 12
Guidance                        n = 1
Guideline                       n = 1
Position statement              n = 1
a: Overall improvement evaluated by mother

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Frenotomy Events</th>
<th>Placebo Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berry 2012</td>
<td>21</td>
<td>14</td>
<td>30</td>
<td>1.67 [1.08, 2.57]</td>
</tr>
<tr>
<td>Hogan 2005</td>
<td>19</td>
<td>1</td>
<td>20</td>
<td>19.00 [2.81, 128.69]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>47</td>
<td>50</td>
<td>100%</td>
<td>2.88 [1.82, 4.57]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 9.89, df = 1 (P = 0.002); I² = 90%
Test for overall effect: Z = 4.50 (P < 0.00001)

---

b: Latch evaluated by LATCH score

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Post-frenotomy Mean</th>
<th>Pre-frenotomy Mean</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geddes 2008</td>
<td>9.4</td>
<td>7.9</td>
<td>1.50 [0.85, 2.15]</td>
</tr>
<tr>
<td>Srinivasan 2006</td>
<td>9.2</td>
<td>6.7</td>
<td>2.50 [1.93, 3.07]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>51</td>
<td>51</td>
<td>2.07 [1.64, 2.49]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 5.22, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 9.52 (P < 0.00001)

---

c: Nipple pain evaluated by pain score

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Post-frenotomy Mean</th>
<th>Pre-frenotomy Mean</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argiris 2011</td>
<td>1.47</td>
<td>6.63</td>
<td>-5.16 [-5.97, -4.35]</td>
</tr>
<tr>
<td>Ballard 2002</td>
<td>1.2</td>
<td>6.9</td>
<td>-5.70 [-6.44, -4.96]</td>
</tr>
<tr>
<td>Geddes 2008</td>
<td>0.5</td>
<td>6.3</td>
<td>-5.10 [-6.00, -4.20]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>123</td>
<td>123</td>
<td>-5.10 [-5.60, -4.69]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 11.63, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 19.79 (P < 0.00001)

---

Figure 2. Meta-analysis of breastfeeding
a: Overall improvement evaluated by mother; b: Latch evaluated by LATCH score; c: Nipple pain evaluated by pain score