

Acute Flaccid Myelitis and Bone Health

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Overview

- **Bone mineral density loss and treatment options in AFM**
- Clinical case presentations

Bone Mineral Density: The Problem

Problems:

Individuals with AFM develop secondary loss in bone mineral density.

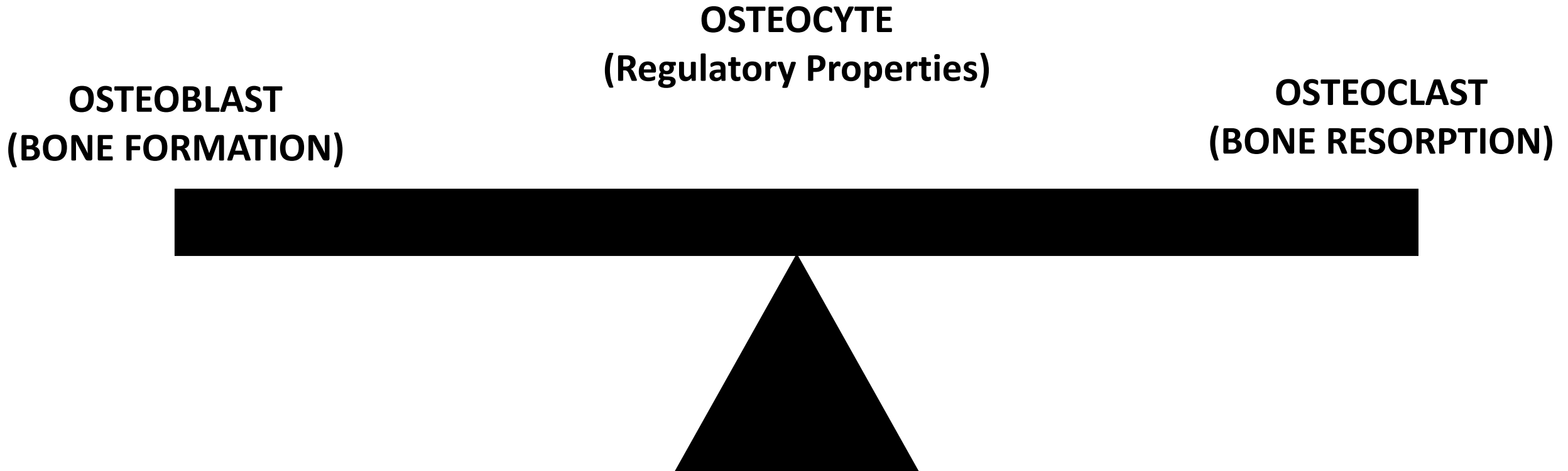
This loss has rapid onset, has associated hypercalcemia, and can increase risk of fractures or other orthopedic consequences.

There is limited evidence on the best treatment modalities for Acute Flaccid myelitis.

Bone Health Goal:

The clinical goal is to prevent fractures and other orthopedic complications and facilitate continued recovery from time of AFM diagnosis.

Bone Density Balance



Mechanical Unloading of Bone in AFM

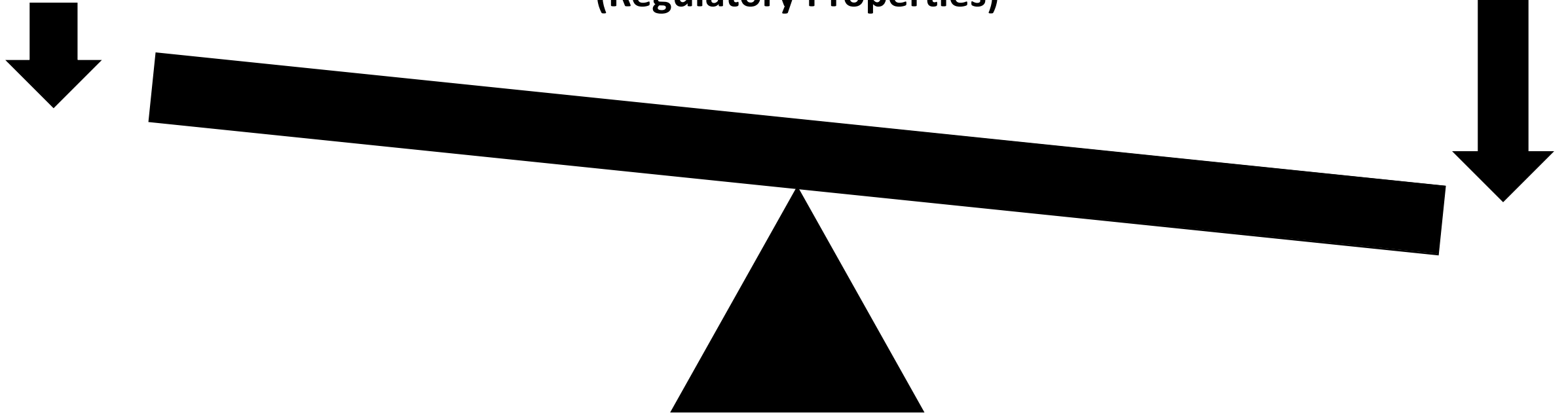
- Mechanical forces promote maintenance of bone mineral density
 - Weight bearing, gravity dependent activity
 - Muscle strengthening activity
- AFM (loss of weight bearing, onset of flaccidity)
 - Osteoblast increased activity in early stages and apoptosis in later stages (reduction in bone formation)
 - Osteoclast activation with onset within 1 month of injury
 - Osteocyte abnormal signaling, felt to have fast onset

Bone Density Balance in AFM: Bone Breakdown

**OSTEOBLAST
(BONE FORMATION)**

**OSTEOCYTE
(Regulatory Properties)**

**OSTEOCLAST
(BONE RESORPTION)**



Acute Flaccid Myelitis – Clinical Observations

- Reduction in bone mineral density with fast onset is associated with an increased risk of fractures.
- Hypercalcemia, occurring within first 3 months after AFM onset, increases risk of calcium oxalate renal stones.

Treatment Options

CLASS	MECHANISM	BENEFITS	LIMITATIONS
Bisphosphonates (Pamidronate, Zoledronate)	Antiresorptive	<ul style="list-style-type: none"> - Longest experience in pediatric populations - Long lasting effects 	<ul style="list-style-type: none"> - Use can be limited to 3-5 years duration, drug holidays
RANKL inhibitor (Denosumab)	Antiresorptive	<ul style="list-style-type: none"> - Mechanism of action specific to known target in AFM 	<ul style="list-style-type: none"> - Limited use in pediatric populations - Concern for rapid bone loss when stopped
Parathyroid hormone (Forteo, Tymlos)	Anabolic	<ul style="list-style-type: none"> - Potential use in later stages - stimulates bone formation 	<ul style="list-style-type: none"> - Limited duration - Possible osteosarcoma association
Anti-sclerostin antibody (Evenity, Setrusamab)	Anabolic	<ul style="list-style-type: none"> - Potential use in later stages - stimulates bone formation 	<ul style="list-style-type: none"> - Limited duration - Possible cardiovascular risks
Anti-TGFB antibody (Fresolimumab)	Anabolic and antiresorptive	<ul style="list-style-type: none"> - Potential utility in treating both sides of equation 	<ul style="list-style-type: none"> - Off site effects

Overview

- Bone mineral density loss and treatment options in AFM
- **Clinical case presentations**

Clinical Case Presentations

- Limited experience exists, specific to the presentation of AFM and treatment of low bone density.
- Based on SCI experience, we have a treatment goal of 4mg/kg/year of Pamidronate while on full therapy.
- 3 cases:
 - 1) Patient 1 has had significant clinical improvements in addition to regular bisphosphonate therapies
 - 2) Patient 2 has had limited/slow clinical improvements and inconsistent bisphosphonate therapy
 - 3) Patient 3 has elected not to receive bisphosphonate therapy

Patient 1

- 8 year old, previously healthy male, with onset of AFM in 10/2018. There was initial right sided weakness that progressed to flaccidity throughout. He is dependent on tracheostomy and GTube feeding
- Hypercalcemia 2 months after AFM onset and treatment with low-dose pamidronate at that time. This was repeated for re-emergence of hypercalcemia 3 months after AFM onset.
- 18 months after diagnosis he has had improvement in strength and mobility and walking with gait trainer.
- Treatment of bone mineral density with pamidronate has been continued over the course of 18 months. He has not had recognized fracture.

Patient 1: Evaluation of Bone Mineral Density

Region	3 months after onset	16 months after onset
Lumbar Spine	0.482 g/cm ² (Z-score -1.3)	0.470 (Z-score -1.9)
Left Femoral Neck	0.493 g/cm ² (Z-score -2.4)	0.490 (Z-score -2.7)
Left Total Hip	0.591 g/cm ² (Z-score -1.5)	0.514 (Z-score -2.7)
Right Femoral Neck	0.406 g/cm ² (Z-score -3.5)	0.592 (Z-score -1.4)
Right Total Hip	0.519 (Z-score -2.4)	0.480 (Z-score -3.2)
Left Distal Femur	0.474	0.377
Right Distal Femur	0.479	0.431
Total (minus head)	0.469 (Z-score -3.2)	0.452 (Z-score -4)

Pamidronate: 3.86 mg/kg/year

Patient 2

- Nearly 4 year old, previously healthy female, with onset of AFM in 10/2018 resulting in incompleting tetraplegia and dependence on tracheostomy and Gtube feeding.
- Hypercalcemia was noted 3 months after AFM diagnosis and pamidronate was started.
- 18 months after diagnosis she has not had significant improvements in mobility.
- Treatment of bone mineral density with pamidronate has been continued over the course of 18 months. She has not had recognized fracture.

Patient 2: Evaluation of Bone Mineral Density

Region	3 months after onset	15 months after onset
Lumbar Spine	0.516 g/cm ² (Z-score 0.9)	0.494 (Z-score 0.1)
Left Femoral Neck	0.403 g/cm ² (Z-score NA)	0.318 (Z-score -3.8)
Left Total Hip	0.545 g/cm ² (Z-score NA)	0.430 (Z-score -2.0)
Right Femoral Neck	0.303 g/cm ² (Z-score NA)	0.215 (Z-score -5.7)
Right Total Hip	0.514 (Z-score NA)	0.379 (Z-score -2.8)
Left Distal Femur	0.469	0.217
Right Distal Femur	0.496	0.212
Total (minus head)	0.45 (Z-score NA)	0.337 (Z-score NA)

Pamidronate: 2.71 mg/kg/year

Patient 3

- Nearly 2 year old, previously healthy male, with onset of AFM in 10/2018 resulting in incompleting tetraplegia and dependence on tracheostomy and Gtube feeding.
- Hypercalcemia was noted 3 months after AFM diagnosis and no bisphosphonate was provided. This self-resolved and no history of renal stones.
- 18 months after diagnosis he has had improvements in mobility.
- Treatment of bone mineral density with pamidronate was not started. He has not had recognized fracture.

Patient 3: Evaluation of Bone Mineral Density

Region	5 months after onset	16 months after onset
Lumbar Spine	0.413 g/cm ² (Z-score -1.0)	0.407 (Z-score -1.4)
Left Femoral Neck	0.260 g/cm ² (Z-score NA)	0.201 (Z-score NA)
Left Total Hip	0.376 g/cm ² (Z-score NA)	0.312 (Z-score NA)
Right Femoral Neck	0.361 g/cm ² (Z-score NA)	0.387 (Z-score NA)
Right Total Hip	0.507 (Z-score NA)	0.454 (Z-score NA)
Left Distal Femur	0.398	0.230
Right Distal Femur	0.505	0.362
Total (minus head)	NA	0.370 (Z-score NA)

Pamidronate: No treatment

Case Presentation Summary

- Limited data exist, specific to bone density and treatment in AFM
- Bisphosphonate therapy has been used for a handful of children with AFM and treatment appears to be well-tolerated. Future, longitudinal data, will help to characterize benefits of treatment.
- Disease severity influences bone density, with more severe presentations demonstrating greater loss in bone density.

Bone Health in an Acute Flaccid Myelitis – a cohort

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Table 1. Demographics of the sample (n=73) and those with DXA¹ scan (n=33)

Sex (male/female)	51/22
Age at paralysis onset (average)	4months-15 years (5.3 years)
Total MMT ² Manual Muscle Test	0 - 76
PAMS ³ (n= 54)	30 - 100
Number of fractures (upper/lower limb)	19 (9/10)
Community ambulatory (yes/no)	38/35
Patients that underwent DXA (male/female)	22/11
Time to DXA	3-57 months

¹ Dual-energy X-ray absorptiometry

² Manual Muscle Test

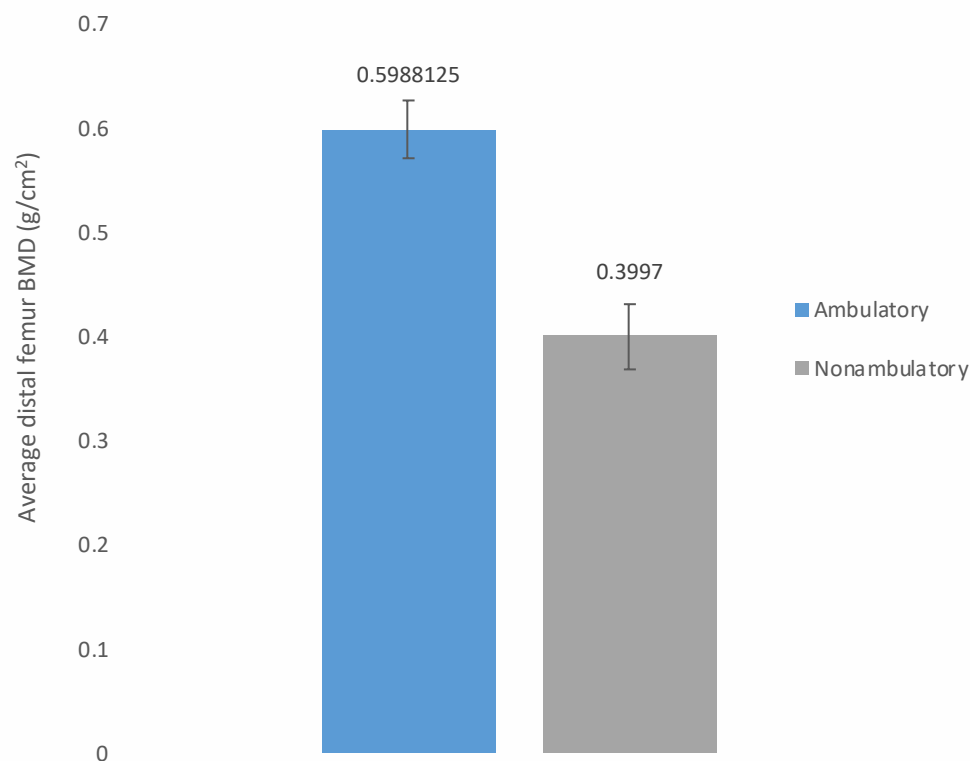
³ Physical Abilities and Mobility Scale

- Of the 73 participants, 33 (45%) had bone density measured by dual energy absorptiometry (DXA)
- 26 of them (78.7%) were diagnosed with low bone mass (LBM)
- 19 fractures occurred post onset of neurologic deficit in 11 of the children in the cohort (15 %) (9 in the arms, 10 in the legs, but only one of them in a child that was walking)



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UNLOCKING POTENTIAL

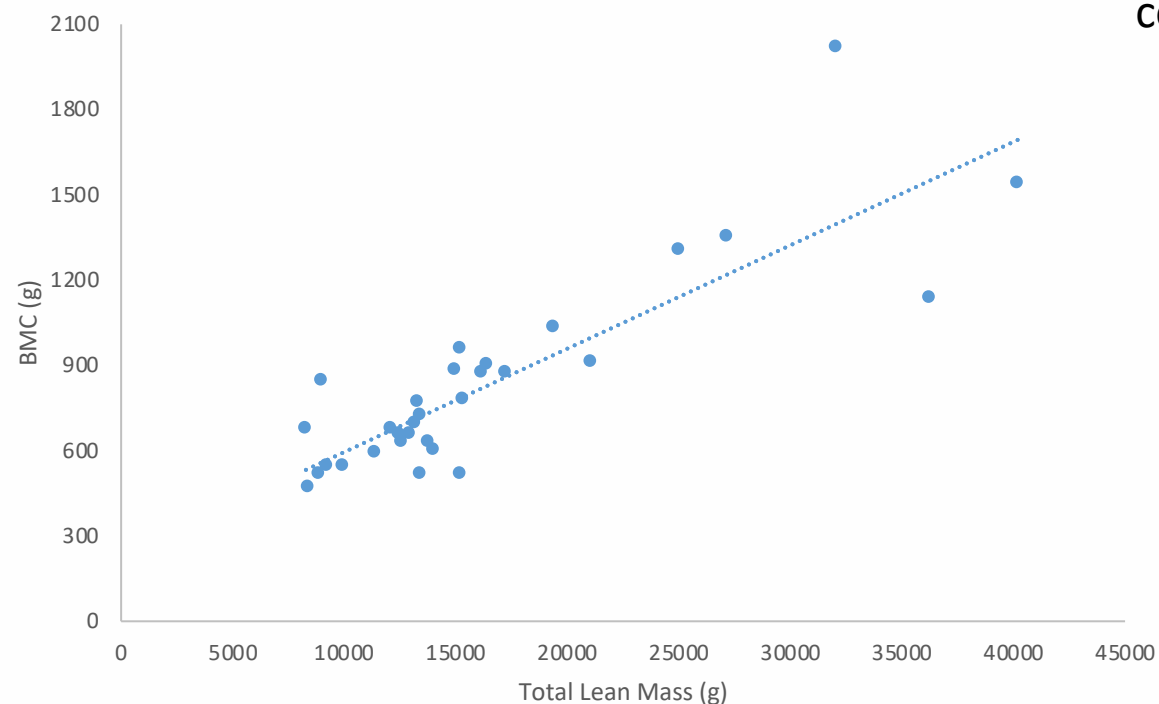
Figure 1. Average distal femur bone mineral density (BMD) in ambulatory vs. non-ambulatory patients with acute flaccid myelitis. Error bars represent +/- the standard error of mean. $P < .005$.



Bone density in the lower limbs (distal femur) was associated with ambulatory status.



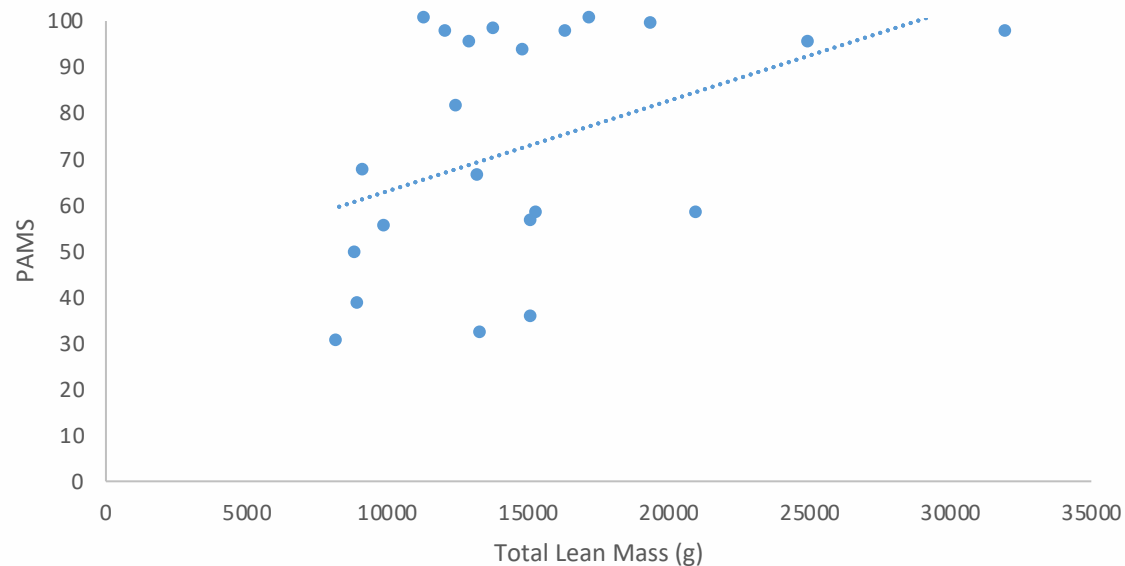
Figure 2. Total lean mass and total bone mineral content (BMC). Each point corresponds to one patient's total lean mass (g) and BMC (g). Dotted line represents the linear association. $r=.852$, $p<0.001$



Lean muscle mass
correlated with bone mass



Figure 3. Total lean mass and functional performance (PAMS). Each point corresponds to one patient's total lean mass (g) and PAMS score. Dotted line represents the linear association. $r=.433$, $p<.05$



Lean muscle mass correlated with functional performance as assessed by Physical Abilities and Mobility Scale (PAMS), but necessarily with muscle strength (MMT)



THANK YOU

- We have been fortunate to be part of the rehabilitative care of dozens of families with AFM

"We" is actually a very large team!

- Nurses, MD's
- PT, OT, SLP, TR, techs
- Social workers, Case mangers

Specific Thank You to:

Janet Dean

Carlos Pardo

Michelle Melicosta

Natalie Curley

Shannon Inches

Anna Schneider



And, most of all, Our Kiddos and their Parents



Join us in the **Sessions area** First Panel Discussion and Q/A



A Patient perspective

Sarah Todd Hammer



Respiratory health in AFM

Michelle Melicosta, MD

Kofi Anoh, RRT-NPS



Symptom Management

Joyce Oleszek, MD.



ABT in AFM

Courtney Porter, PT



Bone in AFM

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