Title: Limb Lengthening for Achondroplasia

Date: 22 June 2007.

Context and policy issues:

Skeletal dysplasias are a group of over 200 genetic disorders that affect the size and shape of the limbs, trunk and skull, typically resulting in short stature. Achondroplasia is the most frequently encountered form of nonlethal skeletal dysplasia. It affects about 0.5 to 1.5 in 10 000 births, making it the most common cause of short-limbed dwarfism. In addition to short stature, individuals with achondroplasia often develop pronounced forward curvature of the spine in the lumbar region (lordosis) and spinal stenosis later in life, which may require surgery to correct. Other features of achondroplasia include neurological complications, craniofacial abnormalities, sleep-disordered breathing, thoracolumbar kyphosis, angular deformities of the knee and leg, otitis media, deafness, speech delay, weight gain and obesity. Functional, cosmetic and psychological problems may also be encountered.

Lengthening of the arms and legs of individuals with achondroplasia can potentially result in height gains of up to 30cm and may improve function. The Ilizarov technique is a method of distraction osteogenesis developed in Russia in the 1950’s and introduced in North American in the 1980’s. In addition to limb lengthening in achondroplasia, the Ilizarov technique is used to correct limb length discrepancy, deformities, joint contractures, nonunion of fractures and reconstruction following trauma, tumors, and infection. The procedure involves a partial cut of the bone cortex followed by a short resting period. The bone is then slowly distracted at a rate of about 1mm per day using a circular (Ilizarov) or uniplanar external device attached to the bone by means of pins or wires. Slow progressive elongation allows new bone to regenerate across the gap but prevents bone segments from rejoining. The external device remains in place about 1 to 2 months per centimeter of bone lengthened, allowing the newly formed bone to consolidate. The Ilizarov technique has a number of advantages in that it allows new bone to form without the use of bone grafting, does not require the ends of the bones to be internally

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fixated and allows for simultaneous correction of angular deformities. Complications are, however, relatively common with the procedure, some of which include infection, pain, swelling of the limb, neurovascular complications, contractures of the soft tissues, subluxation and dislocation of adjacent joint, bone-related problems at the lengthened site and psychological problems.5,7

Limb lengthening in achondroplasia is a contentious issue. A number of insurers in the United States cover the Ilizarov technique to correct significant limb length discrepancies, bone defects and deformities, but consider the technique cosmetic when used to correct short stature.8-10

The American Academy of Pediatrics' Health Supervision for Children with Achondroplasia does not specifically endorse or condemn limb lengthening, but states “Extended limb lengthening using a variety of techniques has been used far more elsewhere than in North America. It can result in substantial increases in ultimate height. However, it is arduous, not without risk, and costly. Most families alternatively choose to modify the environment to accommodate the child rather than the converse.”11

Similarly, the Little People of America’s Medical Advisory Board does not advocate or condemn symmetric extended limb lengthening.12 In a position paper (Appendix), the Medical Advisory Board states “There are no established medical indications for symmetric extended limb lengthening (ELL). While it may have benefit in preventing certain orthopedic and neurological complications in some skeletal dysplasias, the procedure is primarily being performed for adaptive, cosmetic, and psychosocial reasons.”12 The Medical Advisory Board recommends that individuals who are considering limb lengthening be old enough to participate in discussions of its risks and benefits.12 Individuals who choose to undergo the procedure are cautioned to select a multidisciplinary program with expertise in skeletal dysplasia that is equipped to follow patients for 10 years or longer.12

Research question:

What is the clinical effectiveness of limb lengthening surgery for children with achondroplasia compared to no treatment for quality of life, spinal stenosis, leg numbness, back pain and posture?

Methods:

A limited literature search was conducted on key health technology assessment resources, including PubMed, EMBASE, The Cochrane Library (Issue 2, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI's HTAIS, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2002 and the present, and are limited to English language publications only.

Summary of findings:

Search Results
The literature search did not produce any health technology assessments, systematic reviews, meta-analyses or controlled studies that evaluated limb lengthening relative to no treatment in children with achondroplasia. Although surgical protocols may involve a series of lengthening surgeries in all four limbs of individuals with achondroplasia,13 the literature search did not locate any such reports. Two case series reports that described outcomes of lengthening the lower limbs of individuals with achondroplasia using the Ilizarov technique were identified.14,15
We did not specifically search for studies published prior to 2002, but several older case series reports were identified. These studies did not, however, include the outcomes of interest. They reported outcomes primarily dealing with the bone (i.e. percent lengthening, healing index, and days with external fixator in place) and complications. As the Ilizarov technique originated in Europe, there may be reports published in languages other than English that were not identified by the search.

Case Series Reports

Vaidya et al. reported outcomes of 24 individuals with achondroplasia who underwent tibial lengthening using the Ilizarov technique. Ilizarov device was used to externally fixate the tibia. In total, 47 limbs were lengthened (bilateral tibial lengthening in 23 patients and unilateral tibial lengthening in one patient). Deformities were gradually corrected as part of the operative procedure and several patients also underwent femoral lengthening. The average patient age was 12.9±7.5 years old and the average duration of follow-up was 2.4±1.0 years. Following surgery, the average gain in tibial length was 6.8 ± 1.3 cm or 41.3% of the original length. In 76% of cases, the total amount of tibial lengthening exceeded 40%. The average time of external fixation was 131 ± 29 days. The average healing index (the number of days required for the complete healing of 1 cm of lengthened bone) was 26.1 ± 3.3 days per centimeter of lengthening. Statistically significant improvements in measures of angular deformity of the tibia were also observed. Overall, 46 complications were observed in 29 limbs, the most common of which were pin tract infections and ankle equinus contractures. Complications necessitated 29 additional surgical procedures.

Vargas Barreto et al. reported the outcomes of 58 individuals who underwent 94 tibial lengthening procedures using the Ilizarov technique with external fixation using the Ilizarov device. Twenty-two individuals had achondroplasia or hypochondroplasia. The remaining individuals had limb length discrepancy (n=21) or short stature (n=15) due to another cause (i.e., Turner Syndrome, Noonan Syndrome or constitutional short stature). A number of individuals with short stature underwent simultaneous lengthening of the opposite femur and tibia. It was not reported whether correction of a deformity was part of the operative procedure. Outcomes in achondroplasia were not reported separately but were included in the short stature group (n=37). For short stature, the average age at the time of surgery was 21 years old. The average tibial lengthening was 9.1 cm. On average, lengthening occurred over 152 days and the average healing index was 54.2 days per centimeter of lengthening. A total of 54 complications were observed in the short stature group. The authors did not provide a detailed report of specific complications, but 36 complications were reported as minor, while 18 complications required additional surgical intervention.

While these case series reports may be useful from a descriptive perspective, they lacked methodological rigor. For instance, the reports included small patient populations that were heterogeneous in terms of surgical procedure and pathology. Some individuals had the tibiae and femora lengthened while others had only the tibia lengthened. The overall outcome of lengthening both tibiae and femora was not reported. This question may be of interest given that combined lengthenings could increase the total gain in height and possibly function. Further, the second case report presented the results of individuals with short stature of different etiologies as a single group. This makes interpretation challenging as that the authors stated in their discussion that individuals with Turner Syndrome had more complications than short stature of other etiologies. The usefulness of these reports was also limited by their focus on the effect on bone, rather than on longer term outcomes such as quality of life, function, spinal stenosis and other neurological complications of achondroplasia. The duration of follow-up, however,
was likely insufficient to assess the impact of limb lengthening on these outcomes.\textsuperscript{14} Finally, both reports lacked sufficient detail with respect to methods. Details about the patient populations were limited to age and indication for lengthening.\textsuperscript{14,15} Vargas Barreto et al. did not report the duration of follow-up or whether deformities were also corrected.\textsuperscript{15} Neither report gave details of the surgical technique or device that was used for lengthening of the femur.\textsuperscript{14,15}

Conclusions and implications for decision or policy making:

Given the quality of these studies\textsuperscript{14,15}, the outcomes measured and the duration of follow-up, it is difficult to draw any conclusions with respect to the long-term impact of limb lengthening in achondroplasia. While there is evidence that gains in height can be attained, it is not clear how this would impact function, quality of life or common complications of achondroplasia. Because of the lack of long-term data, the potential for complications, and physical demands of the procedure, limb lengthening in achondroplasia remains controversial.

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Appendix 12:

Extended Limb Lengthening

Little People of America Medical Advisory Board
Position Summary, 2006

The following position summary is not intended to either advocate for or condemn extended limb lengthening. It is meant to be a measured summary of information that may be of value to members of the small stature community and members of Little People of America.

The techniques for leg lengthening were originally developed for correction of limb length discrepancy and are an accepted therapy for this. Over the past two decades the procedure has been expanded to allow for symmetric lengthening in individuals of short stature. Although this newer application has generated widespread interest, it has also created controversy among both medical professions, and persons of short stature and their families.

There are no established medical indications for symmetric extended limb lengthening (ELL). While it may have benefit in preventing certain orthopedic and neurological complications in some skeletal dysplasias, the procedure is primarily being performed for adaptive, cosmetic, and psychosocial reasons.

Research is being done on the safety and long-term functional outcome of this procedure. Currently no prospective, randomized studies have yet been completed.

The possible complications of ELL are numerous. These include:
- Nerve injury (usually temporary);
- Infection;
- Angulation;
- Non-union;
- Increased contractures (of the hip, knee and/or ankle);
- Fractures;
- Unequal limb lengths;
- Increased risk for late onset osteoarthritis.

Although the acute complication rate associated with ELL has been reduced, it is still substantial.

This is what patients should have prior to initiation of ELL:
- Confirmation of a specific short-stature diagnosis. The relative risks and benefits of ELL are different in different types of skeletal dysplasias.
- Counseling concerning the natural history and genetic implications of the relevant skeletal dysplasia, independent of ELL.
- Adequate discussion of the benefits and risks of ELL (including medical complications, financial issues, educational and psychological concerns).

Prospective patients should be of an age to participate fully in these discussions and in the decision-making process.
We recommend that before, during and after ELL operative procedures, evaluation should include:

- Orthopedic assessment;
- Physical therapy assessment, including evaluation of mobility, activity, functional limitations, etc.;
- Clinical neurological evaluation;
- Peripheral vascular assessment;
- Psychological evaluation, including self-image, body image, peer relationships, and family relationships.

All of these evaluations will require the cooperative involvement of orthopedic surgeons, physical and occupational therapists, medical geneticists, radiologists, psychologists and/or psychiatrists, and social workers in longitudinal management. We caution prospective patients and their families to seek out institutions that offer the broad multidisciplinary approach that is needed. An institution should have a program with special emphasis and expertise in skeletal dysplasia. The institution should be equipped to follow the patient for a decade or more.

Complete success of ELL is not guaranteed. Furthermore, ELL will not change other health related needs of individuals of short stature. They will still need to have ongoing care by someone knowledgeable about the natural history of their specific diagnosis.

ELL is a complex procedure with far-reaching implications. Interested individuals should carefully assess the institution and personnel, as well as all risks and benefits of ELL prior to committing to this procedure.

Approved by the LPA Medical Advisory Board and LPA Board of Directors July 2006.