

Project Title

Association of Nitrogen Balance with Skeletal Muscle Mass in Singapore's T2D Population

Project Lead and Members

Project lead: Kwan Tsz Kiu

Project members: Lim Su Chi (Clinical Director, Co-investigator),

Keven Ang (Manager, Co-investigator),

Serena Low Kiat Mun (Consultant, Collaborator)

Organisation(s) Involved

Yishun Health

Healthcare Family Group(s) Involved in this Project

Allied Health

Applicable Specialty or Discipline

Nutrition and Dietetic, Geriatrics, Endocrinology, Clinical Research Unit

Project Period

Start date: 21 May 2021

Completed date: Ongoing

Aims

Utilizing data from the SMART2D cohort, this cross-sectional pilot study aims to:

- 1) Measure spot urinary urea nitrogen (UUN) to derive nitrogen balance (NBAL)
- 2) Examine the correlation of NBAL with skeletal muscle mass (SMM), and other frailty parameters

Background

See poster appended/ below

Methods

See poster appended/ below

Results

See poster appended/ below

Lessons Learnt

Since the magnitude of nitrogen balance (NBAL) determines the extent of muscle catabolism, protein intake deficit can be calculated and precise protein amount can be prescribed for patient to achieve nitrogen equilibrium, and improve/maintain skeletal muscle mass to prevent/delay the progression of frailty/malnutrition. Further evaluation of NBAL as an objective indicator of patient's nutritional status, as compared to other conventional subjective malnutrition screening tools, will be beneficial for early detection of malnutrition risk. Further studies are recommended for the application of NBAL in T2D patients presenting with sarcopenic obesity and diabetic kidney disease.

Conclusion

See poster appended/ below

Additional Information

Physical activity and diet data are currently being collected to be integrated for future analysis to study their association with Nitrogen Balance.

Singapore Health & Biomedical Congress (SHBC) 2022: Best Poster Award (Allied Health) (Posters category) – (Bronze Award)

Project Category

Applied/ Translational Research, Quantitative Research

Keywords

NBAL (Nitrogen Balance), Malnutrition Risk Detection

Name and Email of Project Contact Person(s)

Name: Kwan Tsz Kiu (Yishun Health)

Email: kwan.tsz.kiu@ktp.com.sg

Association of nitrogen balance with skeletal muscle mass in Singapore's T2D population

Kwan, TK¹, Tay, YQ¹, Ang, K¹, Low, S^{1,2}, Lim, SC^{1,2,3,4}¹Clinical Research Unit, KTPH, Singapore, ²Diabetes Centre, AdMC, Singapore³Saw Swee Hock School of Public Health, NUS & NUHS, Singapore, ⁴Lee Kong Chian School of Medicine, NTU, Singapore

1. Background

- Poorly controlled diabetes accelerates the catabolic effect of insulin deficiency, resulting in muscle wasting.
- Adequate protein intake is integral to preserve muscle mass². Inaccuracies observed in self-reported dietary data underscores the need to objectively predict protein intake.
- Nitrogen balance (NBAL) reflects the equilibrium between protein intake and losses. The magnitude of negative NBAL can determine the extent of muscle catabolism (Fig 1).

Aim To study the association of NBAL and SMM in T2D population

$$\text{NBAL} = \text{Nitrogen Intake} - \text{Nitrogen Loss}$$

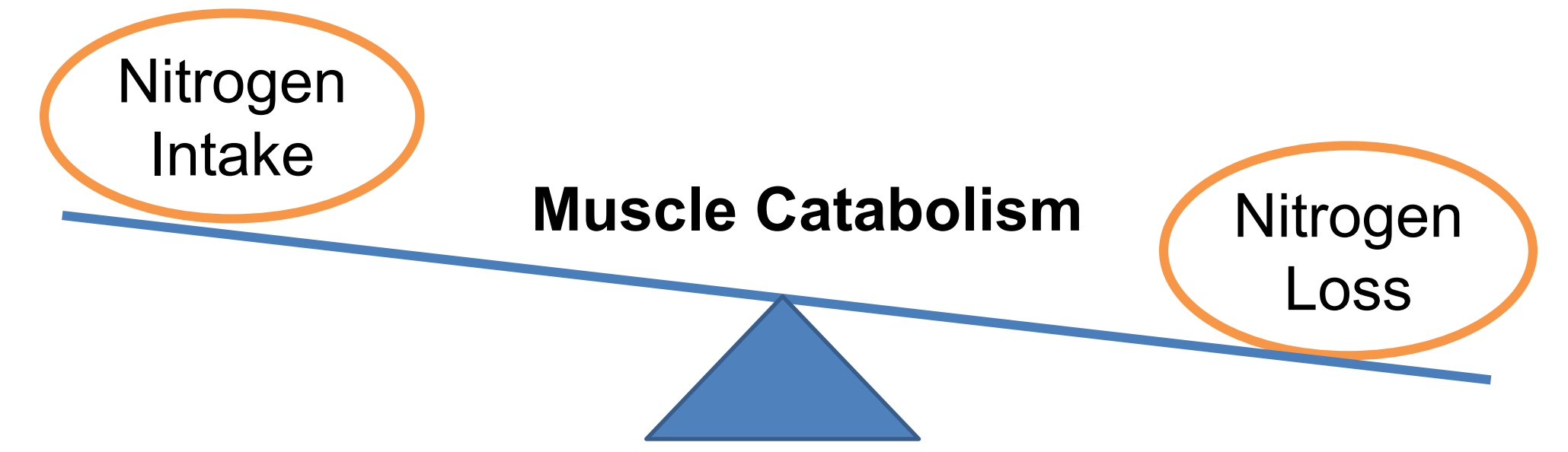


Fig 1. Muscle Catabolism with negative NBAL

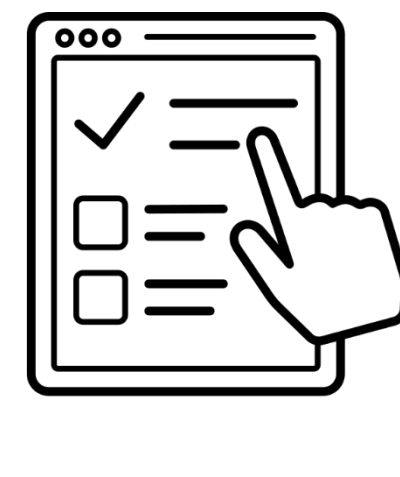
2. Methods

Study population: cross-sectional study of 161 T2D participants from the SMART2D cohort.**Data collection:**

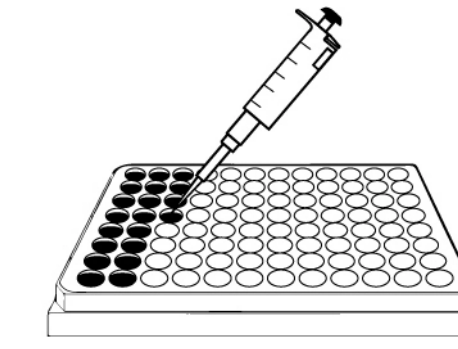
- Bioelectrical Impedance analysis:**
 - Phase Angle (PhA)
 - SMM



- Dynamometer:**
 - Hand grip strength (HGS)



- Lifestyle data**
 - Food Frequency Questionnaires (FFQ)
 - Global Physical Activity Questionnaire (GPAQ)



- ELISA**
 - Spot urine urea nitrogen (UUN)¹

Statistical Analysis:

- One way (ANOVA) or χ^2 test: comparisons of continuous and categorical variables across tertiles
- Pearson's correlation: NBAL, SMM, PhA and HGS
- Univariate and multivariate regression analysis models of NBAL and SMM: adjusted for various patterns of variables

Exclusion: ESRD, malignancy, active inflammation, Hx of dementia

$$\text{NBAL} = \text{Nitrogen Intake} - \text{Nitrogen Loss}$$

$$= \frac{\text{Daily Protein intake (g)}}{6.25} - \text{UUN} + \text{miscellaneous losses}$$

* Maroni method: applicable regardless of renal function³
 # Urinary biomarker of protein intake ¹miscellaneous losses

Fig 2. Calculation of NBAL (g N/day)

3. Results

Table 1. Characteristics of participants (n=161) stratified according to tertiles of NBAL

Characteristics of participants (n=161) (mean \pm SD)*	Overall n (%)	T1 (Low) 55 (34.2%)	T2 53 (32.9%)	T3 (High) 53 (32.9%)	P for trend
*NBAL (g N/day)	-1.78 \pm 0.53	-2.31 \pm 0.16	-1.83 \pm 0.12	-1.20 \pm 0.43	<0.001
*Age (years)	59.26 \pm 12.07	64.12 \pm 9.75	64.72 \pm 7.47	65.12 \pm 7.47	<0.001
Male (%)	87 (54.0%)	18 (11.2%)	28 (17.4%)	41 (25.4%)	<0.001
Ethnicity (%),					
Chinese	91 (56.5%)	39 (24.2%)	26 (16.1%)	26 (16.1%)	0.155
Malay	27 (16.8%)	7 (4.3%)	10 (6.2%)	10 (6.2%)	
Indian	30 (18.6%)	8 (4.9%)	12 (7.4%)	10 (6.2%)	
Others	13 (8%)	1 (0.6%)	5 (3.1%)	7 (4.3%)	
*BMI (kg/m ²)	26.97 \pm 5.28	22.49 \pm 2.46	26.91 \pm 2.71	31.69 \pm 5.30	<0.001
*HbA1c (%)	7.92 \pm 1.62	7.94 \pm 1.82	7.72 \pm 1.40	8.10 \pm 1.61	0.496
*DM duration (years)	15.92 \pm 9.95	17.29 \pm 10.27	18.09 \pm 10.33	12.37 \pm 8.30	0.005
*PhA (°)	5.05 \pm 0.76	4.81 \pm 0.61	5.01 \pm 0.73	5.34 \pm 0.84	0.001
*SMM (kg)	24.07 \pm 6.23	18.94 \pm 2.95	23.54 \pm 3.91	29.91 \pm 5.66	<0.001
*HGS (kg)	24.79 \pm 8.98	20.41 \pm 5.69	24.54 \pm 7.90	29.57 \pm 10.41	<0.001
*MET-minutes	1402.26 \pm 2256.22	1254.62 \pm 1625.79	1244.91 \pm 2182.68	1712.83 \pm 2829.78	0.476

Differences between NBAL tertiles are not significant for SBP, DBP, TC, LDL, TG, HDL and eGFR

Fig 3. Pearson's Correlation of NBAL (g N/day) and Log-transformed SMM (kg)

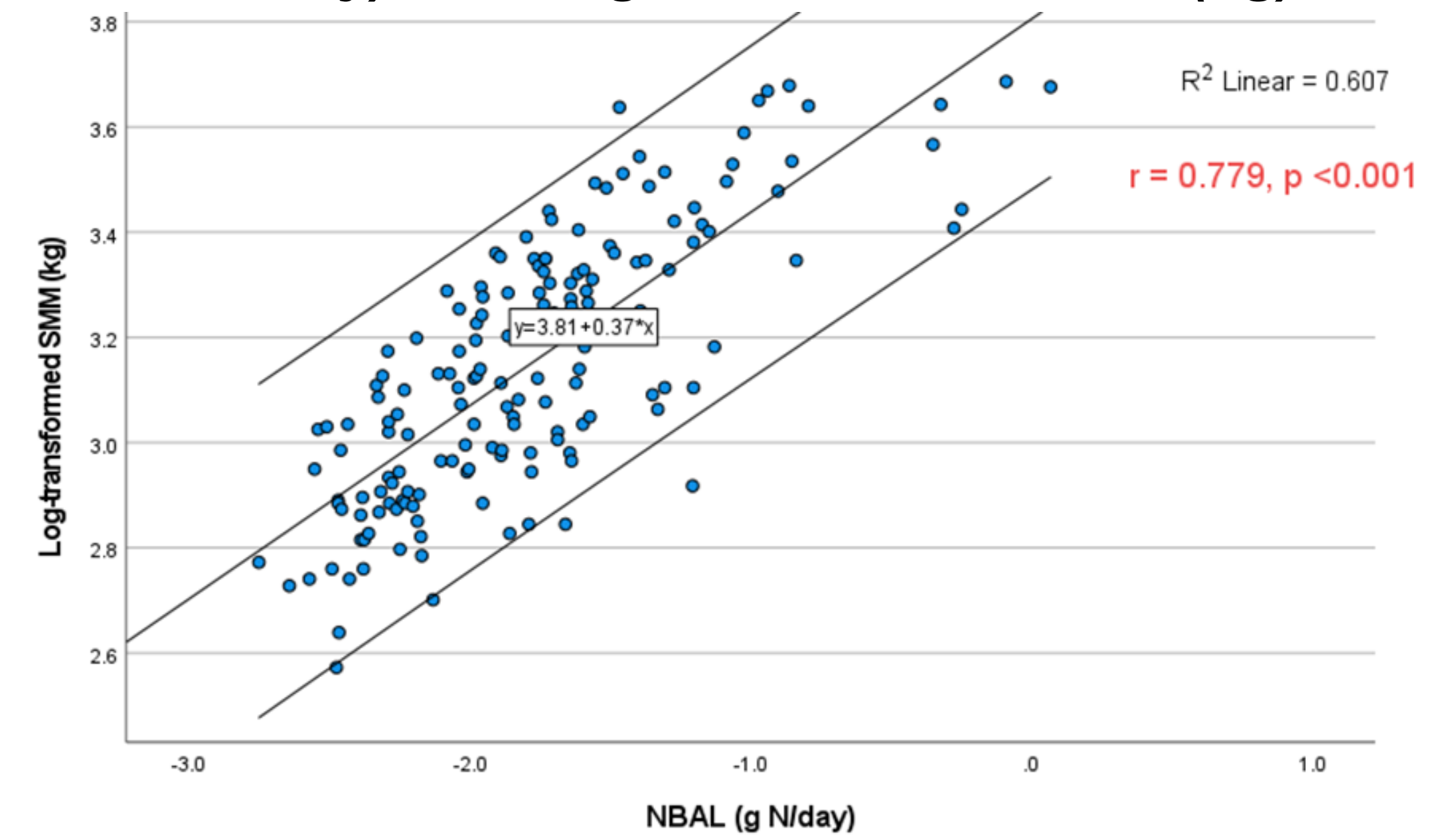


Table 2. Pearson's correlations between NBAL and parameters (n=161)

Variable	r	P Value
PhA (°)	0.351	<0.001
HGS (kg)	0.425	<0.001

Table 3. Multivariable Regression of NBAL (g N/day) and SMM (kg)

Models	β	NBAL Tertiles	β	SE	P-value
Univariate	9.26	T1* vs T2	0.22	0.03	<0.001
		T1* vs T3	0.45	0.03	<0.001
Model 1 ^a	0.24	T1* vs T2	0.17	0.02	<0.001
		T1* vs T3	0.28	0.02	<0.001
Model 2 ^b	0.54	T1* vs T2	0.15	0.02	<0.001
		T1* vs T3	0.25	0.02	<0.001

* Reference

^a Model 1: Adjusted for age, sex, ethnicity^b Model 2: Adjusted for age, sex, ethnicity, BMI, eGFR, HbA1c, DM duration, LDL, Met-minutes

References

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4. Discussion & Conclusion

- Mean predicted protein intake is 44.7g/day for men and 38.9g/day for women (data not shown), below recommended protein intake of 66g/day and 55g/day respectively².
- T3 NBAL is significantly higher than T1. Using T1 NBAL as reference, participants in T3 NBAL are significantly older, has more males, higher BMI, shorter duration of DM, higher PhA, higher SMM and higher HGS (Table 1).
- Significant positive correlations were found between NBAL with log-transformed SMM, PhA and HGS (Fig 3; Table 2).
- Overall, the univariate model shows NBAL is positively and significantly associated with SMM ($\beta = 9.26$, $p < 0.001$). Using NBAL T1 as a reference, both T2 and T3 are positively associated with SMM after adjusting for age, sex and ethnicity in Model 1. The association remains statistically significant when further adjusted for eGFR, HbA1c, DM duration, LDL and Met-minutes in Model 2 (Table 3).
- NBAL is independently associated with SMM and a possible predictor of adequacy of protein intake.
- Future directions: 1) To conduct longitudinal study to determine clinical implications of NBAL 2) To examine sources of protein intake (i.e. protein quality) and other nutrients associated with SMM

Acknowledgements

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