Review

Reoccurrence rate in Ponseti treated clubfeet: A meta-regression

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1. Background

Reoccurrence of deformity, defined as any surgical or non-surgical treatment post initial correction, occurs in 7–64% of children with idiopathic clubfeet who were treated with Ponseti management [1–4]. Previously, the most cited cause of reoccurrence for this group was non-compliance with foot abduction orthosis [1,2,4–9]. Researchers found that 78% of children who are noncompliant with brace wear experience a reoccurrence, compared to only 7% of children who are compliant [4]. Other cited causes of reoccurrence are: low socioeconomic status [2], parental education level less than high school [5], gender (females are 5× more likely to reoccur) [8,10], initial severity rating (the higher the rating the more likely to reoccur) [10], decreased dorsiflexion range of motion [1,8], and everter muscle weakness [1,8]. While previous researchers have reviewed the topic of clubfoot reoccurrence, statistical techniques have not been used to assess the overall rate and cause of reoccurrence for children with clubfeet. Therefore, the purpose of this study is to conduct a review, of studies that report reoccurrence rates in children with clubfoot, and use meta-regression to predict the variables that explain the variance in proportion and effect sizes for clubfoot reoccurrence rate. This analysis will identify factors that contribute to an increased chance of reoccurrence.

2. Methods

A PubMed, Medline and Google Scholar search was conducted for the years of 1990–2017 using the following key words: "clubfoot" or "talipes equinovarus" and "reoccurrence" or "relapse". PubMed and Medline returned a manageable number of articles to review. However, Google Scholar returned too many articles to reasonably screen. Therefore, the word "children" was added to the Google Scholar search in order to decrease the number of results (Table 1). Articles were screened using the criteria in Fig. 1. A total of 17 studies were chosen for inclusion, with three studies providing an additional three subject groups, for a total of 20 samples for analysis.

The effect size statistic (ESp) utilized in this study was proportion (p), where the number of subjects who reoccurred (k) was divided by the total number of subjects (n): $ES_p = p = \frac{k}{n}$ [11]. For statistical analysis in clubfoot literature, it is common to pool bilateral and unilateral clubfeet into one subject group, with the total number of subjects and the total number of clubfeet being reported [12]. Due to this, the proportion of study population that experienced reoccurrence will be calculated one of two ways; n is either the total number of subjects or the total number of clubfeet and k is either the number of subjects or number of clubfeet that reoccurred.

After an extensive review of the methods and procedures of the chosen studies, eight variables were chosen for inclusion in the meta-regression (Table 2). The variables chosen were: gender, sample size, laterality, age at initial presentation, mean number of casts, percent of subjects who underwent tenotomy as part of Ponseti treatment, mean follow-up time, and brace compliance. These variables were chosen as they were commonly reported and have been listed in previous literature as possible causes or contributors to reoccurrence. Other variables previously reported to be important factors (height, weight, parental education level, and socioeconomic status, initial severity/range of motion/muscle strength) were assessed and subsequently discarded due the sparse inclusion of these variables in the methods and results of the studies chosen for analysis.

IBM SPSS Statistics v.24 (IBM Corporation, Armonk, NY, 2016) was used to run custom macros that calculated central tendency statistics and a weighted generalized least squares regression. The effect sizes calculated were outside the predefined range of < 0.20 or > 0.80, therefore the data was transformed into logits for statistical analysis [11]. To transform into logit the following equation was used $effect\ size\ logit = \ln(\frac{Effect\ Size}{1 - Effect\ Size})$. Upon completion of statistical analysis, the logit results were then converted back into effect sizes using the following equation $effect\ Size = \frac{e^{Effect\ Size\ Logit}}{e^{Effect\ Size\ Logit} + 1}$ [11]. Interpretation of results will be discussed in terms of the original values and the final effect sizes converted from logits. For Example: If the calculated effect size is 0.15.

Central tendency macros, custom built for use in SPSS, calculated the following statistics for the 20 samples: mean, minimum, maximum, weighted standard deviation, ± 95% confidence interval, standard error, z score, p-value, random effects variance, and homogeneity analysis (Q). The mean and 95% confidence interval describe the

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Table 1
The number of article returned for three electronic databases; PubMed, Medline and Google Scholar.

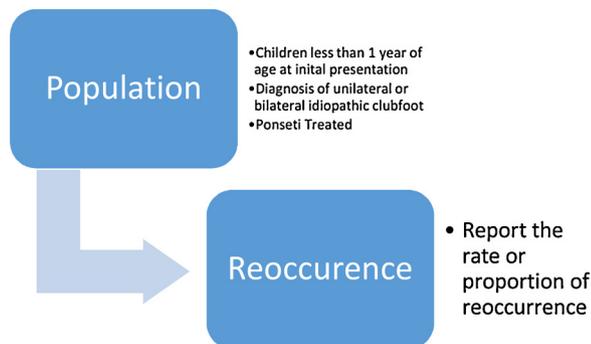| Key words	PubMed	Medline	Google Scholar	Google Scholar + children
Clubfoot and reoccurrence	226	564	10100	8920
Clubfoot and relapse	326	114	2620	2410
Talipes equinovarus and reoccurrence	270	50	5620	5260
Talipes equinovarus and relapse	332	29	1790	1750

Fig. 1. Screening criteria for article review.

average proportion of children with clubfoot that will experience a reoccurrence in deformity. The homogeneity analysis is an indicator of how heterogeneous the distribution of effect sizes is among the 20 samples. A significant homogeneity analysis indicates that the variability across effect sizes is greater than what is expected from sampling error alone. Indicating that the variables listed above may influence reoccurrence and that further analysis is warranted.

Lastly, a weighted generalized least squares regression was used to predict variables that explained the excess variance in effect size. This approach assesses the relationship between the mean effect size and the study variables. The results of which are the variables, in combination or in isolation, that best explain the excess variance of the mean effect size. The regression will be calculated for each individual variable's dummy variable and then the significant variables will be combined into one regression analysis. If the combined regression homogeneity test is significant, then the model will sufficiently explain the variability across effect sizes. If the homogeneity sum-of-squares is not significant, then the unexplained variability is no greater than that from sampling error alone [11].

3. Results

Table 3 presents the effect size statistics for the proportion of subjects/clubfeet that experienced a reoccurrence. If the effect size was calcualted using either the number of feet or the number of subjects. The distinction between the use of feet or subjects is listed under the Total Number Reoccurred column. If feet is listed in the Total Number Reoccurred column the effect size is equation is $Effect\ Size\ (feet) = \frac{Total\ Number\ Reoccured}{Total\ Number\ of\ Clubfeet}$. If subjects is listed in the Total Number Reoccurred column the effect size equation is $Effect\ Size\ (subjects) = \frac{Total\ Number\ Reoccured}{Total\ Number\ of\ Subjects}$. Sixteen of the twenty subject groups used the number of clubfeet to calculate reoccurrence rate, the remaining four measurements utilized the number of subjects. Reoccurrence rates ranged from 11 to 83%, indicating effect size statistics of 0.11–0.83.

Table 4 presents the central tendency results of the logit and converted data. The mean effect size is 0.30 with a 95% confidence interval of $0.28 - 0.33$. This indicates, that on average, 30% of subjects will experience a reoccurrence. The overall homogeneity Q was 97.6 with a p-value of < 0.001; indicating that the variance in effect sizes is due to more than random sampling error.

A weighted generalized least squares regression was used to predict which study variables, in combination, would explain the excess variance in the proportion of subjects who experience a reoccurrence. The 12 dummy variables from Table 2 were entered into the regression analysis (see Table 5 for results). Four dummy variables were found to be significant: Laterality (Unilateral or Bilateral), Tenotomy (yes or no), mean follow-up ≤ 2 years and mean follow-up > 2 years. These four variables were then entered into a regression analysis, which resulted in the variable mean follow up > 2 years falling out. A final weighted generalized least square regression was run with three variables: Affected, Tenotomy and mean follow up ≤ 2 years (Table 6). The model was significant and explained 46.5% of the variance in effect size. The coefficients for Affected, Tenotomy and mean follow up ≤ 2 years are 0.77, 0.60, and 0.29 respectively. These coefficients indicate that children who have unilateral clubfoot deformity, who have had a tenotomy and are less than 2 years of follow-up are at the highest risk of experiencing a reoccurrence.

4. Discussion

The purpose of this study was to review previously reported reoccurrence rates for children with clubfoot and use a meta-regression to predict the variables that explained the variance in proportion effect sizes for clubfoot reoccurrence rate. The goal was to identify factors that could help identify children that may be at risk of a reoccurrence. Seventeen studies, with a total of 20 samples, were identified and used to calculate effect size. The mean effect size for the 20 samples was 0.30 (95% Confidence Interval (CI) $0.28 - 0.33$). This indicates that the average proportion of children that experience a reoccurrence of deformity is 30% (CI 28%–33%). Previous literature has reported a wide range of reoccurrence rates (7–64%) [1–4]. Creating a mean rate of reoccurrence, using the 20 samples from this study, is more representative of the entire clubfoot population and not an individual study population. Using a mean reoccurrence rate of 30% allows clinicians to more accurately inform patients and families of the average reoccurrence rate.

Overall, the homogeneity for the 20 samples was 97.6 with a p-value of < 0.001. This indicates that the variance in proportion of children who experience a reoccurrence can be attributed to more than random sampling error and that additional factors should be taken into account. Eight variables were assessed for each of the 20 samples; percentage of males and females, the study sample size, laterality (percent of bilateral vs. unilateral), age at initial presentation, mean number of casts, percent with tenotomy as part of Ponseti treatment, mean follow-up time and brace compliance. Therefore, a logistic regression was used to assess the study variables in combination. A final model, explaining 46.5% of the variance in the proportion of children experiencing a reoccurrence, was found using three variables (laterality, tenotomy and follow-up time). The coefficients for laterality, tenotomy and follow-up time are 0.77, 0.60, and 0.29 respectively. These coefficients indicate that children who have unilateral clubfoot deformity, who have had a tenotomy and are less than 2 years of follow-up are at the highest risk of experiencing a reoccurrence.

Previously, researchers have reported conflicting evidence on the difference in the severity of deformity between bilateral and unilateral clubfeet. Some researchers found no difference between unilateral and

Table 2

List of the study variables to be used for meta-regression; with the dummy variables used in the regression listed.

Variable	Code	Dummy variables	Notes
Gender	1 = majority male, 2 = majority female, 3 = mixed gender (equal % of males to females.)	MalesA: 1 = 1, 2&3 = 0; MalesB: 3 = 1, 1&2 = 0	Majority = > 75%
Subject sample size	1 = < 50, 2 = > 50	SS: 1 = 1, 2 = 0	
Laterality	1 = majority unilateral, 2 = majority bilateral, 3 = mixed	Affected: 1 = 1, 2&3 = 0	Majority = > 75%
Average age at initial presentation	1 = < 3 months, 2 = > 3 months, 3 = classified as infants no age given	Age: 1&3 = 1, 2 = 0	
Mean number of casts	1 = < 5 casts, 2 = > 5 casts, 3 = not specified	CastsA: 1 = 1, 3&2 = 0; CastsB: 2 = 1; 1&3 = 0	
Percent with tenotomy as part of Ponseti treatment	1 = > 90%, 2 = 80–89%, 3 = 70–79%, 4 = < 69%, 5 = not specified	Tenotomy: 1&2 = 1, 3–5 = 0	
Mean follow-up time	1 = ≤2 years, 2 = > 2 years, 3 = not specified	MFUTA: 1 = 1, 2&3 = 0; MFUTB: 2 = 1, 1&3 = 0	
Brace compliance	1 = < 50%, 2 = > 50%, 3 = not specified	BraceA: 1 = 1, 2&3 = 0; BraceB: 2 = 1, 1&3 = 0	

Table 3

Effect size statistic: the percent of subjects/clubfeet that experiences a reoccurrence.

Samples	Total number of subjects	Total number of clubfeet	Total number reoccurred	Effect size statistic	Percent reoccurred
Dobbs (2004)	51	86	27 feet	0.31	31%
Haft (2007)	51	73	21 subjects	0.41	41%
Richards (2008)	176	267	93 feet	0.37	37%
Avilucea (2009)	50	68	8 feet	0.16	16%
Avilucea (2009)	50	74	18 feet	0.36	36%
Park (2009)	33	48	19 feet	0.40	40%
Goriainov (2010)	50	80	17 feet	0.21	21%
Janicki (2011)	17	30	25 feet	0.83	83%
Janicki (2011)	28	39	12 feet	0.31	31%
Ramirez (2011)	53	73	24 feet	0.33	33%
Zionts (2012)	57	84	40 feet	0.48	48%
Goldstein (2015)	86	86	28 subjects	0.33	33%
Ohalloran (2015)	45	71	18 feet	0.18	18%
Hosseinzadeh (2016)	101	148	42 feet	0.28	28%
Mageshwaran (2016)	20	26	3 feet	0.15	15%
Mageshwaran (2016)	20	25	4 feet	0.20	20%
Changulani (2006)	66	100	31 feet	0.32	32%
Abdelgawad (2007)	89	137	14 feet	0.14	14%
Goksan (2006)	92	134	27 subjects	0.31	31%
Colburn (2003)	34	57	4 subjects	0.11	11%

Table 4

Logit and converted central tendency results.

	Effect size logit	Converted effect size
Mean	−0.83	0.30
Minimum	−2.17	0.10
Maximum	1.61	0.83
Standard deviation	0.55	0.63
± 95% Confidence interval	−0.94 to −0.72	0.28–0.33
Random effects variance (v)	0.26	
Homogeneity analysis (Q)	97.55	
Homogeneity(Q) p-value	< 0.001	

Table 5

Results of the logistic regression on individual dummy variables. Red indicates a significant homogeneity analysis.

	Q	df	p	R-square	k
SS	0.005	1	0.9437	0.0001	20
MalesA	3.301	1	0.0692	0.0338	20
MalesB	3.301	1	0.0692	0.0338	20
Affected	7.4085	1	**0.0065**	0.0759	20
Age	0.0372	1	0.8471	0.0004	20
CastA	0.7702	1	0.3802	0.0079	20
CastB	0.3822	1	0.5364	0.0039	20
Tenotomy	10.2145	1	**0.0014**	0.1047	20
MFUTA	21.6644	1	**0.0000**	0.2221	20
MFUTB	21.87	1	**0.0000**	0.2242	20
BraceA	0.0081	1	0.9281	0.0001	20
BraceB	0.0741	1	0.7855	0.0008	20

bilateral clubfeet [13], whereas others found that bilateral clubfeet are more severe [12]. Despite conflicting reports in the past, the results of this meta-regression show that children with unilateral clubfoot are at a higher risk of experiencing a reoccurrence. The exact mechanism for why laterality was a significant predictor of reoccurrence is unclear and the conflicting results reported previously further confound this issue. More research is needed to ascertain the effect of laterality on the rate of reoccurrence for children with clubfoot.

Equinus is the most difficult of the clubfoot deformities to correct [4] and researchers have found that performing an Achilles tenotomy, as part of Ponseti management, can help increase the amount of ankle dorsiflexion [14]. The range of children that will receive a tenotomy as part of Ponseti management ranges from 12 to 90% [2,3,5–7,14–17]. Children who require a tenotomy may have a foot that is rigid and less

complaint with non-operative treatment, whereas those whose equinus deformity is flexible may better accommodate non-operative treatments. Despite successful correction of equinus with the initial tenotomy, logistic regression shows that the positive history of tenotomy is a predictor of reoccurrence. Researchers have found that the first deformity to reoccur is the last addressed, equinus [18]. The rate of revision for persistent equinus, post initial tenotomy, is 18% [10], indicating that almost 1 in 5 children who receive a tenotomy will experience a reoccurrence of equinus deformity. Therefore, children who

Table 6
Final logistic regression with three significant variables.

Significant variable regression results						R-square
	Q	p-Value	Mean effect size (logit)			
Model	45.3318	< 0.001	−0.83			0.4647
Residual	52.2209	< 0.001				
Total	97.5527	< 0.001				
	B	Standard error	± 95% Confidence interval	Z	p-Value	Beta
Regression coefficients logits						
Constant	−0.8788	0.071	−1.0180 to −0.7396	−12.3754	< 0.001	< 0.001
Tenotomy	0.4072	0.1165	0.1789–0.6355	3.4959	< 0.001	0.3562
Follow up	−0.8653	0.1613	−1.1815 to −0.5491	−5.3642	< 0.001	−0.5504
Affected	1.1904	0.3727	0.4599–1.9209	3.194	< 0.001	0.3268
Regression coefficients converted						
Constant	0.2934	0.5177	0.2654–0.323			
Tenotomy	0.6004	0.529	0.5446–0.6537			
Follow up	0.2962	0.5402	0.2347–0.3660			
Affected	0.7668	0.5921	0.6129–0.8722			

require the initial tenotomy may be predisposed to reoccurrence, due to a more rigid foot, as opposed to those children who do not receive a tenotomy, who may have a more flexible foot.

Previously researchers have found that 6% of children over the age of 7 will reoccur, whereas, upwards of 64% will reoccur before the age of 5 years [1–4]. Additionally, the highest risk of reoccurrence has been reported during the rapid growth period between 3–5 years of age [1]. Previous research supports the results of this study, children whose follow-up time is less than 2 years post-initial treatment are at the highest risk of reoccurrence.

One potential limitation of this study is the use of clubfeet vs. subjects to calculate effect size. For statistical analysis on clubfeet it is common to pool bilateral and unilateral clubfeet into one subject group, with the total number of subjects and the total number of clubfeet being reported [12]. Typically, children with bilateral clubfoot are included with both feet as independent observations [19]. However, several researchers have found using bilateral and unilateral clubfeet in the same analysis is confounding [20]. Bilateral clubfeet tend to be highly correlated; 85% have the same severity classification score, the mean number of casts applied for each side is not significantly different, the need for tenotomy is not different, and 89% of patients who reoccur do so bilaterally [19]. Therefore, it may not always be proper to include both sides of bilateral subjects, as this could artificially inflate sample size and lead to false conclusions [12,19]. The subjects utilized in the 20 samples from this meta-regression, were a mixture of bilateral and unilateral clubfeet. However, due to the nature of meta-regression, the problem of pooling data from both sides of bilateral subjects cannot be addressed. The results of this study do indicate that unilateral clubfeet are at a higher risk of reoccurring. Due to the problems stated above caution may need to be taken when stating that unilateral clubfeet are at higher risk. It may behoove future researchers to consider bilaterality as a potential confound and the utilization of statistical methodologies that account for laterality should be considered.

In conclusion, the purpose of this study was to use meta-regression to assess reoccurrence rates in children with clubfoot. This study is the first to use statistical methodology to assess variance in the proportion of clubfoot subjects who experience a reoccurrence. This study can be used to help guide clinicians in the management of clubfoot deformity. Results show that children with unilateral clubfoot, who underwent a tenotomy as part of Ponseti management and who had less than 2 years follow-up were at the highest risk of reoccurrence. Therefore, clinicians who treat children meeting this criteria should be cautious, as it could be an indication that the child is at risk. Children meeting this criteria should be monitored more closely to assess clubfoot progression.

Disclosure

The authors of this original manuscript meet the authorship requirements and do not have disclosures.

CRediT authorship contribution statement

Juanita Wallace: Methodology, Writing - original draft, Writing - review & editing. **Hank White:** Methodology, Writing - original draft, Writing - review & editing. **Joel Eastman:** Methodology, Writing - original draft, Writing - review & editing. **Sam Augsburger:** Methodology, Writing - original draft, Writing - review & editing. **Xi Ma:** Methodology, Writing - original draft, Writing - review & editing. **Janet Walker:** Methodology, Writing - original draft, Writing - review & editing.

References

[1] Chu A, Lehman W. Persistent clubfoot deformity following treatment by the Ponseti method. J Pediatr Orthooaedics B 2012;21:40–6.
[2] Zhao D, Liu J, Zhao L, Wu Z. Relapse of clubfoot after treatment with the Ponseti method and the function of the foot abduction orthosis. Clin Orthop Surg 2014;6:245–52.
[3] Zionts LE, Zhao G, Hitchcock K, Maewal J, Ebramzadeh E. What's new in idiopathic clubfoot. J Pediatr Orthop 2015;35:547–50.
[4] Hosseinzadeh P, Steiner R, Hayes C, Muchow R, Iwinski H, Walker J, et al. Initial correction predicts the need for secondary Achilles tendon procedures in patients with idiopathic clubfoot treated with Ponseti casting. J Pediatr Orthop 2016;36:80–3.
[5] Dobbs MB, Rudzki JR, Purcell DB, Walton T, Porter KR, Gurnett CA. Factors predictive of outcome after use of the Ponseti method for the treatment of idiopathic clubfeet. J Bone Joint Surg 2004;86(1):22–7.
[6] Radler C. The Ponseti method for the treatment of congenital club foot: review of the current literature treatment recommendations. Int Orthop 2013;37:1747–53.
[7] Hosseinzaheh P, Milbrandt Todd A. Congenital clubfoot. JBJS Rev 2014;2(3):e3.
[8] O'Shea RM, Sabatini CS. What is new in idiopathic clubfoot? Curr Rev Musculoskelet Med 2016;9:470–7.
[9] Hosseinzadeh P, Kelly DM, Zionts LE. Management of the relapsed clubfoot following treatment using the Ponseti method. J Am Acad Orthop Surg 2017;25:195–203.
[10] Goldstein RY, Seehausen DA, Chu A, Sala DA, Lehman WB. Predicting the need for surgical intervention in patients with idiopathic clubfoot. J Pediar Orthop 2015;35:395–402.
[11] Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. West Sussex, UK: John Wiley & Sons, Ltd; 2009.
[12] Gray K, Barnes E, Gibbons P, Little D, Burns J. Unilateral versus bilateral clubfoot: an analysis of severity and correlation. J Pediatr Orthooaedics B 2014;23:397–9.
[13] Zionts LE, Jew MH, Ebramzadeh E, Sangiorgio SN. The influence of sex and laterality on clubfoot severity. J Pediatr Orthop 2015;37(2).
[14] Lebel E, Karasik M, Bernstein-Weyel M, Mishukov Y, Peyser A. Achilles tenotomy as an office procedure: safety and efficacy as part of the Ponseti serial casting protocol for clubfoot. J Pediatr Orthop 2012;32:412–5.
[15] Scher DM, Feldman DS, van Bosse HJ, Sala DA, Lehman WB. Predicting the need for

tenotomy in the Ponseti method for correction of clubfeet. J Pediatr Orthop 2004;24:349–52.

[16] Dobbs MB, Gurnett CA. Update on clubfoot: etiology and treatment. Clin Orthop Relat Res 2009;467:1146–53.

[17] Hosseinzadeh P, Peterson ED, Walker J, Muchow RD, Iwinski HJ, Talwalkar VR, et al. Residual forefoot deformity predics the need for future surgery in clubfeet treated by Ponseti casting. J Pediatr Orthopaedics B 2016;25:96–8.

[18] Bhaskar A, Patni P. Classification of relapse pattern in cubfoot treatd with Ponseti technique. Indian J Orthopadeics 2013;47(4):370–6.

[19] Gray K, Gibbons P, Little D, Burns J. Bilateral clubfeet are highly correlated: a cautionary tale for researchers. Clin Orthop Relat Res 2014;472:3517–22.

[20] Halanski MA, Davison JE, Huang JC, Walker CG, Walsh SJ, Crawford HA. Ponseti method compared with surgical treatment of clubfoot. J Bone Joint Surg Am 2010;92:270–80.