QUESTION

Should Portable rhythm monitors (at least annually) vs. Holter monitors only for symptoms be used for asymptomatic patients with Friedreich ataxia?	
POPULATION:	asymptomatic patients with Friedreich ataxia
INTERVENTION:	Portable rhythm monitors (at least annually)
COMPARISON:	Holter monitors only for symptoms
MAIN OUTCOMES:	Mortality; Clinically significant arrhythmia;
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In a natural history study of 456 patients, 131 had Holters (Mejia et al, 2021). Eight (7.8%, n= 103) had diminished cardiac function, and 74 (74.0%, n = 100) had ventricular hypertrophy. Ninety patients (83.0%) had atrial ectopy (supraventricular ectopy [SVE]): 85 (78.0%) with rare SVE (>0% to 5%) and five (5.0%) with frequent SVE (>10%). Twenty-five (19.0%) had supraventricular runs, and one (0.8%) had atrial fibrillation/flutter. Forty-five (41.0%) had ventricular ectopy (VE): 43 (39.0%) with rare VE (0% to 5%) and two (2.0%) with moderate VE (5% to 10%). Compared with patients with none and rare SVE, patients with frequent SVE had longer disease duration (18.3 versus 4.6 versus 9.0 years, P=0.0005).	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the monitoring cardiac function. 7 out of 7 indicated the consequences of cardiac function. 4 out of 7 indicated cardiac monitoring was urgent; 2 out of 7 was probably urgent and 1 indicated it was urgent if the person has cardiac symptoms. 4 out of 7 indicated cardiac monitoring was a priority; 2 out of 7 was probably a priority and 1 indicated it was a priority if the person has cardiac symptoms. (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 three 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.	Detection of treatable and/or preventable arrhythmias

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 three 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.	Over medicalisation with unnecessary testing; detection of abnormalities of uncertain significance (e.g. premature atrial contractions without sustained arrhythmia)

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 - not measured	CRITICAL[a]	-
Clinically significant arrhythmia - not measured	CRITICAL[b]	-

a. Identified as critical (4/6), important (1/6) and low importance (1/6) by people with FA and critical by expert authors on this topic.
b. Identified as critical (3/6), important (1/6) and low importance (1/6) by people with FA and critical 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.	

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 indicated using portable rhythm monitors to monitor hear function was reasonable, 1 out of 3 indicated it probably wasn't reasonable and 1 person needed more information on its benefits and potential harms. (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**
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

There is not sufficient evidence to make a recommendation about Holter monitoring for individuals with Friedreich ataxia who do not have symptoms suggesting they might have an arrhythmia.

Justification

There is a lack of evidence for benefit of Holter monitoring for individuals with FRDA without symptoms suggesting an arrhythmia, while risks include over-medicalization with unnecessary testing and detection of abnormalities of uncertain significance (e.g., premature atrial contractions without sustained arrhythmia).

Subgroup considerations

None.

Research priorities

Longitudinal research to evaluate whether Holter findings predict clinically actionable outcomes in FA.

Studies evaluating utility of commercially available devices (such as AppleWatch, mobile applications for ECG evaluation) for symptomatic arrhythmia detection.

Reference

Mejia E, Lynch A, Hearle P, Okunowo O, Griffis H, Shah M, et al. Ectopic burden via Holter monitors in Friedreich ataxia. Pediatr Neurol. 2021;117:29-33.