QUESTION

Should advance care planning vs. no advance care planning be used for patients who have reached adulthood, developed major complications such as diagnosis with heart failure, significant change in their mobility, dysphagia, or barriers to communication with Friedreich ataxia??

POPULATION:	patients who have reached adulthood, developed major complications such as diagnosis with heart failure, significant change in their mobility, dysphagia, or barriers to communication with Friedreich ataxia?
INTERVENTION:	advance care planning
COMPARISON:	no advance care planning
MAIN OUTCOMES:	Medical treatment that aligns well with patient values and preferences; Medical treatment that aligns well with patient values and preferences; Medical treatment that aligns well with patient values and preferences ; Patient and caregiver satisfaction; Patient and caregiver satisfaction;

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 advance care planning. 4/6 indicated that the problem was serious, 2/6 indicated probably serious. 4/6 indicated that the problem was urgent, 2/6 indicated probably not urgent. 3/6 indicated that the problem was a priority, 2/6 indicated probably a priority, 1/6 indicated probably not 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		

Outcomes	№ of	Certainty of	Relative	Anticipated absolute effects* (95% CI)

	participants (studies) Follow-up	the evidence (GRADE)	effect (95% CI)	Risk with no advance care planning	Risk difference with advance care planning
Medical treatment that aligns well with patient values and preferences assessed with: Goals of care preferences	246 (1 RCT)[1]	⨁◯◯◯ Very low[a,b,c,d,e]	-	246 participants with advanced heart failure and an estimated likelihood of death of >50% within 2 years were recruited and randomised to either a video-assisted intervention or verbal control arm. Patients' goals-of-care preferences were categorised as follows: life-prolonging care, limited medical care, comfort care, or unsure. Patients' CPR preferences were categorised as "yes, attempt CPR," "no, do not attempt CPR," or "not sure." Similarly, we categorized intubation preferences as "yes, attempt intubation," "no, do not attempt intubation," or "not sure." Patients' knowledge of goals of care was assessed using 5 true/false questions and 1 multiple choice question, for a summary score of 0 to 6 (higher score reflects greater knowledge). Goals-of-care, CPR, and intubation preferences between the video-assisted intervention and verbal control arms were compared.using $\chi 2$ tests. Participants' goals-of-care preferences in both arms were similar at baseline. After the intervention, more participants in the intervention arm preferred comfort care compared with those in the verbal control arm. In the video-assisted arm, 22% preferred life-prolonging care, 25% preferred limited medical care, 51% preferred comfort care, and 2% were uncertain. In the verbal control arm, 41% preferred life-prolonging care, 22% preferred limited medical care, 30% preferred comfort care, and 8 (7%) were uncertain (p<0.001).	
Medical treatment that aligns well with patient values and	282 (1 RCT)[2]	⨁◯◯◯ Very low[a,f,g]	-	282 patients with heart failure were randomised to advanced care planning (ACP, n=93) or control arms (n=189). The ACP arm had lower decisional conflict (p<0.01) and were more likely to have discussed preferences with surrogates	

These 246 patients were all older than 64 years of age which is not the age profile of those with FRDA

Individuals with FRDA likely view heart failure differently and may have a preference for not prolonging life with serial advanced interventions.

	preferences assessed with: Decisional conflict scale				(*p*=0.04). Subsequent follow ups showed no difference.	
	Medical treatment that aligns well with patient values and preferences assessed with: Preferred Place of Death	205 (1 RCT)[3]	⊕◯◯◯ Very low[a,d]	-	205 terminally ill patients with lung, heart and cancer disease were randomised to receive usual care, or usual care plus advance care planning (ACP). The intervention consisted of a discussion between the clinician, patient and relatives about preferences for end of life care. Differences in fulfilment of preferred place of death (PPOD) were calculated using χ2 test among cases where both PPOD and actual place of death (APOD) was known. Differences in APOD were calculated using χ2 test. No significant differences in fulfilment of PPOD (35% vs 52%, *p*=0.221) or in amount of time spent in hospital among deceased patients (49% vs 23%, *p*=0.074) were found between groups. A significant difference in APOD was found favouring home death in the intervention group (17% vs 40%, *p*=0.013). (Skorstengaard et al 2019).	
	Patient and caregiver satisfaction assessed with: EQ5D index	50 (1 RCT)[4]	⊕◯◯◯ Very low[a,d]	-	50 patients hospitalised with acute heart failture or acute coronary syndrome with predicted 12 month mortality risk >20% were randomly allocated (1:1) to Future Care Planning (FCP) or usual care for 12 weeks upon discharge and then crossed over for the next 12 weeks. There were no differences in EQ5D index at baseline and no significant adjusted mean difference at the 12 or 24 week time points. 19 carers from the early intervention group, and 13 from the delayed intervention group contributed to questionnaire data on the EQ5D index at 5 time points during the trial. There were no differences in mean EQ5D index scores between intervention groups.	These 282 patients were all older - approximately 64 years of age which is not the age profile of those with FRDA. Mean age is 69 years, which is not the age profile of those with FRDA. Regarding the place of death, the people who have had FRDA for a long time may have different views on their preferred place of death than the patients in this study, so that the study findings are not directly applicable to FRDA.
	Patient and caregiver	50 (1 RCT)[4]	⊕◯◯◯	-	50 patients hospitalised with acute heart failture or acute coronary syndrome with	

satisfaction assessed with: EQ5D Visual Analogue Scale		Very low[a,d]		predicted 12 month mortality risk >20% were randomly allocated (1:1) to Future Care Planning (FCP) or usual care for 12 weeks upon discharge and then crossed over for the next 12 weeks. There were no differences in EQ5D VAS at baseline and no significant adjusted mean difference at the 12 or 24 week time points. 19 carers from the early intervention group, and 13 from the delayed intervention group contributed to questionnaire data on the EQ5D VAS at 5 time points during the trial. There were no differences in mean EQ5D VAS scores between intervention groups.

1. El-Jawahri A., Paasche-Orlow M.K. Matlock D. et al. Randomized, controlled trial of an advance care planning video decision support tool for patients with advanced heart failure. Circulation; 2016.
2. Malhotra C., Sim D. Jaufeerally F.R. et al. Impact of a Formal Advance Care Planning Program on End-of-Life Care for Patients With Heart Failure: Results From a Randomized Controlled Trial. J. Card. Fail; 2020.
3. Skorstengaard M.H., Jensen A.B. Andreassen P. et al. Advance care planning and place of death, hospitalisation and actual place of death in lung, heart and cancer disease: a randomised controlled trial. BMJ Support Palliat Care; 2019.
4. Denvir MA, Cudmore S Highet G et al. Phase 2 Randomised Controlled Trial and Feasibility Study of Future Care Planning in Patients with Advanced Heart Disease. Sci. rep; 2016.

a. No participants with a diagnosis of FRDA included in any of the studies (all with advanced heart failure).
b. Confidence intervals not reported
c. Unvalidated outcome measures (questionnaires developed for study).
d. Data collectors or clinicians providing intervention not blinded to group allocation.
e. Loss to follow up at 1 and 3 month assessment.
f. Lack of uptake of intervention in advance care plan arm (unequal n in groups).
g. Usual care not described.

Patients were all over 70 years and did not have a lifetime illness like FRDA.

In paediatrics, progressive diseases often prompt decision makers to be more proactive in ACP than is the case with “static conditions” with stably high medical complexity.

In addition to these clinical trials, a 2014 systematic review of studies in progressive and life-threatening illnesses (not FRDA) found that ACP increases compliance with patients' end of life wishes, decreases the use of life-sustaining treatment, increases hospice/PC, reduces hospitalizations (Brinkman-Stoppelenburg et al, 2014).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know		These 246 patients were all older than 64 years of age which is not the age profile of those with FRDA. Individuals with FRDA likely view heart failure differently and may have a preference for not prolonging life with serial

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no advance care planning	Risk difference with advance care planning
Medical treatment that aligns well with patient values and preferences	246 (1 RCT)[1]	⨁◯◯◯ Very low[a,b,c,d,e]	-	246 participants with advanced heart failure and an estimated likelihood of death of >50% within 2 years were recruited and randomised to either a video-assisted intervention or verbal control arm. Patients' goals-of-care preferences were categorised as follows:	

	assessed with: Goals of care preferences				life-prolonging care, limited medical care, comfort care, or unsure. Patients' CPR preferences were categorised as "yes, attempt CPR," "no, do not attempt CPR," or "not sure." Similarly, we categorized intubation preferences as "yes, attempt intubation," "no, do not attempt intubation," or "not sure." Patients' knowledge of goals of care was assessed using 5 true/false questions and 1 multiple choice question, for a summary score of 0 to 6 (higher score reflects greater knowledge). Goals-of-care, CPR, and intubation preferences between the video-assisted intervention and verbal control arms were compared.using $\chi 2$ tests. Participants' goals-of-care preferences in both arms were similar at baseline. After the intervention, more participants in the intervention arm preferred comfort care compared with those in the verbal control arm. In the video-assisted arm, 22% preferred life-prolonging care, 25% preferred limited medical care, 51% preferred comfort care, and 2% were uncertain. In the verbal control arm, 41% preferred life-prolonging care, 22% preferred limited medical care, 30% preferred comfort care, and 8 (7%) were uncertain (p<0.001).	advanced interventions.
	Medical treatment that aligns well with patient values and preferences assessed with: Decisional conflict scale	282 (1 RCT)[2]	⊕◯◯◯ Very low[a,f,g]	-	282 patients with heart failure were randomised to advanced care planning (ACP, n=93) or control arms (n=189). The ACP arm had lower decisional conflict (p<0.01) and were more likely to have discussed preferences with surrogates (p=0.04). Subsequent follow ups showed no difference.	
	Medical treatment that aligns well with patient values and	205 (1 RCT)[3]	⊕◯◯◯ Very low[a,d]	-	205 terminally ill patients with lung, heart and cancer disease were randomised to receive usual care, or usual care plus advance care planning (ACP). The intervention consisted of a discussion between the clinician, patient and	

	preferences assessed with: Preferred Place of Death				relatives about preferences for end of life care. Differences in fulfilment of preferred place of death (PPOD) were calculated using χ2 test among cases where both PPOD and actual place of death (APOD) was known. Differences in APOD were calculated using χ2 test. No significant differences in fulfilment of PPOD (35% vs 52%, *p*=0.221) or in amount of time spent in hospital among deceased patients (49% vs 23%, *p*=0.074) were found between groups. A significant difference in APOD was found favouring home death in the intervention group (17% vs 40%, *p*=0.013). (Skorstengaard et al 2019).	These 282 patients were all older - approximately 64 years of age which is not the age profile of those with FRDA.
	Patient and caregiver satisfaction assessed with: EQ5D index	50 (1 RCT)[4]	⨁◯◯◯ Very low[a,d]	-	50 patients hospitalised with acute heart failture or acute coronary syndrome with predicted 12 month mortality risk >20% were randomly allocated (1:1) to Future Care Planning (FCP) or usual care for 12 weeks upon discharge and then crossed over for the next 12 weeks. There were no differences in EQ5D index at baseline and no significant adjusted mean difference at the 12 or 24 week time points. 19 carers from the early intervention group, and 13 from the delayed intervention group contributed to questionnaire data on the EQ5D index at 5 time points during the trial. There were no differences in mean EQ5D index scores between intervention groups.	Mean age is 69 years, which is not the age profile of those with FRDA. Regarding the place of death, the people who have had FRDA for a long time may have different views on their preferred place of death than the patients in this study, so that the study findings are not directly applicable to FRDA.
	Patient and caregiver satisfaction assessed with: EQ5D Visual Analogue Scale	50 (1 RCT)[4]	⨁◯◯◯ Very low[a,d]	-	50 patients hospitalised with acute heart failture or acute coronary syndrome with predicted 12 month mortality risk >20% were randomly allocated (1:1) to Future Care Planning (FCP) or usual care for 12 weeks upon discharge and then crossed over for the next 12 weeks. There were no differences in EQ5D VAS at baseline and no significant adjusted mean difference at the 12 or 24 week time points. 19 carers from the early intervention group, and 13 from the delayed intervention group contributed to questionnaire data on the EQ5D VAS at 5 time points during the trial

				There were no differences in mean EQ5D VAS scores between intervention groups.

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3. Skorstengaard M.H., Jensen A.B. Andreassen P. et al. Advance care planning and place of death, hospitalisation and actual place of death in lung, heart and cancer disease: a randomised controlled trial. BMJ Support Palliat Care; 2019.
4. Denvir MA, Cudmore S Highet G et al. Phase 2 Randomised Controlled Trial and Feasibility Study of Future Care Planning in Patients with Advanced Heart Disease. Sci. rep; 2016.

a. No participants with a diagnosis of FRDA included in any of the studies (all with advanced heart failure).
b. Confidence intervals not reported
c. Unvalidated outcome measures (questionnaires developed for study).
d. Data collectors or clinicians providing intervention not blinded to group allocation.
e. Loss to follow up at 1 and 3 month assessment.
f. Lack of uptake of intervention in advance care plan arm (unequal n in groups).
g. Usual care not described.

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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	Low certainty of the evidence as per the evidence profile table.	While the groups in these papers are generally much older than FRDA populations with heart disease, there is relevance with regard to their health condition and the interventions they might be offered for their heart failure. We say “low certainty” because of the significant differences between the study populations.

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	See table below	1) Advance care planning program 2) Future care planning 3) Advance care planning using a video support tool All the above interventions have a value in FRDA based on our expert opinion. A further consideration is that it is now considered that loss of dignity is the more important issue for those with FRDA rather than the development of heart failure, so it is important to consider how dignity can be maintained in management of HF.

Outcomes	Importance	Certainty of the evidence (GRADE)
Medical treatment that aligns well with patient values and preferences assessed with: Goals of care preferences	CRITICAL[a]	⨁◯◯◯ Very low[b,c,d,e,f]
Medical treatment that aligns well with patient values and preferences assessed with: Decisional conflict scale	CRITICAL[a]	⨁◯◯◯ Very low[b,g,h]
Medical treatment that aligns well with patient values and preferences assessed with: Preferred Place of Death	CRITICAL[a]	⨁◯◯◯ Very low[b,e]
Patient and caregiver satisfaction assessed with: EQ5D index	CRITICAL[a]	⨁◯◯◯ Very low[b,e]
Patient and caregiver satisfaction assessed with: EQ5D Visual Analogue Scale	CRITICAL[a]	⨁◯◯◯ Very low[b,e]

a. Identified as critical by expert authors on this topic.
b. No participants with a diagnosis of FRDA included in any of the studies (all with advanced heart failure).
c. Confidence intervals not reported
d. Unvalidated outcome measures (questionnaires developed for study).
e. Data collectors or clinicians providing intervention not blinded to group allocation.
f. Loss to follow up at 1 and 3 month assessment.
g. Lack of uptake of intervention in advance care plan arm (unequal n in groups).
h. Usual care not described.

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	Favors the intervention	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Yes - 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
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	Probably favors the intervention	**Favors the intervention**	Varies	Don't know

	JUDGEMENT						
			comparison				
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 advance care planning (ACP) for individuals with Friedreich ataxia who have reached adulthood, have major complications such as heart failure, have experienced a significant change in their mobility, have dysphagia or have barriers to communication, bearing in mind that the only published literature on ACP is in heart failure. ACP should also address the "future loss of dignity" by putting in place a safeguard that a person's own values and wishes be respected in their care. This would help to implement a degree of control over a disease which is often out of the control of a person with Friedreich ataxia.

Justification

The Friedreich's ataxia clinical management guideline patient and parent advisory panel felt this was a serious topic that needed to be addressed, and depending on the person's circumstances, could be urgent. It has not been studied in those with FRDA to date. Studies have demonstrated that an ACP program can be effective in facilitating end of life care consistent with patient preferences (Brinkman-Stoppelenburg et al., 2014)

Subgroup considerations

Advance care planning is more important in adults with Friedreich ataxia, particularly since the life expectancy is between 40 and 50 years of age. For children and teenagers, if there is any evidence of life-altering or life-limiting illness, ACP should be discussed with them. The parent often makes several decisions for those under the age of consent, but children can often be included in a sensitive way and assent to healthcare decisions, and teenagers can often take a more active role in decision making.

Research priorities

This is a new topic for this version of the guidelines. At this time, it would be useful to know how many of those with FRDA have appointed medical decision makers in case they are unable to communicate for themselves and have expressed their preferences regarding goals of care and any end of life wishes to appointed decision makers. Research could also help guide the best practices for having ACP conversations between family members and with care teams, acknowledging that sensitivity and clear education on this topic are important to productive and authentic conversations. It would also be helpful to know if those with FRDA change their preferences in their advance care plan over time.

Reference

Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. Palliat Med. 2014;28(8):1000-25.