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Conclusion: The current study provides a method to quantify knee height asymmetry. Using this method, it was shown that knee height asymmetry is frequent in youth with limb-length discrepancy in both pre- and post-corrective surgery states. The relatively high incidence of knee height asymmetry highlights the importance to investigate the impact of knee height asymmetry in youth living with a limb-length discrepancy.

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Response to Reviewers:
Reviewer #1: Comment 1. Please read and include the following references in the discussion section:

Response 1. All references have been added to the manuscript’s discussion and reference sections. This is highlighted in yellow in the text.
Incidence of Knee Height Asymmetry in a Pediatric Population of Corrected Leg Length Discrepancy:
A Retrospective Chart Review Study

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Keywords: gait; knee height asymmetry; leg length discrepancy; pelvic obliquity.
Introduction

Leg Length Discrepancy (LLD) is a common disorder that estimated to be from 40% to 70% of the population [1, 2]. A study found that LLD greater than 20 mm affects approximately one person in every 1000 [3]. LLD can be corrected in different ways, according to the length of the discrepancy and presence of angular deformity, through lengthening, shortening or growth arrest. Usually, the primary goal is to equalize the leg lengths; and maintaining symmetry between segments of both body sides is not always considered. Segmental asymmetries ultimately will lead to the knee joints being misaligned in the coronal plane. This situation has been referred to as a knee height asymmetry (KHA)[4, 5].

KHA can arise from four conditions: First, preoperatively in patients with short femur or tibia and an uncorrected LLD (Figure 1a). Second, in patients with short femur and a corrected LLD who wear a shoe lift postoperatively (Figure 1b). Third, in patients with a LLD who underwent a corrective surgical intervention at an adjacent or adjacent-contralateral, non-affected leg segment, such as in a LLD due to a short femur that was fully or partially corrected with tibia lengthening (Figure 1c). Finally, it can be observed in individuals with above knee amputations [6].

The potential consequences of KHA on the patients have been acknowledged in two publications [4, 5]. In these publications, it was suggested that KHA of less than 40 mm does not result in functional or cosmetic disabilities. However, none of the authors cited above have provided scientific evidences to support their claim. Perhaps one of the main reasons for this lack of support is that there is currently no clear methodology to quantify KHA. There is also a scanty data with regard to the incidence of KHA and to the average size of KHA in the context of LLD.

The purpose of the present study is to provide a methodology to quantify KHA, and to establish the incidence of KHA in a patient population attending the limb length discrepancy clinic in a pediatric-orthopedic hospital center.
Materials and Methods

Charts review

A retrospective chart review was performed on all patients who visited the limb length discrepancy clinic at the Shriners Hospital for Children-Canada from December 2009 to December 2015. The Institutional Review Board of McGill University approved the study. Hospital charts were reviewed to identify the age, sex, medical diagnosis, leg length discrepancy and the site of the affected lower-limb segment. Inclusion criteria were referral to the LLD clinic and availability of full antero-posterior lower-limb standing x-rays. Exclusion criteria were absence of pre- or post-surgery data or absence of full antero-posterior lower-limb x-rays, absence of knee joint (arthrodesis; knee disarticulation). In addition, precise measurement of pelvic obliquity, KHA and LLD can be affected by hip deformities/contractures and severe bowing of long bones [7]. Therefore, to avoid confusion with regard to KHA and LLD, we excluded patients with cerebral palsy, hip contracture, hip dysplasia (Proximal femoral focal deficiency, Perthes disease, Developmental Dislocation (Dysplasia) of the Hip) and severe genu varum or valgum including patients with osteogenesis imperfecta.

Diagnoses have been classified into: congenital, idiopathic, traumatic, infection, neurologic and developmental. Congenital diagnosis indicates deformities presented at birth. Idiopathic limb deformity group includes patients with limb deformity without known cause or patients with no documentation indicating the diagnosis. Limb deformities that resulted from infectious or traumatic events are classified into infection and trauma groups, respectively. Developmental ones indicate diagnosis of known developmental diseases, like developmental dysplasia of the hip. Patients with neurological disorders, like cerebral palsy, were classified as neurological causes.

Radiographic Measurements

Full standing antero-posterior radiographs were used to measure LLD and KHA, which allows full-length weight-bearing view [4]. When possible, LLD and KHA measurements were taken on preoperative and postoperative x-rays. If the patient had more than one surgery, measurements were taken based on the last surgery. In case the patient had multiple consecutive corrective surgeries with external fixator, without any fixator-free period, then the preoperative measurements were taken before applying the fixators and the postoperative measurements were obtained after fixator removal. Lower limb lengths were measured by the
mechanical axes of both limbs, which was defined as the distance (in mm) from the center of the femoral head to the midpoint of the ankle joint [8] (Figure 2a). LLD was measured by subtracting length of both limbs.

To quantify KHA, pelvic obliquity (mm) and the difference in the knee joint line’s height (mm) was computed. Pelvic obliquity was measured by calculating the difference between the levels of both femoral heads. The difference of knee joint lines was measured by taking the difference in height of the mid-point of both joints’ lines, (i.e., the mid-point between the tibial spine and femur inter-condylar notch). KHA was obtained by subtracting pelvic obliquity from knee height joint line (Figure 2).

Figure 3 depicts the following methodology: A positive value was given if the right hip or left knee was higher than the left hip and right knee and a negative value was given if the left hip or right knee was higher than the right hip and left knee respectively. If no pelvic obliquity was observed, then KHA was measured as the difference in knee joints lines’ height (Figure 3). All measurements were done from standing antero-posterior radiographs using the McKesson Radiology Station software (version 12-1-1; McKesson Corporation, San Francisco, USA).

Reproducibility analysis was conducted on a subset of 15 randomly chosen participants. Leg length, pelvic obliquity and knee height asymmetry measures were all done a second time by the same rater. Results showed coefficients of variation of 0.69, 7.80, and 12.52 % for leg length, pelvic obliquity and knee height asymmetry, respectively. ICCs [95% Confidence intervals] were high with ICCs of 0.999 [0.996-1.000], 0.994 [0.983-0.998], 0.934 [0.996-1.000] for leg length, pelvic obliquity and knee height asymmetry, respectively.

Data and Statistical Analyses

Descriptive statistics are presented as means and standard deviations. For individuals with pre- and postoperative radiographs, a repeated measure ANOVA design was used to determine the difference in KHA and LLD between pre- and postoperative measurements. All tests were 2-tailed and throughout the study and $p = .05$ was considered significant. These calculations were performed using the PASW Statistics software version 24.0 (SPSS Inc, Chicago, Illinois).

Results

A total of 358 individuals visited the LLD clinic at the Shriners Hospital for Children-Canada between December 2009 and December 2015. A total of 52 individuals met inclusion criterion and were included (see
Figure 4) in the study (22 Females/30 males; mean [SD] age at surgery = 13.8 [4.6] years). On average, X-rays were taken 10 ± 11 months prior to surgery and 12 ± 12 months post-surgery.

Within the 52 individuals included in the study, a proportion of 52% (n=27) of the population visited the clinic due to congenital causes and 48% (n=25) for other causes (Figure 5). All individuals underwent corrective surgeries. There were three main corrective interventions that were performed, representing 90% of all surgeries: Epiphysiodesis, distraction osteogenesis and hemi-epiphysiodesis were performed in 46%, 33% and 12%, respectively (Table 1). Within these three intervention categories; 40% of them were done at the femur only; 17% at the tibia only and the remaining 33% were performed at both the femur and tibia. The remaining 10% of surgical corrective interventions was composed of femoral shortening, intramedullary rodding, and osteotomy.

The 52 individuals included had both pre- and postoperative full standing lower-limbs x-rays. In the preoperative state, 67% of the studied population had a KHA of 20 mm or less, 25% had a KHA between 20 mm and 40 mm and 8% had a KHA of over 40 mm (Table 2). The average KHA preoperatively for all 52 individuals was 17 ± 14 mm (range: 0-59 mm), which represents roughly 2.5% of total limb length. In the postoperative state, the proportion of individuals in each of the three KHA size categories remained largely unchanged as compared to the preoperative state: 69% had a KHA of 20 mm or less, 27% had a KHA between 20 mm and 40 mm and 4% had a KHA of over 40 mm (Table 2). The averaged postoperative KHA for the 52 individuals was 14 ± 2 mm (range: 0-49 mm), which represents 2.2% of total limb length.

Changes between preoperative and postoperative LLD and KHA were also assessed. About KHA, there was no significant change in KHA size between preoperative and postoperative states (p = 0.22). In 48% (31 individuals) KHA increased by an average of 6.6 ± 10.0 mm from pre- to post-intervention whereas in the other 52% KHA decreased by an average of 10.2 ± 12.0 mm. In contrast, the absolute LLD decreased significantly between preoperative and postoperative states with an averaged reduction in LLD of 16.0 ± 18.8 mm, or put in other words, a reduction of 68% (p < 0.001) of the original LLD.

Out of the 52 individuals who had both pre- and postoperative x-rays, two showed an increase in KHA of more than 20 mm postoperatively and another one had a 14-mm increase in KHA.

Discussion
The goal of the present retrospective study was to provide a method to measure KHA and to estimate the incidence of KHA in a population visiting a LLD clinic. We have suggested that KHA could be determined by computing both pelvic obliquity and knee's height joint lines. Using this method, it was found that the incidence of pre-surgical KHA between 20 mm and 40 mm was 25% and was 8% for KHA over 40 mm.

Our data indicates that the average amount of KHA, did not change after a corrective surgery was performed. Around half the participants had a reduction in KHA whereas the other half had an increase following surgery. In two cases an increase of KHA of over 20 mm was reported postoperatively. In these cases, KHA increased due to an incomplete correction at the affected site being fully corrected by lengthening at the ipsilateral non-affected site: a short left tibia was partially lengthened and femur lengthening of the same side was performed to complete LLD correction. In another patient KHA increased by 14 mm. This patient had both shorter femur and tibia on the same side. Full compensation occurred only at the femur, which introduced the KHA. Taken together these results indicate that KHA was not considered in many of the interventions that were performed.

The consequences of a KHA on the individual functional status are unknown at present, even though it was suggested that under 40 mm of KHA there should not be any functional limitations [4]. It is not possible to conclude on this point based on the current data, but it should be mentioned that a LLD of 20 mm is sometimes considered as a limiting factor in an individual functionality due to abnormal gait patterns and lower back pain [9]. It is therefore plausible that a KHA of 20 mm could limit an individual's functionality [10].

KHA implies a change of length and weight of lower limb segments between one body side and the other, and is therefore susceptible to interfere with normal biomechanical gait patterns. In the long run, altered gait patterns can cause pain secondary to increased joints’ loads [11]. Gait is certainly one of the most fundamental abilities that are directly related to an individual's quality of life [12]. For example, in ambulatory children with cerebral palsy it has been shown that the severity of gait pathology was inversely proportional to the child's quality of life [12]. For these reasons, preserving gait or limiting gait impairments is often considered crucial in neurological and orthopedic pediatric conditions such as cerebral palsy and leg length discrepancy [13, 14]. The fact that 33% of the studied population remained with a KHA of 20 mm and over despite having received a corrective surgery for their LLD, warrants the need for studies assessing the consequences of KHA on the patient’s functional status.
In that regard, a previous study on lower limb fractures healing and rehabilitation recommend short-(6 months) and long-term (> 12 months) laboratory gait analyses along with follow-up gait analyses done in home-based settings (with insole pressure system) follow-ups [15]. This recommendation is based on the observation of significant functional improvements between 6 and 12 months post-surgery [15]. Own clinical observations suggest that functional improvements can occur until 24 months post-surgery warranting long-term follow-ups of locomotor function. Gait analysis in home-based settings could also contribute to better understand and personalize weight-bearing rehabilitation programs. These programs have been shown to be poorly adapted to individuals, leading to poor patient’s compliance.

At the psychosocial level, it has been shown that youth may report cosmetic complaints because of a LLD, which may be associated with low self-perception [16, 17]. Based on these observations, it can be suggested that correcting the absolute LLD by introducing a significant KHA might result in cosmetic concerns. In that matter, a recent study using dynamic gait computational model showed that a knee height altered by 10% of total leg length can lead to the an altered perception of the knee joint position from an external observer [18]. Our current data indicates that 5 individuals had a KHA of more than 10% of total leg length postoperatively (data not shown).

**Study Limitations**

One limitation of the study is that 229 individuals who visited the LLD clinic did not have adequate lower-limbs x-rays to measure KHA. In the field of LLD, standing posture is preferred because many LLD are associated to or origin directly from limb misalignment [19]. In addition, due to the three-dimension structure of bones, it is suggested that three dimensional radiographs will provide a better support to understand long-term functional consequences of KHA and LLD’s surgical interventions [20]. One recommendation would thus be to assess limb length and KHA in an upright weight-bearing posture in order to monitor the measurements more precisely [19].

Another limitation of this study is that the timing of preoperative and postoperative radiography was not standardized. This might have led to an underestimation of KHA in preoperative radiographs whereas it might have led to an overestimation of KHA in the postoperative radiographs due to incomplete distraction or epiphysiodesis. However, we ran an additional analysis in which it was shown that removing individuals with
radiographs taken 7 months or more preoperatively or 7 months or less postoperatively did not affect the proportion of patients with KHA nor did it change the average size of KHA. Based on our method for x-ray review, preoperative x-rays were chosen before any lengthening frame was applied. Postoperative x-ray data were collected from the first postoperative whole lower limb standing x-ray after device removal. This explains the relatively long period between the preoperative and postoperative x-ray and the surgery.

Finally, it has been shown that more complex surgical interventions (e.g. a multi-segment distraction osteogenesis) are more likely to lead to long-term functional deficits compared to simpler ones (e.g. a single segment distraction osteogenesis) and should be considered as a confounding factor in post-surgery functional analyses [21].

Conclusions

This retrospective chart review study has showed that the incidence of KHA is frequent in youth with LLD in both pre- and post-corrective surgery states. Furthermore, this study provides a method to quantify KHA and the relatively high incidence of KHA highlights the importance to investigate further the impact of KHA in youth living with a LLD.

Acknowledgements

We appreciate the contribution of physiotherapists Monica Chan, Gloria Thevasagayam and Rochelle Rein for clinical feedback, as well as Kathleen Montpetit, MSc, OT, from the Shriners Hospitals for Children-Canada for assistance with ethics submission.

Compliance with Ethical Standards:

Conflict of Interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval: For this type of study, formal consent is not required.
References


Figure Captions

Figure 1. Illustration of potential causes of knee height asymmetry: a) Short femur and short tibia, b) Short femur and tibia, corrected with shoe-lift, c-d) Corrective surgery done at remote site (ipsilateral or a different segment of the contralateral site)

Figure 2. Illustration of lower limb and knee height measurements: a) Leg Length Measurement, b) Knee Height Joint Lines with Pelvic Obliquity, c) Knee Height Joint Lines Measurements Without Pelvic Tilt

Figure 3. Method to compute knee height asymmetry. A positive value was given if the right hip or left knee was higher than the left hip and right knee and a negative value was given if the left hip or right knee was higher than the right hip and left knee respectively. If no pelvic obliquity was observed, then KHA was measured as the difference in knee joints lines’ height

Figure 4. Consort Flow Chart

Figure 5. Frequency of diagnosis of the 52 patients included in the study who underwent LLD corrective surgeries
## Table 1. Types and number of observed interventions

<table>
<thead>
<tr>
<th>Interventions</th>
<th>n</th>
<th>Femur (n)</th>
<th>Tibia/fibula (n)</th>
<th>Femur and Tibia (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epiphysiodesis</td>
<td>24</td>
<td>12</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Distraction</td>
<td>17</td>
<td>7</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Hemi-epiphysiodesis</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>other</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>21</td>
<td>9</td>
<td>17</td>
</tr>
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</table>
Table 2. KHA et LLD Individuals with both Pre- and Post-surgery Data

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>&lt;20 KHA</td>
</tr>
<tr>
<td>n</td>
<td>35</td>
<td>13</td>
</tr>
<tr>
<td>%</td>
<td>67</td>
<td>25</td>
</tr>
<tr>
<td>Average KHA (mm)</td>
<td>9 (14)</td>
<td>29 (18)</td>
</tr>
<tr>
<td>Average LLD (mm)</td>
<td>26 (15)</td>
<td>43 (14)</td>
</tr>
</tbody>
</table>
Figure 01
Figure 02
Figure 03

KHA = 0mm

KHA = -40mm

KHA = 80mm

Click here to download Figure Figure 3.pdf
Assessed for eligibility (n = 358)

Excluded (n = 306)
- Absence of full standing antero-posterior x-rays (n = 229)
- Missing pre- or post-surgical x-rays (n = 47)
- Severe bone deformities (n = 24)
- Cerebral Palsy (n = 6)

Full data set (pre- and post-surgical x-rays; n = 52)