Multi-organ MRI Improves Risk Stratification And Optimises Treatment Allocation In Clinical Obesity

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BACKGROUND

Obesity is a chronic, relapsing and remitting multisystem disease[1].

Cardiometabolic risk varies significantly among individuals with similar BMI [1].

Anti-obesity medications with GLP-1 RA activity have demonstrated cardiometabolic benefit[2,3].

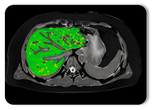
Access to GLP-1 RA-based medications is not equitable or personalised[4].

AIM

To support obesity management by determining whether scalable, standardised multi-organ MR-based imaging has prognostic utility to identify people at high cardiometabolic risk, enabling appropriate allocation of anti-obesity and cardioprotective medications.

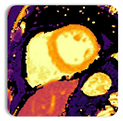
METHODS

Metabolic disease from standardized MRI algorithm for 14 metrics



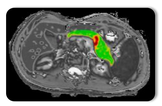
LIVER

Conditions
- MASH
- AIH
- Viral hepatitis



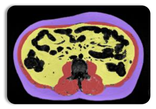
HEART

Conditions
- MI
- Heart failure
- Atrial fibrillation
- Cardiomyopathy
- Myocarditis
- Amyloidosis



Pancreas

Conditions
- Diabetes
- Pancreatitis



Body composition

Conditions
- Obesity
- Sarcopenia

Technical capabilities with non-contrast MRI[5,6]

LIVER

MRI for
- Total fat
- Oedema
- Inflammation
- Fibrosis

HEART

MRI for
- Total fat
- Muscle size
- Muscle stiffness
- Filling pressure
- LV function
- Volumes

Pancreas

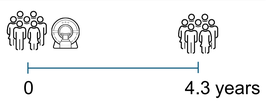
MRI for
- Total fat
- Inflammation
- Fibrosis
- Oedema

Body composition

MRI for
- Visceral fat

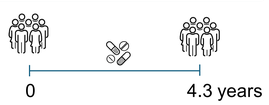
Subcutaneous fat
- Skeletal muscle mass

UK Biobank
Total cohort: **N = 23,087**



- Subjects with baseline MRI & outcome data over 4.3 years.
- Obesity classified as per Lancet Commision[1].
- Cox regression with each clinical parameter individually and in combination with MRI parameter(s).

Subgroup with BMI ≥30kg/m² : N = 4,141



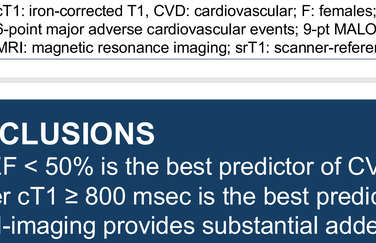
- We used this data from the UK Biobank to model all-cause mortality over 4.3 Years.
- Effects of tirzepatide on body weight and liver ct1 from the synergy- NASH trial[78].
- We modelled the effectiveness of tirzepatide allocation over 4 years in reducing all-cause mortality.

RESULTS

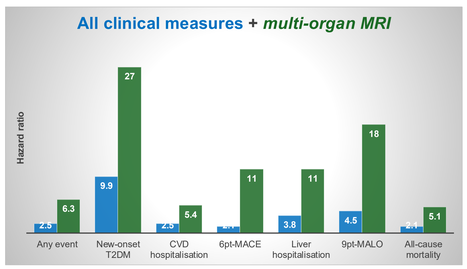
Increased risk of outcomes with obesity

Subgroup with clinical events: N = 2,083

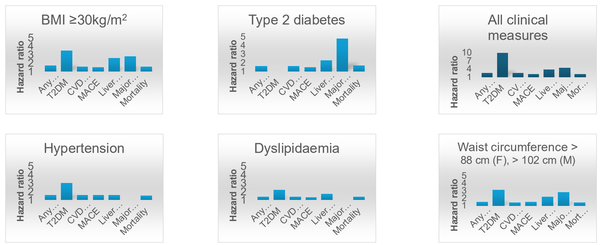
- Mean age: 67 yr, 63% male, 97% white
- Median 2.4 yr time to event



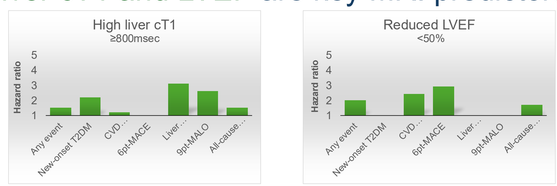
Predicting cardiometabolic risk *with* MRI



Predicting cardiometabolic risk from clinical measures



Liver cT1 and LVEF are key MRI predictors



Predicting effect of tirzepatide treatment

BMI ≥ 30kg/m²	cT1 ≥ 800msec	LVEF < 50%	Patients treated	Lives saved	Number needed to treat
✓			4141	24	172
✓	✓		736	4	175
✓		✓	249	2	146
✓	✓	✓	41	1	41

cT1: MRI-derived measure of inflammation, cell injury, oedema and fibrosis in liver. srT1: MRI-derived measure of inflammation and fibrosis in pancreas. LVEF is an MRI-derived measure of pumping ability in the heart.

cT1: iron-corrected T1, CVD: cardiovascular; F: females; LVEF: left ventricular ejection fraction; 6-pt MACE: 6-point major adverse cardiovascular events; 9-pt MALO: 9-point major adverse liver outcomes; M: males; MRI: magnetic resonance imaging; srT1: scanner-referenced T1; T2DM: type 2 diabetes mellitus.

CONCLUSIONS

- LVEF < 50% is the best predictor of CVD hospitalization and 6 pt-MACE.
- Liver cT1 ≥ 800 msec is the best predictor of new-onset T2DM, liver hospitalization and 9 pt-MALO.
- MRI-imaging provides substantial added value to the prediction of cardiometabolic events.
- Modelling based on tirzepatide's known effects on body weight and MR liver imaging reveals that MR-based cT1 determination has the potential to enhance patient targeting of OMMs to prevent all-cause mortality.

CONTACT

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