Anticoagulation-related quality-of-life associated with extended-interval monitoring: A pre-specified analysis of the FADE-OUT study

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PURPOSE

- The CHEST 2012 Guideline included an option to extend the interval of warfarin monitoring up to every 12 rather than 4 weeks[1]
- Reduced anticoagulation follow-up burden has been proposed to improve quality of life (QoL); but, to our knowledge, this question has not been explicitly studied
- We aimed to assess the impact of a real-world extended-interval warfarin monitoring on QoL, and to identify patient characteristics associated with changes in QoL

METHODS

- FADE-OUT[2] was a prospective single-arm intervention pilot study of extended-interval warfarin monitoring in patients recruited from 5 UF ACR Network clinics; patient enrollment criteria are summarized in **Table 1**
- Study visits were performed at baseline and weeks 6, 14, and 26, and every 12 weeks thereafter to a maximum of 68 weeks of follow-up, or until no longer suitable for extended follow-up
- Patients were removed from the study if they required a warfarin dose change, or were otherwise deemed no longer appropriate for extended-interval monitoring
- The validated 25-question Duke Anticoagulation Satisfaction Scale (DASS) was used to assess QoL at baseline and end-of-study[3]
  - Possible score range: Best QoL 25 – 175 Worst QoL

Table 1. FADE-OUT enrollment criteria.

Inclusion/Exclusion
Male or female aged 18 to 90 years
Anticoagulation indication requiring at least 6 months of therapy
Anticoagulation management by the same anticoagulation clinic for ≥12 weeks prior to enrollment
Stable INR for past 12 weeks noted by maintenance of the same total weekly dose of warfarin
Life expectancy greater than or equal to 24 months
Able to provide informed consent
No thromboembolic event in the previous 12 weeks
Not Pregnancy
Not diagnosed with cancer diagnosis in prior year nor actively receiving cancer treatment

- The primary outcome was change in total DASS score; secondary outcomes were change in sub-scale score (limitations, hassles, psychological impact) and identification of factors associated with changes in QoL
- Change in DASS total and subscale scores were assessed by paired t-test; analysis of variance was used for bivariate analyses and Pearson correlation coefficients were calculated to determine associations between continuous variables
- Study data were managed using REDCap[4]

RESULTS

- Baseline patient characteristics are summarized in **Table 2**

Table 2. Baseline characteristics of 47 study participants.

Characteristic	Mean ± SD or %
Age, years	66.8 ± 12.5
Male	46.8%
Years on warfarin	6.74 ± 6.01
Weeks with stable INR/warfarin dose	33.0 ± 27.76
Number of Medications taken daily	6.9 ± 4.6
Race/Ethnicity	
White (non-Hispanic)	74.5%
Black	21.3%
Indications	
Non-valvular atrial fibrillation/flutter	53.2%
DVT or PE	29.8%

- In patients with complete before ***and*** after DASS Score (N=36) mean ± SD score at baseline was 45.2 ± 14.2 vs. 49.1 ± 14.9 at study end – this was similar to patients with complete before ***and/or*** after DASS scores (**Figure 1**)

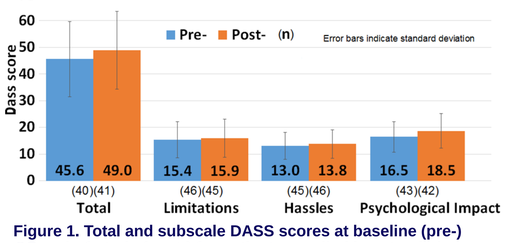

Figure 1. Total and subscale DASS scores at baseline (pre-) *OR* end-of-study (post-) for patients enrolled in extended-interval anticoagulation monitoring

- No significant change was observed in total DASS score comparing baseline and post-extended interval monitoring time points; however, QoL on the psychological impact subscale was significantly worse after extended-interval monitoring (**Table 3**)

Table 3. Mean difference between pre- and post- DASS survey.

Variable	Difference (mean ±SD)	95% CI; p-value
Total score	3.9 ± 13.3	-0.6-8.4; p=0.09
Limitations	0.5 ± 6.5	-1.5-2.5; p=0.61
Hassles	0.8 ± 4.5	-0.6-2.2; p=0.27
Psychological	2.6 ± 6.1	0.6-4.5; p=0.01

Note: Positive changes in score indicate decrease in QoL

- Sensitivity analyses demonstrated no significant association between total DASS score (or any sub-scale score) and whether or not a patient completed the ~68-week extended interval monitoring intervention
- Individual survey questions demonstrating the greatest adverse effect on HrQoL (mean change ≥ 0.5 units):
  - 4b: how much do you feel reassured because of your anti-clot treatment (+0.5) ***psychological impact sub-scale***
  - 4f: overall, how much has anti-clot treatment had a positive impact on your life (+0.67) ***psychological impact sub-scale***
  - 4h: overall, how satisfied are you with your anti-clot treatment (+0.64) ***psychological impact sub-scale***
- No significant association was found between change in total DASS score and sex, employment, or taking the same warfarin dose every day of the week
- No continuous variables were significantly associated with change in total DASS score (**Table 4**)

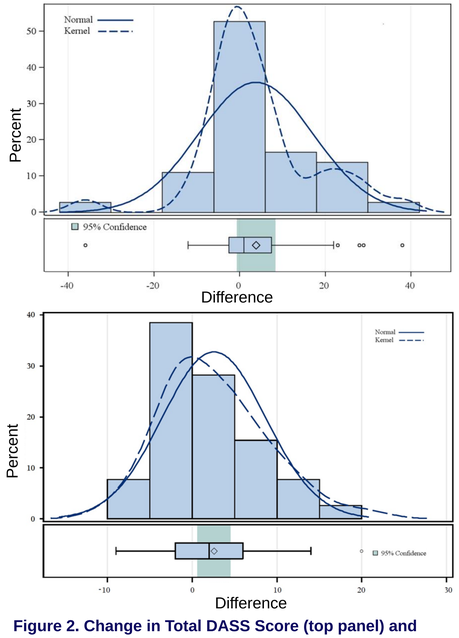

Figure 2. Change in Total DASS Score (top panel) and psychological impact score (bottom panel).

- Increasing years taking warfarin at baseline trended toward an association with decreased hassles sub-scale score
- Greater number of medications may be associated with greater adverse psychological impact

Table 4. Pearson correlation with change in DASS total score and sub-scales.

Variable	Total		Limitations		Hassles		Psychological	
	ρ	P-value	ρ	P-value	ρ	P-value	ρ	P-value
Age (baseline)	-0.04	0.81	0.001	1.00	-0.15	0.34	0.06	0.71
Years on warfarin (baseline)	-0.26	0.13	-0.16	0.30	-0.27	0.07	-0.06	0.72
Weeks with stable INR/warfarin dose (baseline)	-0.13	0.47	-0.11	0.49	-0.06	0.72	-0.12	0.46
Number of medications (baseline)	0.26	0.14	0.17	0.31	0.02	0.89	0.29	0.089
Number of medications (study end)	0.22	0.23	0.11	0.48	-0.11	0.48	0.37	0.026
Weeks of study completed	-0.20	0.24	-0.17	0.27	-0.24	0.12	-0.18	0.27

CONCLUSIONS

- Extended-interval follow up resulted in substantial variation in DASS score change (**Figure 2**)
- Total DASS score trended toward an adverse change in QoL
- In particular, adverse changes were most pronounced in the psychological impact sub-scale
- One plausible reason for the potential decrement is that extended-interval follow-up fosters patient disengagement from self-management activities due to less frequent feedback and patient-provider interaction
- No characteristics were significantly associated with a favorable change in QoL after the extended-interval monitoring intervention
- Study limitations include a relatively small sample size and incomplete data in a minority of patients; due to these limitations and no adjustment for multiple comparisons, these results should be considered hypothesis-generating
- **Additional research is needed to identify who extended interval monitoring may benefit or impair with regards to QoL**
- **Additionally, QoL should be considered with clinical factors and shared-decision making when implementing extended-interval warfarin monitoring.**

REFERENCES

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