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REVIEW ARTICLE

Lower limb lengthening in patients with disproportionate short stature with achondroplasia: a systematic review of the last 20 years

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Parents of children suffering from disproportionate short stature due to achondroplasia may wish to have surgical leg lengthening carried out for the child. The aim is not to increase height, but rather to achieve physiological proportions in the body. In a systematic review of the literature on the topic dating from the last 20 years, the surgical approaches used for this purpose were analyzed in accordance with the Preferred reporting items for systematic reviews and meta-analyses (PRISMA) criteria. Twelve studies show that to date, involvement of the child in decision-making at the start of treatment has been expected and that it is recommended from the age of 12. In highly heterogeneous patient groups, with varying factors involved and different techniques being used, lengthening (often by more than 10 cm) is described. High complication rates are reported, with many setbacks often requiring repeat surgery. Using PALEY'S multiplier method, the expected standing height, sitting height, and leg length can be predicted and an individualized treatment approach can be planned and operative procedures could be started in early childhood as PERETTI suggests. As the patients are unable to be involved in decision-making as young children, these data may provide a basis for offering differentiated advice to parents, who usually consult a pediatric orthopedist at a very early stage in the child's life.

Keywords: Achondroplasia, limb lengthening, congenital short stature, external fixator

Abbreviations: ISI, Institute of Scientific Information; PRISMA, preferred reporting items for systematic reviews and meta-analyses

Implications for Rehabilitation

- Achondroplasia and congenital dysproportional short stature is a condition which restricts quality of life often through stigmatisation.
- Reconstructive surgery by the meaning of deformity correction is a technique available to this patients (Lower) limb lengthening is an operative treatment concepts which tries to better the ratio of disproportion and lengthens the legs not only for improvement of body height
- This systematic review of the literature of the last 20 years describes the most common operative concepts and their limitations

Introduction

Along with hypochondroplasia, achondroplasia represents a separate subgroup of osteochondrodysplasias and creates an external appearance of disproportionate short stature [1,2]. Approximately 80% of cases are caused by new mutations [1–4]. Various efforts have been made to classify the range of congenital skeletal anomalies. On the basis of data from seven population-based birth defect-monitoring programs in the United States, the estimated prevalence of achondroplasia ranges from 0.36 to 0.60 per 10,000 live births (one in 27,780 to one in 16,670 live births) [5].

The disproportion involves extremities that are too short relative to the trunk and head, due to inadequate enchondral ossification in the long bones, with an adult height that is below the third percentile. The prospective final height averages around 136 cm (120–148 cm) and is thus clearly in the short-stature range [1,3]. In Germany, for example, individuals below a height of 140 cm are certified as having a state of severe handicap and are entitled to apply for an appropriate disablement pass. In most countries, buildings, furniture, vehicles and many everyday objects are standardized in size and adapted to physiological growth [6]. The leg length that can be achieved is therefore extremely important in relation to everyday activities such as sitting in a chair with the soles

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on the ground, using toilets, using public transport, climbing stairs, or driving vehicles that have manual gears without needing special adjustment.

The perception of normal proportions has been established by the quotient described in the Zurich longitudinal growth study, based on the ratio of crown-rump length to subischial leg length, or sitting height to subischial leg length [7]. During growth, the proportion consisting of the subischial leg length continuously increases and the proportion consisting of the trunk and head (the sitting height) continuously declines. In individuals with normal growth, the quotient at skeletal maturity is 1.11 ± 0.05 in boys and 1.14 ± 0.05 in girls [6,7]. In achondroplasia, the quotient is often >2.0. A difference in body height also occurs in the process, which may be sufficient to reach the threshold for short stature – often >30 cm.

Among the various surgical options that can be offered to those affected, what is involved is not a cosmetic adjustment of body height, which has been regarded critically in the literature [1,8,9]. The aim of treatment is to calculate the adjustment of leg length (and arm length) required to reach standard proportions and to treat disproportion by achieving proportions that are as physiological as possible. A minimum leg length of 65 cm needs to be achieved, and the threshold for small stature of 140 cm must be exceeded.

In addition to many other orthopedic considerations, the focus since the 1980s has been on options for surgical leg lengthening. The fundamental research conducted by Ilizarov led to a method allowing bilateral lengthening with acceptable risks [10]. It was shown subsequently that psychological aspects of the treatment measures need to be taken into account to enable those affected, whether with or without lengthening operations, to lead happy lives [9].

No satisfactory pharmaceutical or even causal form of treatment for achondroplasia is yet available that would allow growth of the long bones in order to reach normal proportions and a height above the third percentile [2]. However, improvements in implants and standardization of surgical procedures and postoperative courses are increasingly making it possible to use several short lengthening procedures to provide treatment in stages that are socially acceptable for the patients affected and for their relatives [1,9,11–15].

With the information that can now be exchanged among those affected through the Internet, and with relatives who usually have good networks through self-help groups, there is growing awareness that the type of surgery involved should *not* be aimed at creating as much bone and thus adding as much body height as possible, preferably in a single procedure and preferably as quickly as possible. Lengthening to a prospective final height of 124–134 cm in a patient with achondroplasia is not a logical approach. Neither the small stature nor the disproportion would be changed, despite the surgical risks involved and prolonged treatment periods incurred.

Since Paley's review in 1988, in which the lengthening approaches for patients with achondroplasia available at the time were described in detail, no further critical summaries on the topic have appeared in the literature [11]. In the last 20 years technology, medical and surgical skills and protocols should have developed drastically. With a systematic review of the literature from the last 20 years, the present paper sets out the approaches to staged lengthening in patients with achondroplasia that have been described, the ages at which the operations are recommended, and the results and the complication rates presented in studies with a high evidence level (at least level 3B; www.cebm.net).

Materials and methods

Systematic review

A Cochrane Library search (on January 20th, 2010) using the term "achondroplasia" identified four clinical trials and two technology assessments; none of the studies was concerned with surgical approaches.

None of the studies used a protocol in accordance with the PRISMA conditions [16]; two further database searches were carried out, using the inclusion criteria of

- Publication in English and
- Publication date 1989 or later,

and the exclusion criteria of

- Studies not including an outcome for surgical cohorts with extremity lengthening (lower extremity)
- Fewer than five patients with achondroplasia
- Studies not using bone lengthening alone, but primarily administration of growth factors, platelet-rich plasma, or stem cells;
- Those using the method of chondrodiastasis or distraction epiphysiolysis.

The full text of the parameters, variables, and minimum data to be investigated was:

1. Proportion of patients with achondroplasia as a percentage of the total group
2. Age and age range for the patients at the time of surgery
3. Number of operations per patient/number of operations per bone
4. Lengthened bone (femur or tibia)
5. Healing index or wearing time for fixator, in days or months
6. Lengthening achieved in millimeters or centimeters per operation, or in total
7. Surgical method (longitudinal, transverse, cross-leg)
8. Lengthening device used
9. Complications, events influencing the outcome

A search in the "Topics" in the Institute of Scientific Information (ISI) Web of Science (January 20th, 2010; http://isiknowledge.com/wos) using "achondroplasia AND lengthening" produced 39 hits. Twenty-seven studies met the exclusion criteria purely on the basis of the details given in the abstracts.

A PubMed search (January 21st, 2010; http://www.ncbi.nlm.nih.gov) using "('achondroplasia' [MeSH Terms] OR

'achondroplasia' [All Fields]) AND lengthening [All Fields]" produced 63 hits. Forty-nine of the studies met the exclusion criteria purely on the basis of the details given in the abstracts. The remaining 14 papers [1,10,15,17–27] included all 12 of the studies identified in the ISI Web of Science search that were still relevant.

Two reviews from 1991 were excluded [1,10]. The remaining 12 studies were hand-selected and included in the analysis, as they met at least six of the nine comparison criteria listed above [15,17–27].

Statistical data

Microsoft Excel 2003® was used to analyze the statistical data. Descriptive statistics were sufficient, and significance levels did not need to be calculated. Due to the heterogeneity of the literature reports covered in the systematic review, it was not possible to conduct a meta-analysis in accordance to the PRISMA conditions.

Results

The results for the nine basic items for which standard data were recorded are described in particular. In the three relevant studies by Aldegheri et al. included in the review, the groups of patients described suggest that there must have been considerable overlapping of individual patients among the groups [17–19]. Although the numbers for the total groups, at 140 [17],150 [19], and 140 [18], appear to be fairly consistent, the study periods in the "Materials and Methods" sections are given as 1981–1996 [17] and 1990–1995 [19], while a study period is not stated in the 1989 paper [18]. The numbers of patients with achondroplasia in the highly heterogenous groups included vary, with 80 [17], 29 [19], and 45 [18] patients. The other groups, with widely varying numbers, and the heterogeneity of the methods and groups, unfortunately do not allow any further statistical evaluation in relation to complication rates or the healing index.

Sum and proportion of patients with achondroplasia as a percentage of the of the study groups

The systematic review showed wide variation in the size of the groups of patients studied. The size ranges from 12 up to 172 patients. Eight studies did not explicitly investigate patients with achondroplasia as a group during surgical leg lengthening and instead had larger, heterogeneous groups [15,17–20,22,23,26]. The sum of achondroplastic patients ranges from 7 to 80. The proportion of achondroplastic patients at the total amount of patients ranges from 19% [19] to 100% [21,24,25]. Not all parameters were clearly apparent for the groups of achondroplasia patients.

Age and age range for the patients at the time of surgery

The range of average ages in 12 reports, independently of the absolute numbers of patients, was 8.7–16.7 years. Overall, using the age ranges at the time of the first operation given in 11 of the 12 reports, patients with achondroplasia underwent the first lengthening procedure at ages of between 3 and 35 years.

Number of operations per patient/number of operations per bone

Values of this item were provided very inconsistently in the analysed studies. Nine authors are representing results of tibial and femoral lengthening but not of the same patients. For some reasons the intersection could not be determined. At least all authors have concepts for femoral and tibial lengthening procedures. It depends on their surgical approach if they advice two operations in total for at least one lengthening of every bone of the lower limb. A staged approach with two lengthening procedures of tibia and femur is described at least by two authors [15,21].

Lengthened bone (femur or tibia)

There are three tibial study groups [19,22,24] and two groups with only femoral lengthening [22,25]. The remaining eight studies are reporting about femoral and tibial lengthening procedures [15,17,18,20,21,23,26,27]. Due to the uncomparableness of the presentation of the results in these papers no further analysis or meta-analysis was applicable.

Healing index or wearing time for fixator

No unusual healing index values are reported in the various studies; when stated, they range from 20.8 to 39 d/cm.

Lengthening achieved

The average lengthening ranges reported were 5.7–20.5 cm. Four groups of authors report average lengthening of more than 10 cm, although it is not always clear whether the total lengthening described in each patient refers to several operations or a single operation [16,17,19,22]. Villarubias et al. report one operation in the femur and one operation in the tibia, each with a target distraction length of 15–17 cm; however, they do not provide an average value, but only the range of 11–30 cm. A healing index that might allow inferences to be drawn is not given [26].

Surgical method

The approach used for reproportioning in achondroplasia is only clearly stated in a few studies [15,21,22,25]. A staged approach using several lengthening procedures during the course of treatment is explicitly reported by two research groups [15,22]. Four groups describe the use of the longitudinal simultaneous approach, at least for some of their patients [17,20,23,27]. Use of the cross-leg approach was reported in three papers, at least for some of the patients [17,23,27]. The parallel bilateral procedure is described by 10 research groups, at least for some of the patients or for use in the tibia [15,19–27].

Lengthening devices

While two groups of authors still reported use of the Wagner device, sometimes with a modified Wagner technique [23,26], nine research groups used various monolateral fixator models,

usually from the same manufacturer [15,17–20,22,23,25,27]. Use of the devices in the femur and tibia is described. At least three groups of authors used classic Ilizarov ring fixators for tibia lengthening [15,23,24].

Complications

In particular, complications were evaluated using the authors' own classification systems, not established in the literature, and scoring systems were not used to assess the outcomes. The fundamental study by Paley [12] is cited by five research groups, but is then either not used [15,21,22,25] or not used correctly [24]. Some key findings of complications are listed in Table I, that shows the results for the basic items for which standard data were recorded with further explanation in the bottom line of the table.

Absolute numbers and percentage shares were not applicable in four of the twelve studies [15,20,21,25]. The authors of this studies only have mentioned, "yes, there were complications" Some of them were listed exemplarily: Fractures during and after lengthening of the bone, muscle contractures, nerve and vessel injuries during operation, nerve dysfunction because of lengthening tension. In five studies the sum of complication was reported, but their distribution among the patients is missing. Three authors provide absolute numbers and range [17,18,24].

Table I. Results of the analysis of 12 studies with patient groups >5, comparing approaches to lengthening procedures in achondroplasia: surgical procedures, implants, timing of surgery, healing indexes, and complications [15,17–27].

Study No., Year	Patients in Study Group (n)	Achondroplasia Patients (n)	Age at First Op. (y)	Range (y)	Bone	Increased Length (cm)	Range (cm)	Healing Index (days/cm)	Implant	Approach	Complications/ patients with complications
2009 [25][a]	20	20	12.5	8–21	F	9.2	4.5–13.0	39	Monolateral	Transverse	29/n.a.
2006 [24][b]	24	24	12.9	4–35	T	6.84	3.5–10.3	26.06	Ring fixator	Transverse	46/23
2001 [17][c]	140	80	15.1	11–23	F, T	20.5	11–28	n.a.	Monolateral	Longitudinal, cross-leg	39%/31
1999 [19][d]	150	29	16.7	n.a.	T	10.5	n.a.	35.3	Monolateral	Transverse	27/n.a.
1998 [22][e]	121	28	11	4–23	F	13.3	n.a.	20.8	Monolateral	Transverse	60/n.a.
			13	3–38	T	11.5		26.6			81/n.a.
1997 [27][f]	42	35	14.5	10–18	F, T	7.2	4.5–12.0	30.8	Monolateral	Longitudinal, cross-leg, Transverse	44/n.a.
1996 [21][g]	12	12	9.5	6.5–13	F, T	n.a.	2.5–11.0	n.a.	n.a.	Transverse	Yes/n.a.
1995 [15][h]	28	22	8.7	4–17	F, T	5.7	4.0–6.5	n.a.	Monolateral, ring fixator	Transverse	Yes/n.a.
1993 [20][i]	28	7	15	12–19	F, T	6.9	3–10	36	Monolateral	Longitudinal, Transverse	Yes/n.a.
1991 [23][j]	28	17	15.3	4–19	F, T	9.63	6–15		Wagner device monolaterally, ring fixator	Longitudinal, cross-leg, Transverse	71.2%/n.a.
1990 [26][k]	172	?	?	4–30	F, T	n.a.	11–30	n.a.	Wagner device	Transverse	Yes/n.a.
1989 [18][l]	140	45	16.7	12–27	F, T	6.6	3–12	39	Monolateral	N.a.	20/12.1%

Abbreviations: F, femur; n.a., not available/data not provided; T, tibia.

[a]Compares initial bone length with lengthening amount in two groups: A, <50% lengthening in comparison with initial bone length and B, >50%.

[b]Only the tibiae were examined, only with a bifocal technique, 15 × treatment including femoral, lengthening only carried out in combination with deformity corrections.

[c]Unclear in which patients chondrodiastasis was carried out 60 × femorally, 60 × tibially; callotasis in 75%, longitudinal approach used in 30 of the 140 patients, dropouts due to knee problems, cross-leg approach used in 110 of the 140 patients. No data for outcomes or complications, surgical method used, or operated bone on in relation to achondroplasia.

[d]Only the tibia was examined; three groups with different monolateral lengtheners were compared; heterogeneous overall group, no specific approach for achondroplasia, complications not capable of being assigned to specific conditions.

[e]For all patients, lengthening is given per bone, with details given separately for tibia and femur; 100 lengthened segments (56 femurs, 54 tibiae) in achondroplasia.

[f]The first 28 patients underwent longitudinal simultaneous surgery with a 3-month pause between the legs; five patients had cross-leg treatment; nine patients had bifocal transverse parallel tibia.

[g]The question addressed by the study concerned the prospective and achieved height, 20 years' experience; a difference between boys and girls was noted, and it is therefore recommended that boys should be treated starting at the age of eight and girls later; no details on healing course, implants, or complications. However, a staged approach, as 60 bones were lengthened in 30 operations in 12 patients.

[h]A staged approach is presented: first operation on the tibia at age 5; first operation on the femur at age 6; second operation on tibia at age 10–11; second operation on femur at age 12–13. Group included six achondroplasia patients in whom three operations had been carried out, a further seven who had only had two operations, and a further nine with only one operation. The actual average age of the achondroplasia patients cannot be derived from the table of raw data; for the second operation it was 8.3 years (range 5–16 years) and for the third operation 10.5 years (range 9–12 years).

[i]There were only seven patients with achondroplasia in the group; three underwent longitudinal simultaneous lengthening and four had transverse parallel lengthening. It is not clear whether or how many patients underwent chondrodiastasis (four in the overall group) instead of callotasis.

[j]Inconsistent approach: longitudinal simultaneous lengthenings initially, but later in the series a cross-leg approach is used, as well as transverse parallel. Heterogeneous use of implants, with both the Ilizarov ring fixator on the tibia and also bifocal tibial lengthening with a monolateral fixator; overall, the Villarubias method (modified Wagner technique) was used 50 times, monolateral 38 times, and ring fixator six times.

[k]The actual number of achondroplasia patients in the overall group cannot be determined, as they are subsumed into a subgroup of 133 patients within an overall group of 172 patients. Multiple concomitant soft-tissue procedures are described. Two groups who underwent the original Wagner technique are compared with others in whom a technique modified by the authors was used. The age at the first operation was <7 years in the historical group, while in those who underwent the authors' technique the age of 10 years is preferred. No exertion is permitted during the entire treatment period. The overall group was extremely heterogeneous, with an unclear relation to achondroplasia. The approach involved one lengthening each in the femur (15–17 cm) and one in the tibia (15–17 cm). Generally, the study with the poorest level of evidence (expert opinion) of all the papers mentioned in the review.

[l]Heterogeneous group, with no distinction between hypochondroplasia and achondroplasia. Figures for achondroplasia can often not be distinguished. It is recommended that the treatment should be carried out at the end of the growth period. In most of the patients, all four long bones were each lengthened once, but the sequence and approach are not clear. It is assumed that there was a high degree of overlap with the groups described in studies no. 3 and 4 in this table, by the same group of authors.

Discussion

In the approach of Peretti et al. [15] to surgery for children with achondroplasia, in which the lengthening and axis correction procedures are started during early childhood, decision-making and the basic assessment of the pros and cons lie with the parents alone. Involvement of the patients themselves in the decision-making process has usually been required during the last 20 years, implying the level of understanding shown by a 12-year-old, for example. However, the results of the present study show that there is no evidence for a higher or lower complication rate in relation to the age of the first operation. In the systematic review, only four reports were found describing homogeneous groups of patients with achondroplasia [21,23,24,27]. Due to extremely heterogenous patient groups and methodologically weak definition of the groups, it was not fully clear in seven studies to what extent the outcome was related to bone lengthening in each of the groups of achondroplasia patients [15,17–20,22,23,26].

By standardizing the surgical approach, with an acceptable burden for the children affected and several short treatment periods, very good intermediate results can be reported with a high level of evidence.

An evidence level of 3b was only reached in three studies [19,21,24]. These three studies in particular, however, were those in which an approach involving reproportioning was least evident. Vaidya et al. mainly present patients who underwent lengthening in the tibia as well during correction for deformities, in some cases combined with femur lengthening after a slight time delay [24].

In addition, the Paley classification is used imprecisely, and difficulties for which another intervention under anesthesia was required are described as minor complications [24]. Ganel and Horoszowski do not present an outcome study, but instead focus on the question of the extent to which the prospective final height that can be achieved with lengthening operations in achondroplasia patients is affected by gender differences [21]. A difference between boys and girls was noted on the basis of 20 years' experience in 5 girls and 7 boys, and the authors recommend that the operation should be carried out starting at the age of 8 in boys and later in girls, so that at the age of 15 another treatment step for lengthening can take place [21]. Not all of the girls had grown to the predicted extent after the lengthening operations. A simultaneous bilateral and staged procedure is recommended. In 1999, Aldegheri presented a similar group of patients, either overlapping with or duplicating the cases treated in his other studies [17,18]. However, the study only investigates the results of tibial lengthening in three groups using different monolateral lengthening devices made by one manufacturer [19]. A bilateral parallel approach is described.

Overall, the literature for the last 20 years does not include any studies with an evidence grade higher than four that present an approach to lengthening the bones of the extremities in patients with achondroplasia.

There are *four conceivable approaches* to simultaneous lengthening in several segments that have been described for patients with achondroplasia:

1. All four segments at once:
2. Longitudinal simultaneously: the femur and tibia first on one side and then on the other side [17,20,23,27]
3. Cross-leg inverse: right femur and left tibia first, then vice versa [17,23,27]
4. Transverse parallel: both femurs similar first, then both tibiae similar, or vice versa [15,19–27]

The first approach has not yet been used and is not described in any of the studies discussed here.

The second approach, which four of the 12 research groups used at least for a time, leads to relevant leg length differences during the treatment interval, in addition to the existing disproportion. As a distinct case requiring treatment, it would be difficult to compensate for these leg length differences using shoe heightening (6 cm), and an orthoprosthesis would be required. The approach thus inevitably requires a secondary procedure, disregarding the potential social and medical disturbances (and in case of failure, medicolegal consequences as well) that may result.

The third approach, which creates discordance in the height of the knee joints and gait during the treatment interval, also inevitably requires the patients to undergo another operation. We believe that approaches based on the principle of "If you say A, then you'll have to agree to B as well" in connection with what is actually a highly elective procedure need to be reconsidered. A desire on the part of the patient or the parents to achieve an improvement in body proportions and an increase in height to above the threshold for small stature must not lead compellingly to a treatment that may take several years and be associated with complications, the "completion" of which for a single stage of the treatment will necessarily require another procedure to be carried out later. This forcible staged approach should be regarded as obsolete.

In our view, only the fourth approach allows the treatment to be provisionally completed after each individual step, even within the staged approach. At the same time, it also makes it possible to omit a treatment step, to carry it out at a later time, or to select only one of the steps if what is desired is only deformity correction, rather than reproportioning. Further treatment can also be carried out in other locations or institutions (if the parents happen to move house). Changes of opinion regarding further treatment in general due to specific events, whether family-related or treatment-related, can also be taken into account.

- Related to the findings in this review we would consider that using any surgical method other than the bilateral transverse parallel approach in patients with achondroplasia cannot be adequately justified. Ten of Twelve of the authors are using this approach today.
- In patients with achondroplasia, surgical reproportioning can start in the early childhood [2,5,8,10,11,15,21,23,24]. With modern implants, standardized surgical planning

[28], and growth calculations [13], a structured approach to treatment can be applied. Looking at the range of the age at the time of fist operation it becomes much more clearer that six of the 12 authors of the reviewed studies have experience in operative treatment in children younger than 5 years old [15,22–25].

- Waiting until the patient is able to become involved in decision-making may increase the rate of complications. Starting surgical treatment in early childhood – as Peretti et al. and Correll and others stated [1,8,15] – seems to be a debatable approach. It links optimal biologically conditions with optimal healing and anastasis. Now that the technique of leg lengthening is much better, with few complications, this latter point could be answered. Studies with larger cohorts of younger patients will be expected soon.
- The late outcome results of those procedures should be analyzed and further well-structured prospective homogenous studies. Usage of structured predicting and scoring systems like Paley et al. [12,13] suggested and classifying of the late outcome with comparable classification systems is strongly recommended in the future. Otherwise no higher evidence of these procedures in can be expected.

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