Project Title

Association Between Phase Angle and Change in Cognitive Function Over Time in Type 2 Diabetes Mellitus

Project Lead and Members

Project lead: Serena Low

Project members: Lim Su Chi, Subramaniam Tavintharan, Sum Chee Fang, Angela Moh, Keven Ang

Organisation(s) Involved

Khoo Teck Puat Hospital, Admiralty Medical Centre

Healthcare Family Group(s) Involved in this Project

Medical

Applicable Specialty or Discipline

Endocrinology, Neurology

Project Period

Start date: Sep 2014

Completed date: Apr 2019

Aims

To investigate the longitudinal association between phase angle and cognitive function in type 2 diabetes

Background

See poster appended/ below

Methods

See poster appended/ below

Results

See poster appended/ below

Lessons Learnt

- Phase angle could be a novel biomarker for cognitive decline in T2DM
- Non-invasive and potentially applicable in clinical care to supplement assessment of cognitive decline
- Findings pave the way to investigate responsiveness of phase angle to interventions aimed at ameliorating cognitive decline

Conclusion

- Phase angle is positively correlated with MMSE score at baseline.
- Phase angle is associated with increase in MMSE score and lower odds of cognitive decline over time.
- Phase angle is associated with increase in domain score in attention

Additional Information

Singapore Health & Biomedical Congress (SHBC) 2022: Singapore Clinician Investigator Award (Oral category) – (Silver Award)

Project Category

Applied/ Translational Research

Quantitative Research

Keywords

Phase Angle, Type 2 Diabetes, PhA, Cognitive Decline, Marker, Mini-Mental State Examination (MMSE), Endocrinology, Neurology

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Association between phase angle and change in cognitive function over time in type 2 diabetes mellitus

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BACKGROUND

- Phase angle (PhA) is the angle of vector formed by human body's resistance and reactance (Fig.1).
- PhA is determined by lean body mass, total body water (TBW) and ratio of extracellular to total body water (ECW/TBW) ratio (Fig.2)
- It reflects cellular integrity and hydration status.[1]
- Although PhA is a marker of clinical health outcomes, including sarcopenia and frailty,[1] its longitudinal association with cognitive function is unknown.

Fig 1. Phase angle

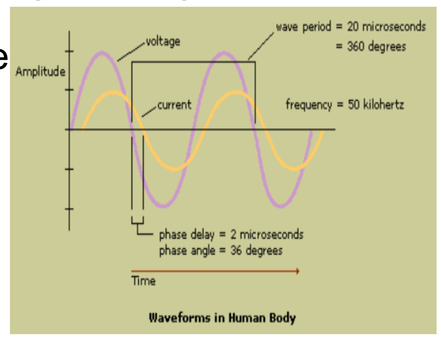
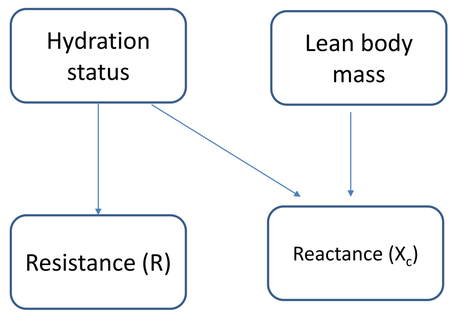


Fig 2. Determinants of phase angle



METHODS

Study Population

Prospective cohort study of 612 patients recruited by the Singapore Study of Macro-angiopathy and Micro-vascular Reactivity in Type 2 Diabetes (SMART).

- Type 2 Diabetes
- ≥ 45 years old

- Active inflammation
- Known neuropsychiatric diseases which could compromise neurocognitive ability
- Inability to give informed consent

Excluded

655 → No MMSE score at baseline (n=19)

637 → No MMSE score at follow-up(n=14)

612

Study Period (Sep 2014-Apr 2019) → (Jul 2019 – May 2022)

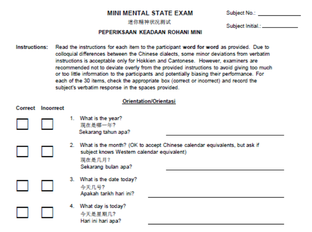
Data collection

1. Questionnaires
2. Clinical measurement
3. Blood samples
4. Geriatric Depression Scale (GDS≥5)
5. Foot screen

Cognitive assessment

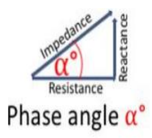
- Mini-mental state examination (MMSE)[2]. See Fig 3
- Domains include orientation, immediate recall, attention, delayed recall and language.
- Outcomes are change in MMSE score and cognitive decline (≥ 2 points drop in MMSE) [3]

Fig 3. MMSE



Body composition

- Bio-impedance analysis: electric currents flow through the body, allowing calculation of impedance and reactance of currents.
- PhA was calculated as arc-tangent (reactance/resistance) x 180 ˚/ π.



Statistical analysis

- Spearman correlation to examine the correlation between MMSE score and clinical covariates
- Linear and logistic regression to examine the association between PhA and cognitive decline.
- Model 1: age, gender, ethnicity, education, geriatric depression scale, neuropathy, DM duration, BMI, HbA1c, systolic blood pressure, low-density lipoprotein cholesterol, estimated glomerular filtration rate, log-transformed urinary albumin-to-creatinine ratio, use of metformin, history of stroke, APOE e4 allele, log-transformed follow-up period, baseline MMSE score.
- Model 2: Model 1 + GPAQ-mets + Energy-adjusted protein intake

RESULTS

- Mean age of the participants was 60.5 ± 7.4 years. Fig. 4 shows baseline characteristics.
- Higher PhA is correlated with younger age, shorter DM duration, lower systolic blood pressure and higher physical activity.
- PhA is positively correlated with baseline MMSE score – total, orientation, language and attention.
- Median follow-up period was 4.6 years (IQR 4.0-5.1, max 7.2). 138 (22.6%) of patients had cognitive decline. Mean change in MMSE was -0.46 ± 2.00. Patients with cognitive decline were older, had fewer than 7 years education, longer DM duration and lower PhA (Table 1).
- Higher PhA is associated with increase in MMSE score over time (Fig. 5) and increase in domain score in attention (Fig. 6).
- PhA is also associated with lower odds of cognitive decline (Fig. 7).

Fig 4. Baseline characteristics

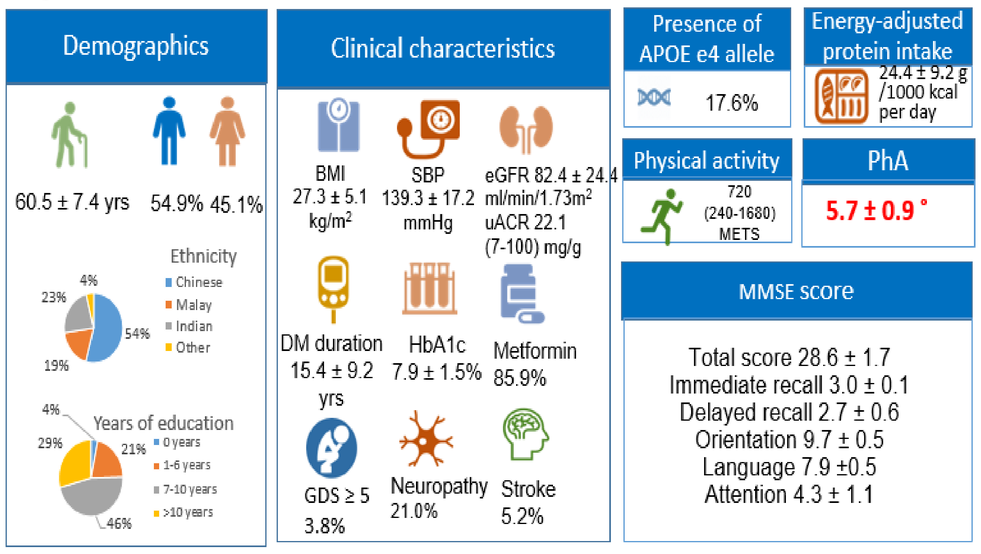
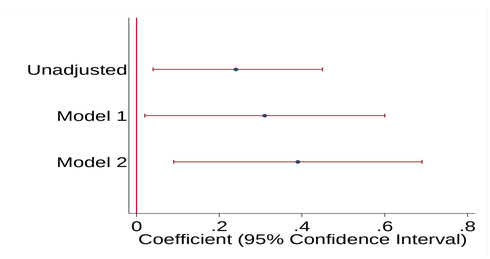


Table 1. Baseline characteristics stratified by cognitive decline

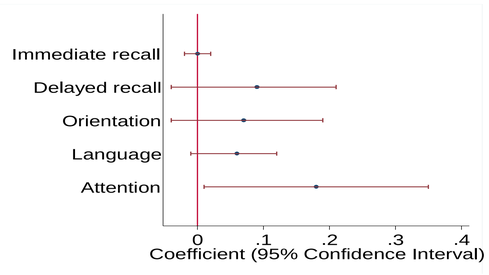
	No cognitive decline	Cognitive decline	P-value
Age (yrs)	59.8 ± 7.3	63.0 ± 7.7	<0.001
Male (%)	270 (57.0)	66 (47.8)	0.058
Ethnicity (%)			0.550
Chinese	260 (55.0)	72 (52.2)	
Malay	90 (19.0)	23 (16.7)	
Indian	103 (21.8)	38 (27.5)	
Other	20 (4.2)	5 (3.6)	
Education < 7 yrs (%)	98 (20.8)	52 (38.0)	<0.001
GDS ≥ 5 (%)	17 (3.6)	6 (4.4)	0.677
Neuropathy (%)	96 (20.3)	32 (23.4)	0.445
Stroke (%)	19 (4.1)	12 (9.0)	0.026
DM duration (yrs)	14.7 ± 8.6	17.7 ± 10.7	<0.001
BMI (kg/m2)	27.4 ± 4.9	26.8 ± 5.6	0.181
HbA1c (%)	7.9 ± 1.5	7.9 ± 1.6	0.925
SBP (mmHg)	138.6 ± 16.8	141.4 ± 18.5	0.095
LDL-C (%)	2.7 ± 0.8	2.5 ± 0.7	0.136
eGFR (ml/min/1.73m²)	83.3 ± 23.8	79.4 ± 26.1	0.102
uACR (mg/g)	23.0 (6.7-109.5)	20.0 (7.7-89.7)	0.819
Phase angle (˚)	5.8 ± 0.9	5.5 ± 1.1	0.004

Fig 5. Association between PhA and change in MMSE score



Coefficient (95% CI) p-value
0.24 (0.04 to 0.45) p=0.019
0.31 (0.02 to 0.60) p=0.035
0.39 (0.09 to 0.69) p=0.012

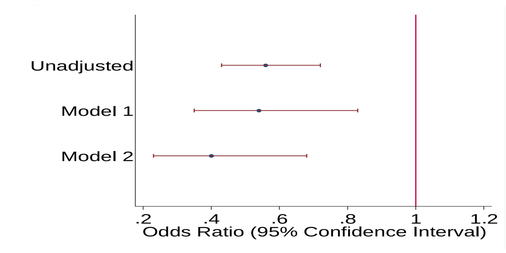
Fig 6. Association between PhA and change in domain scores



Coefficient (95% CI) p-value
-0.00 (-0.02 to 0.02) p=0.857
0.09 (-0.04 to 0.21) p=0.160
0.07 (-0.04 to 0.19) p=0.223
0.06 (-0.01 to 0.12) p=0.077
0.18 (0.01 to 0.35) p=0.043

In fully adjusted Model 2

Fig 6. Association between PhA and cognitive decline



OR (95% CI) p-value
0.56 (0.43 to 0.72) p<0.001
0.54 (0.35 to 0.83) p=0.005
0.40 (0.23 to 0.68) p=0.001

DISCUSSION AND CONCLUSION

- Cardio-metabolic burden is lower in patients with higher PhA.
- PhA is positively correlated with MMSE score at baseline.
- PhA is associated with increase in MMSE score and lower odds of cognitive decline over time. It is associated with increase in domain score in attention.
- Possible mechanism is that higher PhA may decrease ECW, thereby lowering arterial stiffness and arterial pulsatility which are contributing factors for cognitive decline.
- PhA could be a novel biomarker for cognitive decline in T2DM.
- It can be measured non-invasively and is potentially applicable in clinical care to supplement assessment of cognitive decline.

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