

QUESTION

Should lower limb strengthening vs. no treatment be used for ambulant people with Friedreich ataxia?

POPULATION:	ambulant people with Friedreich ataxia
INTERVENTION:	lower limb strengthening
COMPARISON:	no treatment
MAIN OUTCOMES:	Independence of ambulation; Balance; Falls; Walking capacity; Quality of life; Lower limb strength;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>In a study of 54 individuals with FRDA, loss of ambulation was primarily due to ataxia rather than weakness (Pandolfo et al, 2020). Weakness of the lower limbs was absent or minimal in ambulatory patients, whereas it rapidly became prominent 1 year after loss of ambulation.</p> <p>There is no direct evidence that demonstrates muscle weakness leads to decline in ambulation in FRDA; however, there is evidence suggesting changes to skeletal muscles. This includes studies demonstrating deficits in energy production, delayed muscle oxygenation after exercise (Lynch et al, 2002), homogeneously increased muscle density and reduced muscle force (Sival et al, 2011), increased muscle specific fatigue (Bossie et al, 2017), and a reduction of 70% of strength at the time of wheelchair use (Beauchamp et al, 1995).</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic.</p> <p>1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably serious, 5/7 indicated serious, 1/7 indicated didn't know if serious.</p> <p>1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably not urgent, 1/7 indicated probably urgent, 5/7 indicated urgent.</p> <p>1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably a priority, 6/7 indicated priority. (Aug 2020).</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Trivial <input type="radio"/> Small <input checked="" type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 24 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p> <p>There are no studies that have examined the effectiveness of strengthen exercises on ambulation in</p>	<p>Strength training may be a beneficial strategy to maximise ambulatory function in individuals with FRDA; however, there is no published data or clinical evidence to conclusively recommend strength exercises for ambulant individuals. However, muscle strengthening appears to be beneficial when it is incorporated as one component into a program targeting</p>

	<p>individuals with FRDA. However, given there is sparse evidence suggesting muscle weakness contributes to ambulatory decline, four studies have included strength training as a component of their multi-faceted rehabilitation programs for individuals with inherited cerebellar ataxia (Miyai et al, 2014; Milne et al, 2018; Rodriguez-Diaz et al, 2018; Milne et al, 2012).</p>	<p>multiple areas on impairment.</p> <p>In clinical practice, there is uncertainty around the intensity of strengthening due to the underlying movement limitations secondary to ataxia.</p>
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know 	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 24 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>There appears to be no detrimental effects of muscle strengthening. However, progressive resistance programs are generally limited due to a focus on correct movement pattern and control rather than the required repetition max load. Therefore, detrimental effects may not be evident.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ○ Moderate ○ High ● No included studies 	<p>No published evidence.</p>	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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- Important uncertainty or variability
- Possibly important uncertainty or variability
- Probably no important uncertainty or variability
- No important uncertainty or variability

Outcomes	Importance	Certainty of the evidence (GRADE)
Independence of ambulation - not measured	IMPORTANT ^a	-
Balance - not measured	IMPORTANT ^b	-
Falls - not measured	CRITICAL ^c	-
Walking capacity - not measured	IMPORTANT ^d	-
Quality of life - not measured	CRITICAL ^e	-
Lower limb strength - not measured	IMPORTANT ^f	-

- a. Identified as critical (1/6), important (3/6), low importance (2/6) by people with FA and critical by expert authors in this topic
- b. Identified as critical (2/5), important (3/5) by people with FA and important by expert authors in this topic
- c. Identified as critical (3/5) and important (2/5) by people with FA and important by expert authors on this topic
- d. Identified as critical (2/6), important (3/6) and low importance (1/6) by people with FA and important by expert authors on this topic
- e. Identified as critical (3/6), important (3/6) by people with FA and critical by expert authors in this topic
- f. Identified as critical (1/6) and important (5/6) by people with FA and important by expert authors on this topic.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT

RESEARCH EVIDENCE

ADDITIONAL CONSIDERATIONS

<ul style="list-style-type: none"> ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know 	<p>No published evidence.</p>	<p>A survey designed to systematically collect expert-based opinions from clinicians involved in developing the recommendations for this topic and providing clinical care for individuals with Friedreich ataxia, was conducted. Clinical experts from Australia, Europe, UK, South America, Canada and the USA were asked to consider the harms/benefits of lower limb strengthening as a management strategy for ambulant individuals.</p> <p>Reflecting on the impact of lower limb strengthening on <u>Independence of ambulation</u>, 100% (2/2) clinical experts reported a benefit (large, moderate or small), 0% (0/2) reported no effect and, 0% (0/2) reported observing a harm (large, moderate or small).</p> <p>Reflecting on the impact on <u>Balance</u>, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect.</p> <p>Reflecting on the impact on <u>Falls</u>, 100% (2/2) clinical experts reported a benefit.</p> <p>Reflecting on the impact on <u>Walking capacity</u>, 100% (2/2) clinical experts reported a benefit.</p> <p>Reflecting on the impact on <u>Quality of life</u>, 100% (2/2) clinical experts reported a benefit.</p> <p>Reflecting on the impact on <u>Lower Limb Strength</u>, 100% (2/2) clinical experts reported a benefit.</p>
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know 	<p>No published evidence.</p>	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

We suggest lower limb strengthening over no lower limb strengthening in individuals with Friedreich ataxia who are ambulant.

Justification

There is no published evidence examining the effects of lower limb strength training alone for individuals with FRDA. In clinical practice (and some in studies) strength training is included in exercise or rehabilitation programs with an emphasis on correct movement control and pattern with beneficial effects. However, it is difficult to ascertain the direct impact of this management strategy.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia who are ambulant.

Research priorities

Future research should examine the effectiveness of strengthening for ambulant individuals and should explore the best dosage, intensity and timing of implementing a strengthening program.

References

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