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Ground Reaction Forces in Patients with Epidermolysis Bullosa Simplex (EBS)during walking

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Background

- Epidermolysis bullosa is a group of inherited conditions characterized by mutations in 20 genes; the commonest subtype of which, is EBS which affects up to 70% of all patients.
- Multiple proteins are implicated in the pathogenesis of the different subtypes
- Mutations in keratins ***; KRT5*** and ***KRT14*** are most commonly seen in EBS and result in abnormalities affecting the structural stability of the cytoskeleton of the basal keratinocytes (*Circled in yellow in Figure 1)*
- This **leads to blisters and keratoderma** on the hands and feet which can cause significant pain and functional limitations including difficulty walking. (*Figure 2)*

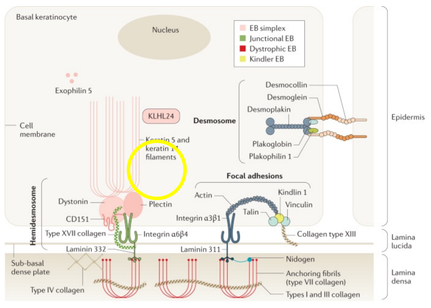


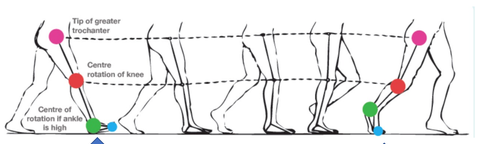
Figure 1. Schematic of affected proteins in EB in the epidermis by Bardhan et al Nature 2020[1] 2.Feet of an affected individual demonstrating marked keratoderma

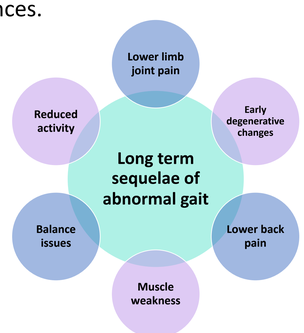
The impact of EBS on gait has not been formally evaluated . This study aims to investigate gait pattern in those with EBS and explore any strategies to modify the distribution of forces under their feet.

Normal Gait cycle

- **Normal gait cycle** is divided into **the braking and pushing phases**
- It is during these phases that the most **pressure** is exerted.
- When impaired can have long term consequences.

NORMAL GAIT PATTERN



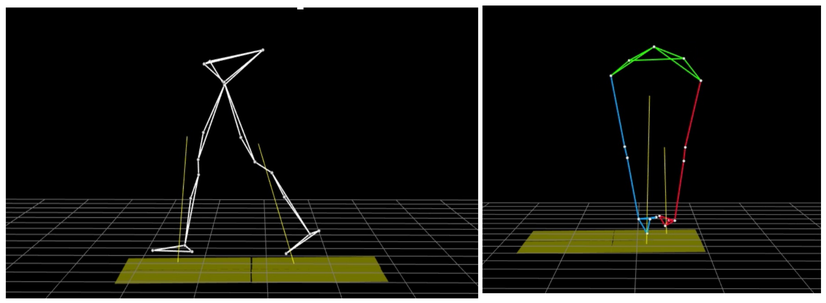


Methods

RECRUITMENT
- 21 patients with a DNA confirmed diagnosis of EBS were recruited from our centre

DATA COLLECTION
- Carried out at the Movement Analysis Laboratory (BTS Bioengineering ,Milan, Italy)
- Height/ weight measured for each participant
- Feet were evaluated for active blistering
- Participants were asked to walk a length of 8metres at spontaneous speed over ground plates that measured ground reaction forces (GRF)
- This was repeated 15-20 times

ANALYSIS
- Each participant was **matched by age/ sex** with controls from the unaffected group from the online database [2]
- Waveforms of the force components were compared between groups using a one dimensional statistical parametric mapping independent t-test
- This was used to identify which phases of gait differed between groups



Figures 4 +5: Screenshots of 3D reconstruction in the Movement Analysis laboratory – optoelectronic system (BTS Bioengineering, Milan, Italy) was used to record kinematics. The system consists of 8 infrared cameras with a resolution of 2,2 Mpixels (2048x 1088 pxs) The cameras tracked the 3D motion of retroreflective markers attached to the subject's skin.

Results

DEMOGRAPHICS

	Participant Group (n=21)	Control Group (n=21)
Male	9	9
Female	12	12
Mean- age	45.8 years	45.0 years
Active blistering	11	-
KRT5 mutation	14	-
KRT14 mutation	7	-

- **We observed a SIGNIFICANT reduction of ground reaction forces in the EBS group when compared with controls**
- **Anterior –Posterior (AP) component during both heel contact (braking phase) (p<0.001) and push phases (p<0.001).** (Figure 6)
- **Medio-lateral (ML) component during heel contact (braking phase) (p<0.01)** (Figure 7)
- Patients **with blisters** showed **lower AP force during the push phase** compared with patients without blisters (p<0.05).

Figure 6a:

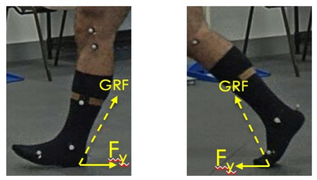


Figure 6b:

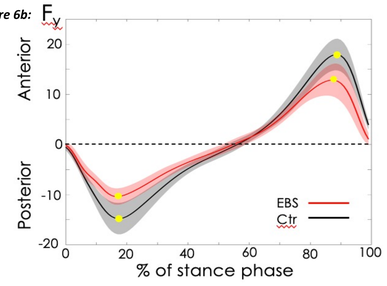


Figure 7a:

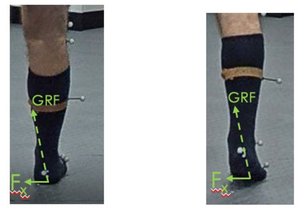


Figure 7b:

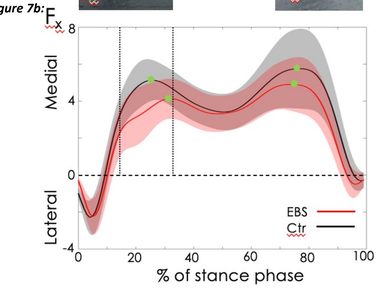


Figure 6a: *Illustration showing plane in which the anterior posterior force is measured in an individual.*
Figure 6b: *Pattern of the anteroposterior force in people with EB (red line) and control group (black line). Both peaks in the EBS group (braking phase and push phase of gait) were smaller than those of the control group showing a reduction in the ground reaction forces*
Figure 7a: *Illustration showing plane in which the mediolateral force is measured in an individual.*
Figure 7b: *Pattern of the mediolateral force in people with EB and a control group. Shows a reduction in both peaks but only statistically significant during the heel contact(braking phase) compared with the control group .*

Discussion

- The reduced GRF is possibly to reduce forces to minimize blistering and pain
- This gait pattern may also impair their stability when walking especially on irregular surfaces/ external forces
- We are exploring methods for rehabilitation and prevention strategies.

Conclusion

- **Our novel results show that patients with EBS adopt a maladaptive gait that results in reduced shear forces during walking**
- **This can lead to long-term sequelae such as early degenerative changes, muscle weakness and reduced balance**

References
1. Bardhan A, Bruckner-Tuderman L, Chapple ILC, Fine JD, Harper N, Has C, et al. Epidermolysis bullosa. Nat Rev Dis Primers. 2020;6(1):78. 2) Schreiber C, Moissenet F. A multimodal dataset of human gait at different walking speeds established on injury-free adult participants. Sci Data. 2019;6(1):111.

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debra for people whose skin doesn't work we do