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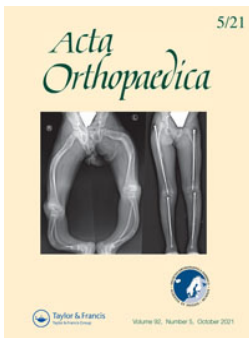
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Prognostic factors for recurrent idiopathic clubfoot deformity: a systematic literature review and meta-analysis

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Background and purpose — After initial clubfoot correction through Ponseti treatment, recurrence rates range from 26% to 48%. Even though various factors have been associated with increased recurrence risk, systematic assessments of the prognostic capacity of recurrence risk factors and their clinical relevance are lacking. Therefore we assessed clinically relevant prognostic factors for recurrent idiopathic clubfoot deformity after initial correction through Ponseti treatment.

Methods — PubMed, Embase, Cinahl, and Web of Science were systematically searched for studies investigating the association between clinically relevant factors and recurrence rates. Prognostic factors were qualitatively assessed and included in the meta-analysis if ≥ 2 studies investigated the same factor and methods were comparable.

Results — 34 articles were included in the qualitative synthesis, of which 22 were also included in the meta-analysis. Meta-analysis revealed that poor evtor muscle activity (OR = 255, 95% CI 30–2,190), brace non-compliance (OR = 10, CI 5–21), no additional stretching (OR = 31, CI 10–101), more casts (OR = 3.5, CI 1.6–7.8), lower education level of parents (OR = 1.8, CI 1.2–2.6), non-marital status of parents (OR = 1.8, CI 1.1–3.0), and higher Dimeglio scores (OR = 1.9, CI 1.2–3.3) were associated with higher recurrence rates.

Interpretation — Brace non-compliance and poor evtor muscle activity have been identified as main recurrence risk factors and are therefore important to be closely monitored during clinical follow-up of clubfoot patients. Adding additional stretching during the bracing protocol might be promising in the quest to prevent relapse, but scientific evidence for clear clinical treatment recommendations is still limited.

Idiopathic clubfoot is typically treated according to the Ponseti method involving repetitive manipulation and casting, in most cases an Achilles tenotomy and a foot abduction brace until the age of 4. The goal of the extensive bracing regime is to prevent recurrence by opposing the deforming forces at the medial ankle–foot joints that persist or reoccur after initial correction of the clubfoot (Ponseti 2002, Dobbs and Gurnett 2009, Hosseinzadeh et al. 2017). However, between 26% and 48% of the children treated with the Ponseti method experience a clubfoot recurrence (Hosseinzadeh et al. 2017). A major challenge of current clubfoot research is to categorize children based on recurrence risk and identify those children in need of preventive interventions to reduce recurrence risk.

Although the exact underlying pathomechanism of clubfoot recurrence remains to be established, it is assumed that recurrences are caused by the same pathology as the initial deformity (Ponseti 2002). After initial correction, persisting or reoccurring retracting fibrosis in the tarsal ligaments and their surrounding structures pulls on the medial ankle and foot joints. In some children these deforming forces cannot be sufficiently opposed by the evtor muscles (e.g., peroneus longus and brevis), since these remain weak (Ponseti 2002, Chu and Lehman 2012, Gelfer et al. 2014). This imbalance between in- and evting ankle–foot joint forces might gradually increase and lead to clubfoot recurrence. In line with this pathomechanism is the finding that children strictly adhering to the bracing regimen are less likely to experience a recurrence as compared with children who have poor brace compliance (Dobbs et al. 2004, Avilucea et al. 2009). Similarly, those children with a better ability to oppose the deforming medial ankle–foot joint forces with activity of their evtor muscles seem to have a lower recurrence risk (Gelfer et al. 2014, Little et al. 2019). Other factors that have previously been associated

with the risk of clubfoot recurrence are accessibility to treatment resources, frequency and number of cast changes, or the severity of the initial deformity (Dobbs et al. 2004, Avilucea et al. 2009, Zhao et al. 2014, Goldstein et al. 2015). The main limitation in current literature is the lack of a systematic overview of relevant recurrence risk factors and their prognostic capacity.

This literature review and meta-analysis provides a systematic overview of factors associated with the risk of recurrence after initial correction with the Ponseti method and quantifies the strength of each recurrence risk factor and its clinical relevance. Based on the proposed pathomechanism of force imbalances in recurrent clubfoot deformity (Ponseti 2002), we hypothesize that brace compliance and evertor muscle function have the strongest prognostic capacity for clubfoot recurrence.

Methods

The systematic literature search and meta-analysis were conducted in accordance with the PRISMA guidelines and registered with PROSPERO (CRD42020172434).

Literature search

Studies published up to March 5, 2020 were systematically searched in 4 databases (PubMed, Embase, Cinahl, and Web of Science). A search string (Appendix 1, see Supplementary data) was formulated for each database using database-specific MeSH terms, title, abstract and text search words, wildcards (*) and Boolean operators (AND and OR). The following terms and their synonyms were used: clubfeet, Ponseti, and recurrence.

Eligibility criteria and study selection

Studies were included if (i) written in English, Dutch, or German, (ii) patients were diagnosed with idiopathic clubfoot deformity and (iii) treated according the Ponseti method, (iv) included the occurrence of recurrent clubfeet deformity, (v) provided statistical assessments of an association between clubfoot recurrence and prognostic factor(s) in terms of odds ratio or other risk estimates such as hazard ratios. Exclusion criteria were (i) < 5 participants, (ii) study was not primary research, (iii) study considered non-idiopathic, secondary recurrence, and/or neglected clubfeet. Neglected clubfeet were defined as: no treatment given before the age the child starts walking (12 months) (Sutherland et al. 1980, Adegbehingbe et al. 2017).

The selection process started by removing duplicates, followed by screening of titles and eventually abstracts and full texts of the respective studies. 2 reviewers (HS and CG) independently assessed the eligibility criteria. If at least 1 reviewer included a title, it was included in the abstract phase. Abstracts and full texts were included if agreement existed between the

2 assessors. Disagreements were solved in a discussion meeting. Reference lists of included articles were checked in additional relevant studies.

Data extraction

Data extraction was performed by HS. In the case of unreported data authors were contacted via email. Data extraction was performed on study characteristics, participant characteristics, treatment details, and the main outcome measures.

Risk of bias assessment

The risk of bias for the individual papers was assessed by 2 independent researchers using the prognostic form of the Cochrane Collaboration's risk of bias tool (Appendix 2, see Supplementary data). Every item was scored with "low risk" (+), "high risk" (-), or "unclear" (?) (Scholten et al. 2013). The forms were compared and discussed for final conclusion. Measurements of prognostic factors were marked as high bias if one of the measurements was done in a self-reporting way. The overall risk of bias was judged to be low if all domains were marked low, moderate if > 2 domains were marked unclear and others low, serious if one domain was judged high risk, critical if multiple domains were marked high risk, and unknown if information on most domains was lacking (Sterne et al. 2016).

Data synthesis and statistical analyses

Qualitative and quantitative data synthesis was performed on all factors found in the included studies. A meta-analysis was performed using Review Manager (RevMan version 5.3) (Cochrane Collaboration 2014) when ≥ 2 studies investigate the same prognostic factor and methods for assessment were comparable. Absolute values of the number of participants were used to perform meta-analyses (Mantel-Haenzel) and determine the recurrence risk in terms of odds ratio (OR) with an 95% confidence interval (CI). Fixed effect was used if heterogeneity was low ($I^2 < 50\%$), and random effect if heterogeneity was high ($I^2 > 50\%$). To improve clinical interpretation of the findings from the random effect meta-analysis, prediction intervals were computed when > 10 studies were included in the meta-analysis (Deeks et al. 2021). In addition, an odds ratio > 3 was marked as of clinical significance (Kraemer 1992, Higgins et al. 2021). To improve overall interpretability, significant findings were also presented as risk percentages using the following computation: risk percentage = $\text{odds}/(1+\text{odds}) * 100$ (Higgins et al. 2021). A risk percentage of 10% would mean that 10 out of 100 children will have a recurrent pathology. Data from studies investigating the association between compliance and recurrence rates was transformed to allow pooling with studies investigating the association of non-compliance. Furthermore, reference groups were determined for categorical and continuous outcomes, based on the cut-off points that were presented in the majority of the studies (Appendix 2, see Supplementary data).

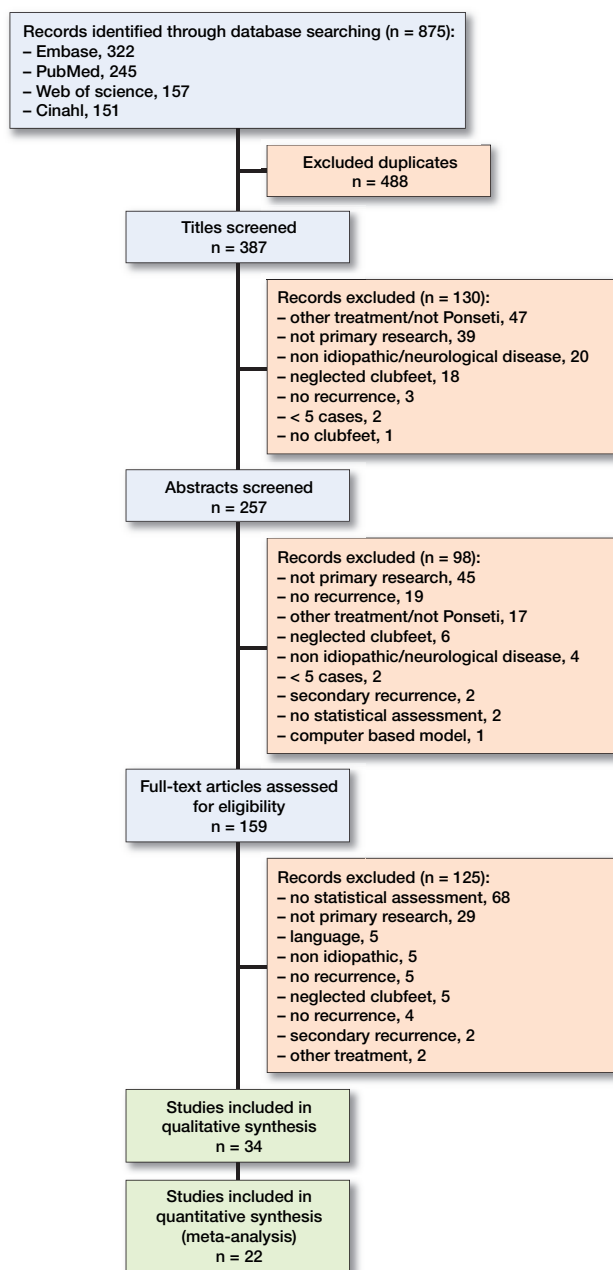


Figure 1. PRISMA flow diagram of results.

Funding and potential conflicts of interest

No funding was received to perform this study. The authors have no conflicts of interest to declare.

Results

Study selection and characteristics

875 articles were identified in the initial search. After study selection (Figure 1), 34 articles were included for qualitative synthesis and 22 for meta-analysis.

Table 1 (see Supplementary data) summarizes the study characteristics of the included articles. This review included 2,987 idiopathic clubfeet treated with the Ponseti method, of which 70% of the patients were male. Sample sizes ranged from 23 to 308 children and the average recurrence rate was 22% (5–49%). The initial age of manipulation by cast treatment was on average 50 days, and the average age at recurrence was 1.6 years. Follow-up period was reported in 31 articles, with an average of 3 years (13 months–8 years). The bracing protocol was documented in 29 studies. Bracing duration ranged between 2 and 5 years. Brace compliance was reported in 21 studies, with an average of 76% (0–100%).

Risk of bias

An overall judgment of the risk of bias assessment is given in Table 1. Although all studies described the prognostic factors clearly and a valid recruitment of participants was performed, all studies showed unclear or high risk of bias on 1 or more items of the checklist (Appendix 3, see Supplementary data).

Prognostic factors for clubfoot recurrence

Musculoskeletal factors

23 studies assessed the association of recurrence rates and 9 musculoskeletal factors (Table 2). 3 factors could be included in a meta-analysis.

2 studies investigated the association between manually tested evertor muscle activity and recurrence risk. Both were included in the meta-analysis. Poor evertor muscle activity was associated with 225 times higher odds of clubfoot recurrence (CI 30–2,190; 99.6% risk; Figure 2A, see Supplementary data) exceeding the threshold value for clinical significance. The assessment of initial Dimeglio score was reported in 11 studies, of which 6 could be included in the meta-analysis. A higher Dimeglio score was associated with 1.9 times higher odds of clubfoot recurrence (CI 1.2–3.3; 66% risk; Figure 2B, see Supplementary data). However, 4 of the 5 studies not included in the meta-analysis did not find an association. The meta-analysis on initial Pirani scores included 3 out of 8 studies, but did not reveal a significant association (Figure 2C, see Supplementary data). This was in line with the remaining 5 studies.

Lower overall joint laxity as measured with the Beighton score was associated with a 5.3 times higher odds of clubfoot recurrence in 1 study (CI 1.3–22). Other investigated musculoskeletal factors showed no clear association with recurrence rates.

Genetics

17 studies assessed the association between 3 genetic factors and recurrence rates (Table 3). 2 factors were included in a meta-analysis and no association was found for family history or gender (Figure 3, see Supplementary data). Based on qualitative synthesis, a significant association was found for

Table 2. Overview and outcome of studies: presented musculoskeletal factors for risk of recurrence

Musculoskeletal factor	Significant association	Not significant association
Decreased dorsiflexion Before tenotomy (radiographic)	(O'Halloran et al. 2015)	(Kang and Park 2015)
After tenotomy (goniometer)	(Hosseinzadeh et al. 2016)	
Decreased lateral tibio- calcaneal angle (radiographic)	(Kang and Park 2015)	(O'Halloran et al. 2015)
Lower joint laxity (Beighton score)	(Cosma et al. 2018)	
Poor evertor muscle activity	(Gelfer et al. 2014), (Little et al. 2019)	
Severity of clubfeet deformity Initial Dimeglio score	(Brazell et al. 2019), (Panjavi et al. 2012), (Sangiorgio et al. 2017)	(Clarke et al. 2011), (Hallaj-Moghaddam et al. 2015), (Jochymek and Peterkova 2019), (Kang and Park 2015), (Kuzma et al. 2019), (Limpaphayom and Sailohit 2019), (Ramírez et al. 2011), (Vo and Huynh 2016)
Initial Pirani score		(Avilucea et al. 2009), (Cosma et al. 2018), (Dinesh et al. 2017), (Gelfer et al. 2014), (Haft et al. 2007), (Jochymek and Peterkova 2019), (Shabtai et al. 2015), (Zhao et al. 2018)
Higher talar dysplasia		(Jochymek and Turek 2018)
Walking age	(Zionts et al. 2014)	(Hallaj-Moghaddam et al. 2015), (Shabtai et al. 2015)

Table 3. Overview and outcome of studies: presented genetic factors for risk of recurrence

Genetic factor	Significant association	Not significant association
Family history Race/ethnicity Sex	(Avilucea et al. 2009)	(Haft et al. 2007), (Panjavi et al. 2012) (Chong et al. 2014), (Haft et al. 2007), (Kuzma et al. 2019), (Zhao et al. 2018) (Avilucea et al. 2009), (Brazell et al. 2019), (Chong et al. 2014), (Clarke et al. 2011), (Cosma et al. 2018), (Hallaj-Moghaddam et al. 2015), (Kang and Park 2015), (Kuzma et al. 2019), (Limpaphayom and Sailohit 2019), (Little et al. 2019), (O'Halloran et al. 2015), (Panjavi et al. 2012), (Ramírez et al. 2011), (Sangiorgio et al. 2017), (Willis et al. 2009), (Zhao et al. 2018)

Table 4. Overview and outcome of studies: presented demographic factors for risk of recurrence

Demographic factor	Significant association	Not significant association
Family Age of parents Economic status Education level	(Mootha et al. 2011) (Avilucea et al. 2009)	(Chong et al. 2014), (Hallaj-Moghaddam et al. 2015) (Cosma et al. 2018), (Kuzma et al. 2019), (Panjavi et al. 2012), (Ramírez et al. 2011), (Sangiorgio et al. 2017) (Kuzma et al. 2019)
Employment Income Insurance Marital status parents	(Avilucea et al. 2009) (Avilucea et al. 2009) (Avilucea et al. 2009)	(Chong et al. 2014), (Kuzma et al. 2019), (Ramírez et al. 2011), (Sangiorgio et al. 2017) (Ramírez et al. 2011), (Sangiorgio et al. 2017) (Kuzma et al. 2019), (Sangiorgio et al. 2017)
Laterality		(Brazell et al. 2019), (Chong et al. 2014), (Clarke et al. 2011), (Kang and Park 2015), (Limpaphayom and Sailohit 2019), (Panjavi et al. 2012), (Ramírez et al. 2011), (Sangiorgio et al. 2017), (Shabtai et al. 2015), (Zhao et al. 2018)

Native American ethnicity and recurrence rates in Avilucea et al. (2009); other studies showed no association with ethnicity.

Demographic factors

15 studies assessed the association between 8 demographic factors and recurrence rates (Table 4). 5 factors were assessed

in a meta-analysis and showed significant associations between recurrence rates and a lower education level of parents (OR = 1.8, CI 1.2–2.6; 64% risk) and non-marital status of parents (OR = 1.8, CI 1.1–3.0; 64% risk; Figure 4A, D, see Supplementary data). No associations were found for income level, insurance or laterality (Figure 4B, C, E, see Supplemen-

Table 5. Overview and outcome of studies: presented treatment factors for risk of recurrence

Treatment factor	Significant association	Not significant association
Additional stretching	(Panjavi et al. 2012)	(Limpaphayom and Sailohit 2019)
Accelerated Ponseti treatment	(Morcuende et al. 2005)	
Brace duration	(Mahan et al. 2017)	
Casting		
Age of completion casting	(Kuzma et al. 2019)	(Ramírez et al. 2011)
Duration casting	(Kuzma et al. 2019)	(Dinesh et al. 2017), (Gelfer et al. 2014), (Haft et al. 2007), (Hallaj-Moghaddam et al. 2015), (Kuzma et al. 2019), (Little et al. 2019), (Morcuende et al. 2004), (Morcuende et al. 2005), (Shabtai et al. 2015), (Zhao et al. 2018)
Number of casts	(Chong et al. 2014)	(Chong et al. 2014), (Gelfer et al. 2014), (Haft et al. 2007), (Hallaj-Moghaddam et al. 2015), (Kang and Park 2015), (Kuzma et al. 2019), (Limpaphayom and Sailohit 2019), (Little et al. 2019), (Liu et al. 2018), (Ramírez et al. 2011), (Mootha et al. 2011), (Morcuende et al. 2004), (Morcuende et al. 2005), (O'Halloran et al. 2015), (Vo and Huynh 2016), (Zhao et al. 2018)
Initial age at start of treatment	(Willis et al. 2009)	(O'Halloran et al. 2015)
Longer follow-up time	(Chong et al. 2014)	(Cosma et al. 2018), (Mootha et al. 2011), (Morcuende et al. 2005), (Morcuende et al. 2004), (Ramírez et al. 2011), (Willis et al. 2009)
Previous treatment		(Janicki et al. 2009)
Surgeon vs. physiotherapist directed treatment		(Chong et al. 2014), (Cosma et al. 2018), (Dinesh et al. 2017), (Hallaj-Moghaddam et al. 2015), (Kuzma et al. 2019), (Little et al. 2019), (Panjavi et al. 2012), (Ramírez et al. 2011), (Willis et al. 2009), (Zhao et al. 2018)
Tenotomy		(Chong et al. 2014), (O'Halloran et al. 2015)
Age at tenotomy		(Tuhano lu et al. 2018)
Local vs. general anesthesia		(Chong et al. 2014), (Cosma et al. 2018), (Limpaphayom and Sailohit 2019)
Type of brace		

tary data). Studies not included in the meta-analysis were in line with these results.

In addition, Kuzma et al. (2019) found no association for employment, but Mootha et al. (2011) found a significant association between lower socioeconomic status and higher recurrence rates. Age of parents was not associated with recurrence rates.

Treatment factors

23 studies investigated the association between 15 treatment-related factors and clubfoot recurrence (Table 5). 5 factors were assessed in a meta-analysis.

2 studies investigated the association between additional stretching as part of the post-corrective treatment and recurrence rates and were included in the meta-analysis. Not applying additional stretching increased the odds for recurrence 32-fold (CI 10–101; 70% risk; Figure 5A, see Supplementary data), exceeding the threshold value for clinical significance. The meta-analysis on the number of casts included 3 out of 11 studies and showed 3.5 times higher odds of recurrence when > 5 casts were applied during Ponseti treatment (CI 1.6–7.8; 78% risk; Figure 5B, see Supplementary data), exceeding the threshold value for clinical significance. Similarly, a higher age at completion of casting was associated with a higher recurrence rate (Kuzma et al. 2019). However, the remaining 8 studies did not find associations between the number of casts and recurrence rates. The initial age at start of treatment (> 3 months), whether other (conservative) treatment preceded Ponseti treatment or whether tenotomy was performed (Figure

5C, D, E, see Supplementary data), were not associated with recurrence rates. This was in line with the additional studies included in the qualitative synthesis, except for one study showing a significant association for the initial age at start of treatment (Willis et al. 2009).

Based on the qualitative analysis only, changing casts every 7 days compared with every 5 days and shorter duration of bracing were associated with an increased recurrence rate. Inconclusive results were found for the duration of follow-up treatment and cast duration. Other treatment-related factors showed no clear association with recurrence rates.

Behavioral factors

Only brace compliance was identified as a behavioral factor (Table 6). 21 articles investigated the association between brace compliance and recurrence rates, of which 17 were included in meta-analysis. The odds of clubfoot recurrence increased 10 times when patients were non-compliant with the bracing protocol (CI 5–21; prediction interval: 0.6–180; 91% risk; Figure 6), see Supplementary data, exceeding the threshold value for clinical significance. The studies not included in the meta-analysis did not report an association between non-compliance and recurrence rates. Average compliance rate was 89% in those studies that did not report associations, ranging from 70% to 100% in the recurrent group, whereas average compliance rate was 66% in those studies reporting significant associations, ranging from 0% to 40% in the recurrent group.

Table 6. Overview and outcome of studies: presented behavioral factors for risk of recurrence

Treatment factor	Significant association	Not significant association
Brace non-compliance	(Abdelgawad et al. 2007), (Avilucea et al. 2009), (Dinesh et al. 2017), (Haft et al. 2007), (Limpaphayom and Sailohit 2019), (Mahan et al. 2017), (Mootha et al. 2011), (Morcuende et al. 2004), (Morcuende et al. 2005), (Panjavi et al. 2012), (Ramírez et al. 2011), (Sangiorgio et al. 2016), (Sangiorgio et al. 2017), (Zhao et al. 2018)	(Chong et al. 2014), (Cosma et al. 2018), (Gelfer et al. 2014), (Kang and Park 2015), (Kuzma et al. 2019), (Little et al. 2019), (Vo and Huynh 2016)

Discussion

This systematic review and meta-analysis aimed to establish clinically relevant factors associated with the risk of clubfoot recurrence after initial correction with the Ponseti method. In line with our hypothesis, brace non-compliance and poor evertor muscle activity were strong prognostic factors for clubfoot recurrence. In addition, children requiring > 5 casts and who did not receive additional stretching had a higher recurrence risk. These 4 risk factors all exceeded the threshold for clinical significance. Furthermore, small associations, not exceeding the clinical significance threshold, were identified between the incidence of recurrence and the severity of the initial deformity as measured with the Dimeglio scoring system as well as lower education level and non-marital status of the parents. However, prediction intervals could only be computed for brace compliance, and these were wide, implying large heterogeneity between studies. Scientists and clinicians should therefore use the estimated OR and risk ratios with caution when predicting recurrence rates in future patient populations.

In line with the proposed pathomechanism of clubfoot recurrence, evertor muscle activity and brace non-compliance were identified as strong prognostic factors for clubfoot recurrence. This data suggests that those patients with high compliance rates and good evertor muscle function are able to oppose potentially reoccurring or persisting deforming medial ankle-foot joint forces after initial correction and prevent recurrence. In line with this idea is our finding that adding stretching to the standard bracing protocol significantly reduces recurrence risk.

The addition of stretching to the bracing protocol was examined in 2 of the included studies following different protocols and showing moderate risk of bias. Limpaphayom and Sailohit (2019) asked parents to perform stretching exercises twice a day for 20 minutes, including passive range of motion of the involved ankle-foot joints and squatting exercises after walking age. 30 children completed this program, of which 8 experienced a clubfoot recurrence. In the group not completing the stretching program, 3 out of 4 children experience a recurrence. Panjavi et al. (2012) asked parents to perform dorsiflexion and abduction stretches 3 times a day, for 10 to 15 minutes. 95 feet completed this stretching program, and

only 3 recurrences were documented, while of the 34 feet not completing the program, 21 recurrences were diagnosed. Even though stretching is not part of the standard Ponseti treatment protocol, this data suggests that stretching might be a promising method to reduce recurrence rates when added to the standard Ponseti treatment. However, current evidence is still limited and more high-quality experimental studies are required to provide clinical treatment recommendations.

Our data suggests that clinical assessments of evertor muscle function seem valid to identify children unlikely to experience a recurrence as long as they comply with the bracing regimen. However, clinical assessments of evertor muscle activity do not seem sensitive enough to accurately identify those children in need of additional treatment to prevent clubfoot recurrence. Little et al. (2019) reported that about 30% of the children unable to evert their ankle joint immediately after casting did not experience clubfoot recurrence. This is surprising, as one could expect that an inability to evert the ankle would lead to excessive inversion during functional activities such as walking and on the long-term recurrence of clubfoot deformity. We propose 2 main reasons for this seemingly contradictory finding.

First, clinical assessments of evertor muscle activity require (voluntary) activation of isolated muscle groups in a static, sitting position. Functional activities such as unperturbed walking are rhythmic and muscle coordination is largely automatized (Dominici et al. 2011, Yang et al. 2019, Bizzi and Ajemian 2020). The possibility exists therefore, that even though children are unable to evert their ankle joint in a static position, they are still able to control ankle-foot joint motion during functional activities such as walking. Second, clinically assessed evertor muscle activity is subjective and some children, especially at this young age, might not understand or have difficulties in following the instructions of the clinician, leading to inaccurate estimates of evertor muscle function. To better identify children in need of additional intervention to prevent clubfoot recurrence, current clinical assessments of evertor muscle function might be complemented with objective and instrumented measurements (e.g., instrumented gait analysis).

Next, we assumed that more severe initial deformities underlie higher congenital deforming forces and are asso-

ciated with a higher recurrence risk. However, our analysis revealed inconclusive findings. The meta-analysis revealed a small but statistically significant association between Dimeglio scores and recurrence rates, whereas the qualitative analysis and analysis on the Pirani scores did not reveal significant associations. The Dimeglio and Pirani scoring systems are widely used and accepted tools to assess clubfoot severity, plan treatment progression, and inform parents of the expected treatment course (Flynn et al. 1998, Wainwright et al. 2002). However, our data and previous studies question their clinical validity in predicting recurrences. In addition, even though radiographic assessments of ankle-foot joint mobility might improve objectivity of joint mobility assessments we did not identify a clear association between radiographic assessments of dorsiflexion range of motion or the lateral tibio-calcaneal angle and recurrence rates. Our findings are in line with previous studies reporting only moderate to poor correlations between Dimeglio and Pirani scores and the number of required cast changes or the need for additional surgery (Chu et al. 2010, Agarwal and Gupta 2014, Gao et al. 2014, Fan et al. 2017). These findings might imply that manual and radiographic assessments of joint mobility and subjective scoring systems of disease severity are not sensitive enough to accurately quantify disease severity and categorize children based on recurrence risk or expected treatment outcome (Dyer and Davis 2006, Cosma and Vasilescu 2015).

Another potential measure of disease severity is the number of required cast changes to correct the initial deformity (Haft et al. 2007, Chong et al. 2014, Zhao et al. 2018). Our data supports the assumption that more severe deformities require more cast changes to achieve correction, provided these were properly executed. In particular, those children who received > 5 cast changes during Ponseti treatment should be monitored more closely to prevent recurrence.

Finally, analyses of demographic factors revealed an association between educational level and marital status of the parents and recurrence rates. The assumption is that parents with lower education levels have more difficulty understanding the importance of preventive bracing and that single parents have less time for caregiving and treatment due to work obligations negatively affecting compliance rates (Dobbs et al. 2004, Avilucea et al. 2009, Mootha et al. 2011). Assuring that parents understand the importance of bracing and providing different sources of information on various educational levels is a potential strategy to improve compliance and reduce recurrence risk. In some cases, sensor-based monitoring might support parents to comply with the bracing regimen (Sangiorgio et al. 2016).

We identified 2 main aspects requiring improvement in future studies to better identify children with recurrence risk. First, future studies should aim to use more objective and possibly instrumented assessments to establish the exact relationship between musculoskeletal factors and recurrence risk. Second, there is a need for consensus on the definition of

recurrent clubfoot deformities. Clubfoot recurrence or relapse is currently defined as either the reappearance of physical qualities of a clubfoot, the need for further treatment after Ponseti treatment or dynamic supination movement while walking (Hosseinzadeh et al. 2019, Thomas et al. 2019). This lack of consensus on a definition impairs comparison between studies, quantification of severity of recurrent deformities, and identification of recurrence risk factors (Gelfer et al. 2019).

The main limitation of this systematic review is that not all included studies were part of the meta-analysis due to a lack of reporting of absolute values. This may have influenced the results and might in part explain the contradictory findings for the Dimeglio score. Furthermore, all included studies demonstrated risk of bias. Alongside this, the average 3-year follow-up period is considered to be too short, because recurrence rates peak around 5 years post initial correction (Stouten et al. 2018). Future studies should incorporate longer follow-up periods (> 5 years) and use randomized controlled, blinded study designs (Wallace et al. 2019).

Conclusion

To conclude, brace non-compliance and poor evertor muscle activity have been identified as main recurrence risk factors and it is therefore important that these be closely monitored during clinical follow-up of clubfoot patients. More experimental evidence is required to conclude whether adding stretching to the standard Ponseti treatment protocol is safe and if it should be added for further reductions in recurrence risk.

Supplementary data

Appendices 1–3, Table 1 and Figures 2–6 are available as supplementary data in the online version of this article, <http://dx.doi.org/10.1080/17453674.2021.1982576>

HS, CG: designed search strategy literature search, performed literature search, study selection, assessment of literature quality, performed data extraction and statistical analysis, writing, and revision of manuscript. SM, MS: study design, additional support for study selection, interpretation of the results, revision of manuscript. ATB: clinical interpretation of the results, revision of the manuscript.

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