QUESTION

Should heart failure medication and devices vs. no medication be used for patients with reduced ejection fraction with Friedreich ataxia?	
POPULATION:	patients with reduced ejection fraction with Friedreich ataxia
INTERVENTION:	heart failure medication and devices
COMPARISON:	no medication
MAIN OUTCOMES:	Mortality - Survival; Progression of heart failure; Worsening of systolic function;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic. 6 out of 7 indicated the consequences of heart failure was serious; 1 individual indicated it was probably serious. 6 out of 7 individuals indicated management of heart failure was urgent; 1 individual indicated it was probably urgent etc. 6 out of 7 indicated heart failure was a priority; 1 indicated it was probably a priority. (July 2020)

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	A search of 3 databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	A search of 3 databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No published evidence.	

Values

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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)
Mortality - Survival - not measured	CRITICAL[a]	-
Progression of heart failure - not measured	CRITICAL[b]	-
Worsening of systolic function - not measured	IMPORTANT[c]	-

a. Identified as critical (3/3) for decision-making by people with FA and identified as critical by expert authors on this topic.
b. Identified as critical (3/3) for decision-making by people with FA and identified as important by expert authors on this topic.

	c. Identified as critical (2/3) and as important (1/3) for decision-making by people with FA and identified as 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
○ 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	No published evidence.	Based on expert consensus.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No published evidence.	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if the intervention was reasonable (weighing up the balance between benefits, harms and costs). 1 out of 3 individuals indicated management with heart failure medication and devices was reasonable; 2 out of 1 was probably reasonable. (August 2020)

SUMMARY OF JUDGEMENTS

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

	JUDGEMENT						
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
○	○	○	●	○

CONCLUSIONS

Recommendation

We conditionally recommend treating individuals with Friedreich ataxia with a reduced left ventricular ejection fraction with medications according to current American Heart Association/American College of Cardiology heart failure guidelines (2013 & 2017 update).

Justification

Medical treatment of an individual with FRDA with reduced ejection fraction should include those with a LVEF <50%, but could also be considered for those with a significant downward trend in ejection fraction over time. This is based on current recommendations of the AHA/ACC (Yancy et al, 2013; Yancy et al, 2017) for treatment of heart failure as there is no evidence to suggest that individuals with FRDA should be treated differently to other people with heart failure and reduced ejection fraction.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia and a reduced ejection fraction, and as indicated in the justification above.

Research priorities

References

Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr., Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013;128(16):e240-327.

Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr., Colvin MM, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137-e61.