QUESTION

Should chest pain management that incorporates FRDA-specific considerations vs. standard chest pain managements without FRDA-specific considerations be used for all people with FRDA who present with chest pain?

POPULATION:	all people with FRDA who present with chest pain
INTERVENTION:	chest pain management that incorporates FRDA-specific considerations
COMPARISON:	standard chest pain managements without FRDA-specific considerations
MAIN OUTCOMES:	Accurate diagnosis; Unnecessary testing;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In a retrospective cross-sectional study, in a cohort of 239 individuals with FRDA, 90% had abnormal electrocardiographic findings (Schadt et al, 2012). In a second cross-sectional study, 49 individuals with FRDA without active arrhythmia, chest pain or acute coronary syndrome, had their cardiac troponin I levels (cTnI) values measured (Friedman et al, 2013). In the asymptomatic individuals, 16.3% had levels typically seen during an acute myocardial infarct and 30.6% were above the 99th percentile range.	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of chest pain and/or raised troponin. 4/6 indicated that the problem was serious, 1/6 indicated probably serious,1/6 indicated they didn't know if serious. 3/6 indicated that the problem was urgent, 1/6 indicated probably urgent, 1/6 indicated they didn't know if urgent, 1/6 indicated that it varied or was sometimes urgent. 3/6 indicated that the problem was a priority, 1/6 indicated probably a priority, 1/6 indicated they didn't know if a priority, 1/6 indicated it varied or was sometimes a priority. (Aug 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 four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 14 December 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	Clinical experience of all of the expert authors is that not taking the listed caveats into account can lead to inappropriate testing and diagnosis.

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 four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 14 December 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	No undesirable effects.

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 directly addressing PICO; however, there is evidence of elevated troponin (Friedman et al, 2013) and abnormal ECG findings (Schadt et al, 2012) in individuals with FRDA.	

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)
Accurate diagnosis - not measured	CRITICAL[a]	-
Unnecessary testing - not measured	CRITICAL[a]	-

	a. Identified as 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.	

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

	JUDGEMENT						
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

We recommend that chest pain assessment in Friedreich ataxia should incorporate the following considerations: coronary artery disease is not more or less common than in the non-Friedreich ataxia population; ECG is usually abnormal in Friedreich ataxia in the absence of coronary disease; troponin can be elevated in patients with Friedreich ataxia for a non-coronary reason and should not be assumed to indicate an acute coronary syndrome; the possibility of increased incidence of pulmonary embolism due to the sedentary nature of the disease. If troponin is elevated, then serial troponin assessment is very important. In the setting of left ventricular hypertrophy an episode of atrial fibrillation can lead to angina-like pain.

Justification

Coronary artery disease in FRDA is not more or less common that in the non-FRDA population. However, clinical experience of all expert authors is that standard chest pain management without considering the listed caveats can lead to inappropriate testing and diagnosis of chest pain for individuals with FRDA. There is evidence for ECG abnormality in FRDA in the absence of coronary disease and elevated troponin levels in people with FRDA for non-coronary reasons.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia who present with chest pain.

Research priorities

Future research should aim to provide further information on ischemic and non-ischemic chest pain in FRDA. It would be beneficial to explore troponin levels in different clinical circumstances, as well as exploring the incidence of chest pain occurrence and related hospital presentations and the patient's troponin profile.

References

Friedman LS, Schadt KA, Regner SR, Mark GE, Lin KY, Sciascia T, et al. Elevation of serum cardiac troponin I in a cross-sectional cohort of asymptomatic subjects with Friedreich ataxia. Int J Cardiol. 2013;167(4):1622-4.

Schadt KA, Friedman LS, Regner SR, Mark GE, Lynch DR, Lin KY. Cross-sectional analysis of electrocardiograms in a large heterogeneous cohort of Friedreich ataxia subjects. J Child Neurol. 2012;27(9):1187-92.