1-1-2016

Quantitative Assessment of Children with Osteogenesis Imperfecta

Adam Graf
Shriners Hospitals for Children

Joseph Krzak
Shriners Hospitals for Children

Angela Caudill
Shriners Hospitals for Children

Ann Flanagan
Shriners Hospitals for Children

Peter Smith
Shriners Hospitals for Children

See next page for additional authors

Published version. *Transitional Care in Osteogenesis Imperfecta: Advances in biology, Technology, and Clinical Practice*, (2016): pp. 217-232. Publisher link.

Authors
Adam Graf, Joseph Krzak, Angela Caudill, Ann Flanagan, Peter Smith, and Gerald F. Harris

13 QUANTITATIVE ASSESSMENT OF CHILDREN WITH OSTEOGENESIS IMPERFECTA

Adam Graf, M.S.[1]
Joseph Krzak, Ph.D., P.T., P.C.S. [1,2]
Angela Caudill, M.P.T.[1]
Ann Flanagan, P.T.[1]
Peter Smith, M.D.[1]
Gerald Harris, Ph.D., P.E.[1,3]

[1] Shriners Hospitals for Children, Chicago, IL
[2] Physical Therapy Program, College of Health Sciences, Midwestern University, Downers Grove, IL
[3] Orthopaedic and Rehabilitation Engineering Center (OREC), Marquette University and The Medical College of Wisconsin, Milwaukee, WI

INTRODUCTION

Assessments of children with Osteogenesis Imperfecta (OI) are typically limited to a physical exam and observations from a clinician during a hospital visit. Often quantitative information such as bone mineral density and outcome questionnaires is obtained, but with the increasing prevalence of motion analysis and other performance type laboratories, there are many other tools available, which could be beneficial to this patient population. These laboratories can provide data supplementary to morphologic and radiographic data that is helpful in tracking changes in the patient's functional abilities, recovery from fracture, and treatment outcomes. This chapter will cover some useful evaluation methods for children with the most commonly seen types of OI and provide some examples of their test results.

METHODOLOGY – EVALUATION TOOLS

It is important to first identify areas of pain and eliminate patients with fractures from being asked to perform functional assessments. Those individuals with minimal-to-no-pain and no fractures could benefit from a variety of assessments such as a thorough physical examination that includes joint range of motion (ROM) measurements and strength testing. Plantar pressures provide a quick evaluation of foot mechanics and can identify biomechanical deformities like pes valgus. Gait analysis quantifies temporal-spatial parameters (i.e. walking speed), joint motion (kinematics), joint forces (kinetics) and muscle activity (electromyography). Postural control testing is useful in ensuring the safety of these patients by identifying standing instability and it also plays a role in the development and completion of gross motor skills. Combined, these tools provide a quantitative assessment of the physical abilities as part of a comprehensive functional evaluation of children with OI. This information can assist in making the best treatment decisions and track patient progress over time.

Pain Assessment

The Faces Pain Scale-Revised[1] is a commonly used tool to have the patient indicate their level of pain on a scale of 0 – 10. Establishing the level of pain is important prior to proceeding with any functional assessment. If pain levels are above the 0 – 1 range certain tests may not produce accurate results.

Physical Exam

A lower extremity physical exam performed by a physical therapist or orthopaedic physician is useful in providing joint range of motion (ROM) and strength measurements. The Minimum Standardized Gait Analysis Protocol (MSGAP)[2] can be used for collecting measurements bilaterally of the subject's hips, knees and ankle joints. Table 1 shows an example of a typical physical exam of a patient with OI type I. Note the abnormal knee hyperextension and ankle hypermobility as well as the hindfoot valgus and some asymmetry.

Table 1. Physical exam measures of a 9 year old female with type I OI.

Physical exam: 9 year old female with OI type I		
LEFT ROM	JOINT MOTION	RIGHT ROM
	HIP	
130	Flexion 0-125°	130
0	Extension (supine, Thomas test) 0°	0
75	Abduction (flexed) 0-45°	75
45	Abduction (extended) 0-45°	48
20	Adduction 0-20°	20
60	Internal Rotation (prone) 0-45°	60
40	External Rotation 0-45°	40
	KNEE	
150	Flexion (supine) 0-140°	150
145	Flexion (prone) 0-140°	145
10 Hyper	Extension 0° (Note Hyperextension)	8 Hyper
10	Popliteal Angle (op extended) 25°	10
80	Straight Leg Raise 0-90°	80
	ANKLE	
50	Dorsiflexion (knee flexed) 0-20°	45
40	Dorsiflexion (knee extended) 0-10°	35
45	Plantarflexion 0-45°	50
45	Adduction (post tib) 0-40°	40
40	Abduction (peroneals) 0-30°	30
	STATIC TRANSVERSE/CORONAL ALIGNMENT	
10° AV	Femoral Anteversion (Ryder)	10° AV
2° Evert	Thigh Foot Angle	14° Evert
5° Invert	Transmaleolar Axis	18° Evert
	STATIC FOOT ALIGNMENT – WEIGHT BEARING	
8° Valgus	Hindfoot	15° Valgus
Decreased	Midfoot (Arch)	Decreased
Neutral	Forefoot	Neutral
Neutral	Great Toe	Neutral

To break the cycle of fracture leading to immobility, leading to weakness, leading to fracture in children with OI, it is helpful to quantify baseline levels of strength and monitor them for deficits in order to maintain the highest level of functional ability. Due to bone fragility, strength assessments must be performed with the utmost concern for the patient's safety. Tests that apply forces or initiate resistance are often avoided in this patient population. Strength can still be assessed by having the patient perform tests without manual resistance, where they initiate the force instead of tests where forces are applied to them. Strength testing methods include:

a) Manual Muscle Test — where the therapist or physician does not apply manual resistance;

b) Functional Assessments of Strength – measure the maximum number of repetitions of movements:
   - Single leg heel rise test[3,4] assigns a plantarflexion strength score based on how many heel rises can be completed out of 20 (Example in Table 2).
   - Lateral/Frontal step ups
   - Sit to stand;

c) Dynamometry – can be used to quantify the strength of isometric muscle contractions. There are hand held devices or larger systems that a patient is seated in and positioned to isolate certain muscle groups. Table 2 displays the results of a single patient's strength represented by the single leg heel rise test score and plantarflexor strength measured using a Biodex System III (Shirley, New York).

Table 2. Strength measures for a 9 year old female with type I OI.

Test	Left	Right	Controls
Heel Rises	20	11	20
Plantarflexion* (PKTQ/BW)%	66.1	63.9	101.7
Dorsiflexion* (PKTQ/BW)%	47.7	47.7	45.5

*PKTQ/BW: This is the peak torque generated during the duration of the trial and divided by the subject's body weight so the value is reported as a percentage of total body weight.

Previous research, as well as the data in Table 2, shows that weakness is prevalent in the OI population. Common areas of weakness include the plantarflexors, shoulder abductors, hip flexors, ankle dorsiflexors and grip strength.[5-7] This weakness may affect exercise tolerance and high level gross motor activities, which results in functional skills ranging from very limited to highly functional depending on disease severity. Weakness does not appear to be progressive. This is similar to Engelbert et al., 2004, who reported that muscle strength did not change significantly over time in children with OI.[8] They found that as children aged, from ~7 years old to ~11 years old, the ability to care for themselves improved along with their overall functional ability.

Pedobarography

Pedobarography is a timely way to quantify foot mechanics during gait. Due to the characteristic ligament laxity in the OI population, pes valgus and decreased medial arches are often seen during static standing and the stance phase of gait. Flatfoot is typically a deformity created by malalignment of several adjacent joints. According to Mosca, "the anatomic characteristics of a flatfoot are excessive eversion of the subtalar complex during weight bearing with plantarflexion of the talus, plantarflexion of the calcaneus in relation to the tibia, a dorsiflexed and abducted navicular and supinated forefoot."[9] Jameson et al. have developed a pedobarographic technique that helps in the identification of poor foot mechanics, or flexible lever arm dysfunction.[10] This is accomplished by tracing the relative movement of the center of pressure across the plantar surface of the foot during the stance phase of gait. By identifying the medial-lateral location of the center of pressure progression (COPP), you can determine if the hindfoot, midfoot and/or forefoot are varus, valgus or neutral. It is hypothesized that improper foot positioning during loading may lead to inadequate shock absorption during initial foot contact and loading response, and it has been found that poor foot mechanics in OI type I can lead to reduced ankle push off power generation during forward propulsion.[11] Figure 1 displays the plantar pressures of a patient with OI next to that of a typically developing child. Notice the increased surface area in contact with the floor at the midfoot and the decreased time spent loading the forefoot.

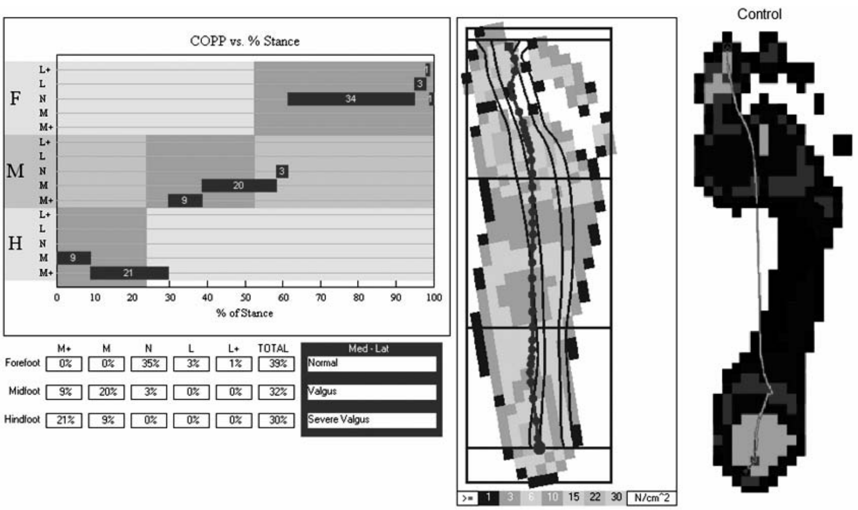

Figure 1. Pedobarography Sample Report. The top left graph shows the % of stance phase that the Center of Pressure Progression (COPP) is within the hindfoot (H), midfoot (M) and forefoot (F). Below the graph shows the % of stance phase that the COPP is normal (N), medial by 2+ std. deviations (M+), medial by one std. dev (M), lateral (L) or lateral by 2+ std. deviations (L+). Next to that is a display that summarizes the COPP location. This subject has a severe valgus hindfoot, valgus midfoot and normal forefoot COPP position, but reduced % of stance on the forefoot.

Gait Analysis

Gait analysis is another tool often used to quantify functional ability by measuring the three dimensional motion of body segments during gait. It can be used to collect data longitudinally and measure changes over time, pre and post intervention, and then compare data to a typically developing individual's gait pattern to identify deficits. Analysis of gait typically involves an observational component including video and photographs, as well as quantitative three-dimensional motion capture data. Useful parameters such as temporal spatial values (i.e. walking speed, step/stride length and foot contact time), kinematics (ankle, knee and hip joint angles/rotations), kinetics (joint forces/moments and powers) and electromyography (muscle activity) can be recorded simultaneously during walking. The recording and analysis of this information can be helpful in evaluating children with OI especially due to the disorder's heterogeneity, even within types.

Gait disturbances in OI are typically caused by underlying bony deformities or by weakness in the musculoskeletal system. These children are not known to have any neurologic conditions associated with the disease. Some individuals with OI are observed using an antalgic gait pattern to minimize the application of forces to weakened or compromised areas, while others may vault or circumduct to accommodate other problems. Gait analysis can help to identify or dissociate between primary gait deviations due to structural deformities that cause biomechanical abnormalities and the compensatory strategies used to maximize ambulatory capacity. Typically, a gait analysis will discover gait abnormalities that then need to be sorted and pieced together to uncover the primary problems. Some examples of this can be seen in Table 3.

Table 3. Gait Abnormalities and their associated problems in children with OI.

Gait Abnormality	Description and secondary gait abnormalities	Primary Problem
Increased Hip Abduction	Increased coronal plane pelvic/trunk motion (Trendelenberg pattern) Attempts to diminish forces generated by muscles that typically stabilize the hip	Gluteal weakness
Fixed Pelvic Obliquity	Vaulting on one side/circumducting on the other Flexed hip or knee	Leg length discrepancy
Decreased Peak Ankle Power Generation	Increased hip and/or knee power generation Prolonged stance phase Excessive ankle dorsiflexion due to ligament laxity	Plantar flexor weakness and/or pes valgus
Knee Hyperextension	Increased power absorption Prolonged stance phase	Ligament laxity and plantar flexor weakness

Temporal Spatial Parameters

Treatment strategies for OI should improve functional abilities, which may in turn affect some time dependent activities such as navigating a crosswalk and keeping up with peers in the community. Analysis of gait can provide insight into the level of these abilities. Table 4 shows examples of these parameters for someone with OI types I, III and IV, all of whom have reduced walking speed compared to typically developing individuals. All groups also show increased time with the foot in contact with the ground, or a delay in their foot off.

Table 4. Temporal spatial parameters for three individuals with OI.

Parameter	Type I	Type III	Type IV	Typically Developing
Walking Speed (m/s)	0.97	0.27	0.69	1.21
Cadence (steps/min)	126	65.7	95.6	122.9
Foot Off (%GC)	63.1	75.0	65.4	60.3
Double Support (%GC)	27.8	48.9	35.2	21.5
Single Support (%GC)	36.5	25.2	33.7	38.8
Step Length (m)	0.47	0.25	0.40	0.6
Stride Length (m)	0.92	0.52	0.85	1.1

Kinematics

Kinematic analysis describes joint angles during the gait cycle. Once the angular position can be calculated, the functional ability of the corresponding muscles and bones that cause that motion can be described in regards to gait. The kinematic analysis of these individuals with OI types I, III and IV reveals several trends that can be seen in the OI population (Figure 2). In these examples, the type I pattern is quite similar to a typically developing pattern, while the type III pattern is distinctly different with many gait deficits. The type IV pattern can be quite variable and in this example falls between the types I and III as far as quality of gait. Gait patterns typically correspond to the severity of the disease in these individuals. Even with the type I pattern, there are several characteristics different from the typically developing group. Here are some other common gait characteristics:

a) Type I common kinematic gait characteristics:
- Similar to typically developing children
- Increased knee hyperextension in midstance
- Increased ankle dorsiflexion throughout the gait cycle
- Reduced peak ankle plantarflexion during push off

b) Type III common kinematic gait characteristics:
- Increased anterior pelvic tilt throughout the gait cycle
- Reduced hip ROM and peak hip extension
- Reduced knee ROM with increased flexion throughout the gait cycle
- Reduced peak ankle plantarflexion during push off

- Variable rotational profiles at hip, shank or foot due to bone deformities

c) Type IV common kinematic gait characteristics:
- Variable gait pattern that can range in quality from that of type I to type III
- Variable rotational profiles at hip, shank or foot due to bone deformities
- Increased knee hyperextension in midstance
- Increased ankle dorsiflexion throughout the gait cycle
- Reduced peak ankle plantarflexion during push off

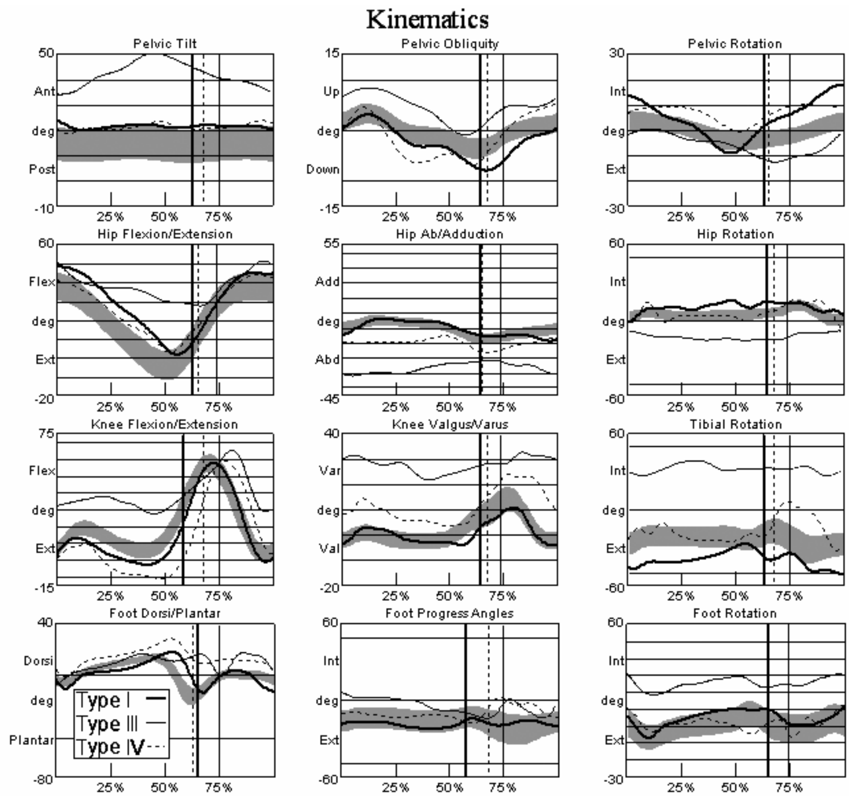

Figure 2. Gait Kinematics for 3 individuals with OI. Gray band is Typically Developing (TD) gait pattern, thick black line is an individual with type I, thin line is type III and the dotted line is type IV. The types I and IV are independent ambulators and the type III subject uses lofstrand crutches.

Kinetics

Kinetic analysis of the lower extremities during gait is somewhat limited by current technology due to the fact that the forceplate must be struck "cleanly", or by one whole foot at a time. This is difficult for individuals who use assistive devices and/or take small steps, which is the case especially in the OI type III population. However, the use of force transducer instrumented crutches, walkers or wheelchairs allows for upper extremity kinetic analysis. Of those who do "cleanly" strike the forceplates, typically individuals with types I and IV, we are able to understand in greater detail the causes of gait deviations seen in the lower extremity kinematic data. Calculating joint moments helps to explain how the body responds to external loading and the changing position of the ground reaction force during gait. Joint power is calculated by measuring the work done over time. The analysis of power data can be viewed as a summary of gait findings because it has components from the kinematic data (joint angular velocity) and the moment data, and provides a description of muscle activity (concentric or eccentric contraction). Kinetic analysis demonstrates that children with OI do typically exhibit several deficits from typically developing kinetic gait patterns (Figure 3):

a) Type I kinetic gait characteristics:
- Similar to typically developing
- Decreased plantar flexor demand
- Decreased peak ankle power generation
- Increased hip power generation as compensation for reduced ankle power

b) Type III kinetic gait characteristics:
- Often limited to upper extremity analysis using instrumented assistive devices

c) Type IV kinetic gait characteristics:
- Similar to type I but may exhibit greater deficits depending on severity
- Increased knee flexor demand due to knee hyperextension in midstance.

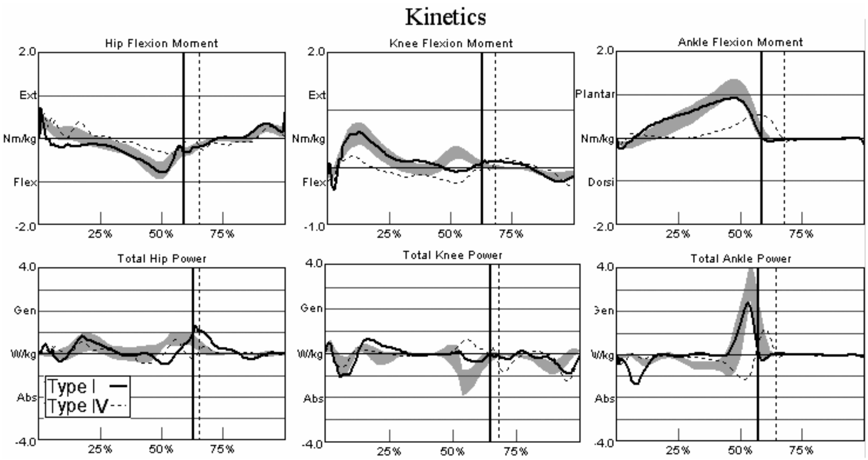

Figure 3. Gait kinetics for two individuals with OI. The Gray band is typically developing, the thick black line is an individual with type I OI and the dotted is type IV. There is no data for type III because all subjects used assistive devices causing inaccurate force plate data.

Postural Control

With a high risk of fracture in the OI population, balance and stability is of the utmost importance. Static and dynamic balance is vital for patient safety but is often difficult to assess in a clinical setting. Many individuals with OI will walk with a gait pattern that increases the duration of stance phase or delay the time until foot off to increase the time both feet are on the ground, thereby increasing stability. Static balance can be effectively evaluated using a system such as the Neurocom® SMART EquiTest® (Natus Medical, Inc., Pleasanton, CA). Postural stability is discussed further in a subsequent chapter.

Energy Efficiency

Many motion analysis laboratories now have systems capable of analyzing expired CO_2/O_2 as a measure of energy efficiency. This information is useful for objectively quantifying and differentiating the gait efficiency of children with OI compared with typically developing individuals. Takken et al. found that fatigue often limits patients with OI during activities of daily living and exercise. This may be a result of hypoactivity, and thus leads to detraining[5] and increase in the fracture cycle. Their findings confirm that OI has a large impact on functional ability depending on severity with common findings of decreased muscle strength and exercise ability.

The Cosmed K4B[2] (Rome, Italy) is an example of a device used to assess cardiopulmonary fitness. It is a wireless, portable system that allows the subject to walk and move at their desired pace making within-subject comparisons possible. There are several parameters that can be generated during the analysis of expired gases that may be useful in treating children with OI including heart rate (HR), energy expenditure (EE), VO_2, energy efficiency index (EEI)[12] and net non-dimensional (NN) scheme outputs.[13] The EEI determines efficiency of movement using HR and walking speed. The NN was introduced as a method to reduce the variability in energy expenditure due to age and stature by appropriate non-dimensionalization,[14] which makes it useful for children with OI. Table 5 and Figure 4 show the results for a 10 year old male with type IV OI during resting, walking and on an ergometer. This individual has a higher heart rate, but is nearly normal in walking efficiency compared to typically developing individuals.

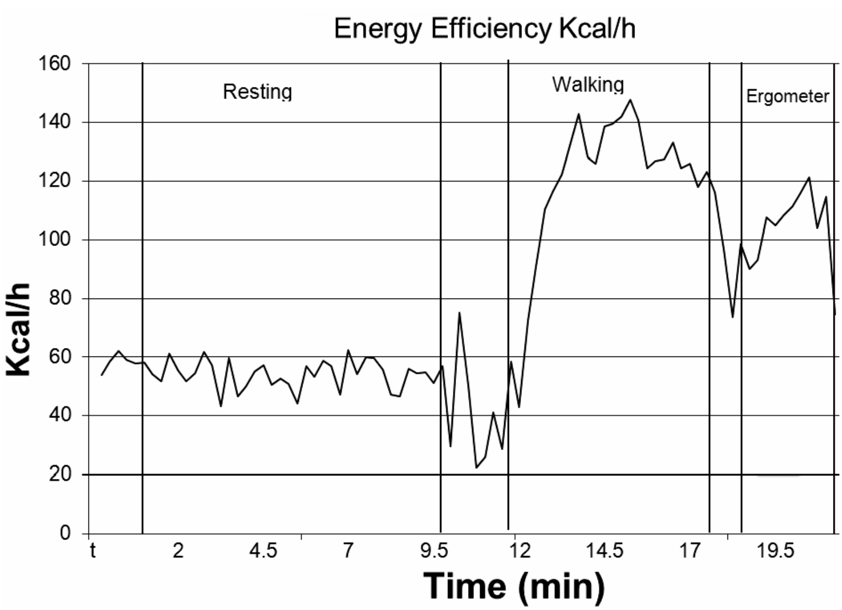

Figure 4. Energy efficiency (Kilocalories/hour) over time for roughly 10 minutes of resting, 6 minutes of walking and 3 minutes of ergometer use.

Table 5. Energy efficiency parameters for a 10 year old male with type IV OI.

Parameter	HR (beats/min)	Eehour (Kcal/h)	VO2 (ml/min)	EEI (beats/min)	Nncost
Resting (10min)	102.6	54.1	179.6	-	-
Walking (6min)	131.4	128.0	440.3	0.70	0.26
Ergometer (3min)	126.6	109.1	366.6	0.62	0.29

Assistive Devices

Assistive devices such as walkers, lofstrand crutches and wheelchairs are often used by children with severe cases of OI. It has been reported by Engelbert et al. that the severity of the collagen defect is the greatest predictor of ambulatory ability in this patient population.[15] Out of 70 children with OI all with type I were able to ambulate and 85% of those walked independently without assistive devices. Individuals with OI types III and IV had a lower chance of walking than those with type I. Rodding of the lower extremities also limited ambulation. It was found that with an increase in the number of rods inserted into the long bones there was a reduction in the subject's walking ability. Children dependent upon assistive devices prove more difficult to evaluate, but still benefit greatly from functional evaluation.

As previously mentioned, it is possible to assess upper extremity joint kinetics using walker or crutch handles that are instrumented with six-degree-of-freedom force transducers in conjunction with a kinematic model. Examples of the use of this technology can be seen in a subsequent chapter.

CLINICAL IMPLICATIONS

Motion analysis laboratories have several tools that may be helpful in assessing the functional ability of children with OI. Prior to performing any tests that require physical activity it is important to consider the classification of OI of the patient. The classification is helpful in understanding disease related characteristics specific to each class and allows for more accurate patient comparisons and expectations. Several studies have determined that strength, functional ability and prognosis for walking are closely associated with the type of OI.[3,5,8,15,16] Sillence et al. reported that rehabilitation should focus on strategies to achieve community walking in type I, exercise or household walking in type III and household or community walking in type IV. Determining the appropriate assessment tools and treatment options may also depend on the classification keeping in mind the wide range of variability in the disease (Table 6). Individuals with OI type I typically are independent ambulators with normal stature and few visible physical abnormalities that would limit function. Upon closer examination however, some characteristics may become apparent such as joint hypermobility and muscle weakness. Ligament laxity could cause knee hyperextension, excessive ankle dorsiflexion and flatfeet. Muscle weakness could be a limiting factor in high level gross motor activities. The short stature and limb deformities prevalent in individuals with type III OI may limit mobility to a wheelchair or necessitate the use of an assistive device to ambulate. If that is the case, upper extremity evaluation tools can be used such as a walker, crutches or a wheelchair instrumented with force transducers to assess loading of the bones and joints during gait. These tools are discussed further in other sections of this book. With the heterogeneous nature of OI type IV, and physical changes that occur with age in these individuals, functional assessment is very useful, though careful consideration needs to be taken in testing selection. These individuals could be administered the same protocol as for type I or type III, depending on their severity.

Table 6. Recommended evaluation tools for types of OI.

OI Type	Evaluations Tools
I,III,IV	Pain Scale
I, III, IV	Physical Exam – ROM, static alignment
I, III, IV	Strength (Manual Muscle Test without resistance
I, IV	Strength (Dynamometer Test — isometric)
I, III, IV	Pedobarography
I, III, IV	Gait Temporal Spatial Parameters
I, III, IV	Gait Kinematics
I,IV	Gait Kinetics
I, IV	Postural Control
III, IV	Instrumented Walker/Crutches/Wheelchair
I, III, IV	Energy Efficiency

The treatment of OI has improved in many ways with advancements in surgical rodding, gene and drug therapy. With increasing treatment options it is important to be able to thoroughly assess these patients in order to focus treatment in the most appropriate areas and to use the most effective methods available. The fundamental variability of this disease also necessitates the use of evaluation tools capable of measuring the abilities of children with a range of body types and functional levels, while still providing the capacity to track changes over time. These methods described in this chapter allow for both quantitative intra- and inter-patient comparison, and therefore lend themselves well to use in a clinical setting as well as for research studies.

ABBREVIATIONS

BW	Body weight
COPP	Center of pressure progression
EE	Energy expenditure
HR	Heart rate
NN	Net non-dimensional
OI	Osteogenesis imperfecta
PKTQ	Peak torque
ROM	Range of motion
TD	Typically developing
%GC	Percent gait cycle

REFERENCES

1. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain.* Aug 2001;93(2):173-183.
2. Davis R DJ, Gorton G, Aiona M, Scarborough N, Oeffinger D, Tylekowski C, Bagley A. A Minimum Standardized Gait Analysis Protocol: Development and Implementation by the Shriners Motion Analysis Laboratory Network (SMALnet). In: Harris G SP, ed. *Pediatric Gait A New Millennium Clinical Care and Motion Analysis Technology*. Piscataway: IEEE; 2000:1-7.
3. Lunsford BR, Perry J. The standing heel-rise test for ankle plantar flexion: criterion for normal. *Phys Ther.* Aug 1995;75(8):694-698.
4. Hislop HJ MJ. *Muscle Testing: Techniques of manual examination*. 6th ed. Philadelphia: W.B. Saunders Company; 1995.
5. Takken T, Terlingen HC, Helders PJ, Pruijs H, Van der Ent CK, Engelbert RH. Cardiopulmonary fitness and muscle strength in patients with osteogenesis imperfecta type I. *J Pediatr.* Dec 2004;145(6):813-818.
6. Montpetit K, Plotkin H, Rauch F, et al. Rapid increase in grip force after start of pamidronate therapy in children and adolescents with severe osteogenesis imperfecta. *Pediatrics.* May 2003;111(5 Pt 1):e601-603.
7. Caudill A, Flanagan A, Hassani S, et al. Ankle strength and functional limitations in children and adolescents with type I osteogenesis imperfecta. *Pediatr Phys Ther.* Fall 2010;22(3):288-295.
8. Engelbert RH, Uiterwaal CS, Gerver WJ, van der Net JJ, Pruijs HE, Helders PJ. Osteogenesis imperfecta in childhood: impairment and disability. A prospective study with 4-year follow-up. *Arch Phys Med Rehabil.* May 2004;85(5):772-778.

9. Mosca VS. The child's foot: principles of management. *J Pediatr Orthop.* May-Jun 1998;18(3):281-282.
10. Jameson EG, Davids JR, Anderson JP, Davis RB, 3rd, Blackhurst DW, Christopher LM. Dynamic pedobarography for children: use of the center of pressure progression. *J Pediatr Orthop.* Mar 2008;28(2):254-258.
11. Krzak J GA, Flanagan A, Caudill A, Smith P, Harris G. Analysis of Push-Off Power During Locomotion in Children with Type I Osteogenesis Imperfecta. *Journal of Experimental and Clinical Medicine.* 2011;3(5):195-199.
12. Rose J, Gamble JG, Lee J, Lee R, Haskell WL. The energy expenditure index: a method to quantitate and compare walking energy expenditure for children and adolescents. *J Pediatr Orthop.* Sep-Oct 1991;11(5):571-578.
13. Schwartz MH, Koop SE, Bourke JL, Baker R. A nondimensional normalization scheme for oxygen utilization data. *Gait Posture.* Aug 2006;24(1):14-22.
14. Baker R, Hausch A, McDowell B. Reducing the variability of oxygen consumption measurements. *Gait Posture.* May 2001;13(3):202-209.
15. Engelbert RH, Uiterwaal CS, Gulmans VA, Pruijs H, Helders PJ. Osteogenesis imperfecta in childhood: prognosis for walking. *J Pediatr.* Sep 2000;137(3):397-402.
16. Sillence DO, Morley K, Ault JE. Clinical management of osteogenesis imperfecta. *Connect Tissue Res.* 1995;31(4):S15-21.