Health-Related Quality of Life (HRQoL) in Fit, Unfit and Frail Patients Enrolled in FiTNEss (UK-MRA Myeloma XIV): A Cross Sectional Study

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Background

Multiple Myeloma is the second most common haematological malignancy with over 5500 patients diagnosed each year. In the UK in 2016-2018, more than 4 in 10 new diagnoses of multiple myeloma (MM) were in people aged at least 75 years old.

Considerable heterogeneity among transplant non-eligible (TNE) patients may be better assessed through assessment of frailty (an interplay between age, physical function, cognition and co-morbidities) then chronological age alone.

However, little is known about the impact of frailty, or the components that contribute to frailty, has on health-related quality of life (HRQoL) in older patients with MM.

Aim

To examine patient-reported outcomes from participants according to frailty categorization and explore the contribution of different elements of the International Myeloma Working Group (IMWG) frailty score (FS) to HRQoL.

Methods

- FiTNEss (UK-MRA Myeloma XIV, NCT03720041) is a phase III, multi-centre, randomised controlled trial for newly diagnosed TNE MM patients, comparing frailty score-adjusted dose reduction with standard up-front dosing and toxicity dependent dose adjustments.

- Frailty was defined using the IMWG frailty score combining age (<75y, 75-80y, >80y), Katz Activity of Daily Living (ADL<=4), Lawton Instrumental Activity of Daily Living (IADL<=5) and Charlson Comorbidity Index (CCI<=1). The UK-MRA MRP uses age, performance status (PS), ISS and CRP. HRQoL was measured by EORTC QLQ-C30 and QLQ-MY20 completed at trial entry.

- One-way ANOVA and two-sample unequal variance t-tests compared subscales. Minimally important differences were medium sized by accepted definitions. P-values were adjusted using a Bonferroni correction for the 19 subscales in each comparison (adjusted P = 0.05/19 = 0.0026).

Results

- Baseline HRQoL was available for 559 trial participants.
- Median age at trial entry was 76y, 307 (54.9%) were male and 427 (76.4%) ECOG PS0-1.
- 160 (28.6%) patients were classified as Fit, 182 (32.6%) were Unfit and 217 (38.8%) were Frail according to IMWG FS. Co-morbidity, ADL and MRP risk scores in *Table 1*

Table 1: Baseline HRQoL characteristics

Baseline HRQoL was available for 559 trial participants			
Age	**<75y**	**75 – 80y**	**>80y**
	183 [32.7%]	248 [44.4%]	80y 128 [22.9%])
Sex		**Male**	**Female**
		307 (54.9%)	252 (45.1%)
Frailty Category (ECOG PS0-1)	**Fit**	**Unfit**	**Frail**
	160 (28.6%)	182 (32.6%)	217 (38.8%)
Co-morbidity & ADLs	**CCI <=1**	**ADL <=4**	**IADL <=5**
	105 (18.8%)	60 (10.7%)	115 (20.6%)
Risk according to MRP	**Low**	**Intermediate**	**High**
	167 (31.0%)	180 (33.5%)	191 (35.5%)

- Significant differences between frailty categories were evident in 7 of 15 C30 subscales and 1 of 4 MY20 subscales.

- The largest differences were between the Fit/Unfit and Frail groups with Physical Functioning only a single nominally different subscale between Fit and Unfit (*Figure 1A*).

- When comparing the elements of the frailty score, ADL score resulted in significantly differences in 11 of 15 C30 and 2 of 4 MY20 subscales (*Figure 1D*) and the IADL 10 of 15 C30 subscales and 4 of 4 MY20 subscales were significantly different (*Figure 1E*).

- C30 or MY20 subscales were not significantly different between age group (*Figure 1B*) and CCI (*Figure 1C*).

- HRQOL domains significantly different for both ADL and IADL were:

  Global Health Status   Physical Functioning   Role Functioning   Fatigue

  Cognitive Functioning   Social Functioning   Pain   Appetite Loss

  Constipation   Dyspnoea   Disease Symptoms   Side Effects

- 10 of 15 C30 subscales and 2 of 4 MY20 subscales were significantly different between MRP risk groups (*Figure 1F*). In contrast, IMWG FS, 5 subscales were nominally significantly different between low and medium risk groups.

Figure 1: EORTC-QLQ-C30 and MY20 subscale score means with associated 95% confidence intervals by group

* = adjusted P = 0.05/19 = 0.0026

(A) IMWG FS   (B) Age   (C) CCI <=1   (D) ADL <=4   (E) IADL <=5   (F) UK-MRA MRP
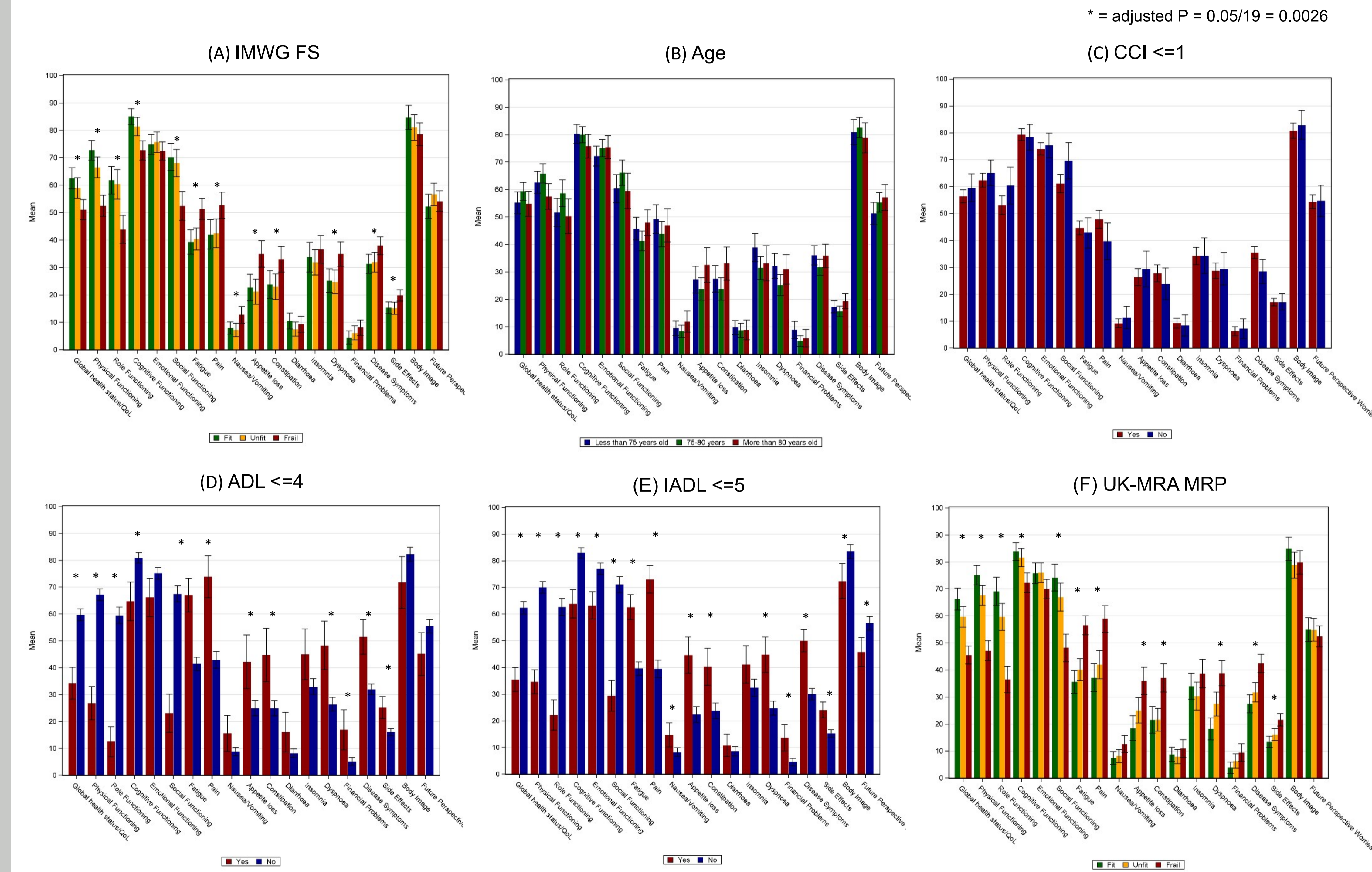
Conclusion

- Frailty as categorised by the IMWG FS is associated with several domains of the EORTC QLQ-C30 and MY20 among newly diagnosed TNE MM patients, with worse functioning and higher symptomology among frailer patients. Examining the elements of the FS show that non-modifiable components age and comorbidities do not contribute to heterogeneity in HRQoL, but ADL and IADL scores are significantly associated with differences in HRQoL. Further interrogation of these measures at an individual level could identify components of frailty that are potentially modifiable by optimising function and participation in daily tasks through rehabilitation. Enhancing ADL scoring may alter frailty categorising as assessed through the IMWG FS, is likely to enhance HRQOL and may impact on treatment tolerability in older patients.

- The MRP risk profile is associated with baseline HRQoL as shown previously, and with several other subscales as shown here. There is evidence that the MRP can delineate subscales, including QL better than the IMWG FS.