

QUESTION

Should heart failure medication and devices vs. no medication be used for patients with preserved ejection fraction with Friedreich ataxia?

POPULATION:	patients with preserved 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
<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>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)</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 type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 	<p>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.</p>	<p>There may be theoretical benefits from medication to prevent progression of HF, but they are unknown in FRDA.</p>

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 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.</p>	<p>Consensus clinical expertise suggests there are potential adverse side effects of medication and devices and the possibility of over-medication for individuals with HF and preserved EF in FRDA.</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												
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 45%;">Outcomes</th> <th style="width: 20%;">Importance</th> <th style="width: 35%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Mortality - Survival - not measured</td> <td>CRITICAL^a</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Progression of heart failure - not measured</td> <td>CRITICAL^b</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Worsening of systolic function - not measured</td> <td>IMPORTANT^c</td> <td style="text-align: center;">-</td> </tr> </tbody> </table> <p>a. Identified as critical (3/3) for decision-making by people with FA and identified as critical by expert authors on this topic.</p> <p>b. Identified as critical (3/3) for decision-making by people with FA and identified as important by expert authors on this topic.</p>			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	-	
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	-														

	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
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input checked="" type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know 	No published evidence.	No routine use of medication or devices in individuals with preserved EF.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> 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 medications or devices was reasonable; 1 out of 3 was probably not reasonable; and 1 out of 3 was not reasonable. (August 2020)

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	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 do not suggest using heart failure medication and/or devices for individuals with Friedreich ataxia with a preserved left ventricular ejection fraction.

Justification

There is no evidence that the use of medication and/or devices has any benefit in reducing the occurrence of cardiac dysfunction in individuals with FRDA with preserved ejection fraction and there are risks of side effects and over-medication if such treatments are used.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia and a preserved left ventricular ejection fraction (i.e. >55%).

Research priorities