**Participant flow**



**Baseline characteristics**

Baseline characteristics, anthropometry and physiological measures for all participants enrolled on the study on low carbohydrate, high protein (LC), or conventional energy restricted (ER) diets

|  |  |  |
| --- | --- | --- |
|   | ER (n = 7)  | LC (n =6)  |
| Age (years) | 55.7 ± 9.2 | 63.5 ± 5.8 |
| Number of females | 4 | 3 |
| Number of smokers | 2 (2 ex-smokers) | 1 (3 ex-smokers) |
| Weight (kg)  | 92.6 ± 10.7  | 87.6 ± 8.0  |
| Height (m)  | 1.67 ± 0.09  | 1.66 ± 0.1  |
| BMI (kg·m-2)  | 33.1 ± 3.0  | 31.8 ± 3.2  |
| Waist to hip ratio  | 0.99 ± 0.06  | 0.95 ± 0.06  |
| Body fat (%)  | 38.3 ± 7.3  | 36.7 ± 9.5  |
| Systolic blood pressure (mmHg)  | 137.1 ± 17.0  | 145.7 ± 12.8  |
| Diastolic blood pressure (mmHg)  | 82.3 ± 11.4  | 77.5 ± 6.8  |

Values are expressed as mean ± SD

Baseline lipid profile, diabetes, and endothelial measures for all participants enrolled on the study on low carbohydrate, high protein (LC), or conventional energy restricted (ER) diets

|  |  |  |
| --- | --- | --- |
|  | ER (n = 7) | LC (n = 6) |
| Cholesterol (mmol·L-1)  | 4.8 ± 0.7\* | 4.0 ± 0.3  |
| Triacylglycerols (mmol·L-1)  | 1.3 ± 0.5  | 1.7 ± 0.6  |
| HDL (mmol·L-1) | 1.4 (1.1 – 3.3)  | 1.4 (1.1 – 1.8)  |
| LDL (mmol·L-1)  | 2.6 ± 0.8  | 1.8 ± 0.3  |
| Cholesterol / HDL ratio  | 3.26 ± 0.89  | 2.92 ± 0.68  |
| HbA1c (mmol/mol)  | 53 ± 8.0  | 47 ± 11.2  |
| Insulin (pmol·L-1)  | 95 (21 – 103) | 57.5 (25 – 186) |
| Glucose (mmol·L-1)  | 7.2 (5.5 – 8.3) | 6.4 (5.6 – 11.4)  |
| HOMA-IR  | 4.14 (1.15 – 6.09) | 2.75 (1.09 – 15.71) |
| vWF(IU·mL-1)  | 0.9 ± 0.4  | 0.8 ± 0.3  |
| sE-selectin (ng·mL-1) | 20.1 ± 18.8 | 23.6 ± 12.9 |

Values are expressed as mean ± SD or median (range)

\*p < 0.05 comparison between groups

Baseline urea, electrolytes and liver function tests for all participants enrolled on the study on low carbohydrate, high protein (LC), or conventional energy restricted (ER) diets

|  |  |  |
| --- | --- | --- |
|  | ER (n = 7) | LC (n = 6) |
| Sodium (mmol·L-1)  | 138.3 ± 2.2  | 138.5 ± 1.8  |
| Potassium (mmol·L-1)  | 4.50 ± 0.34  | 4.35 ± 0.32  |
| Bicarbonate (mmol·L-1)  | 29.0 ± 3.1  | 27.7 ± 3.4  |
| Urea (mmol·L-1)  | 5.96 ± 2.27  | 5.05 ± 1.23  |
| Creatinine(mmol·L-1)  | 73.7 ± 21.4  | 69.8 ± 8.8  |
| Bilirubin(μ mol·L-1)  | 12.0 ± 4.1  | 12.5 ± 4.9  |
| ALT (IU·L-1) | 27.0 (17 – 66)  | 33.0 (15 – 175)  |
| Alkphos(IU·L-1)  | 77.4 ± 16.2  | 85.3 ± 38.3  |
| Gamma GT (IU·L-1)  | 43.0 ± 26.7  | 47.7 ± 26.9  |
| Total protein (g·L-1)  | 70.1 ± 4.4  | 73.0 ± 4.3  |
| Albumin (g·L-1) | 41.0 (38 – 45)  | 41.5 (40 – 43)  |
| Globulin (g·L-1)  | 28.0 (25 – 34)  | 29.5 (29 – 36)  |
| eGFR (ml·min-1) | 90 (72 – 90)  | 90 (63 – 90)  |
| Ketones(mmol·L-1) | 0.2(0.1 -0.2)  | 0.1 (0.1 - 0.2)  |

Values are expressed as mean ± SD or median (range)

**Outcome measures**

Primary outcome measures

**Metabolic parameters of participants at baseline, 4 weeks and 8 weeks following a low carbohydrate, high protein (LC) or conventional energy restricted (ER) diet**

|  |  |  |  |
| --- | --- | --- | --- |
|  | ER (n = 5) | LC (n = 5) | Combined (n = 10) |
|  | Baseline | 4 weeks | 8 weeks | Baseline | 4 weeks | 8 weeks | Baseline | 4 weeks | 8 weeks |
| Sodium (mmol·L-1) | 138 (136 - 140) | - | 139 (138 - 140) | 139 (137 - 141) | - | 139 (135 - 139) | 138.3 ± 1.8 | - | 138.7 ± 1.3 |
| Potassium (mmol·L-1) | 4.5 ± 0.39 | - | 4.6 ± 0.26 | 4.4 ± 0.36 | - | 4.3 ± 0.29 | 4.43 ± 0.36 | - | 4.41 ± 0.30 |
| Bicarbonate (mmol·L-1) | 29 (28 - 31) | - | 29 (28 - 32) | 29 (22 - 30) | - | 30 (25 - 30) | 29 (22; 31) | - | 29.5 (25; 32) |
| Urea (mmol·L-1) | 5.6 (3.2 - 6.1) | - | 4.1 (3.6 - 6.0) | 4.9 (3.3 - 6.8) | - | 7.3 (3.7 - 7.6)\* | 5.0 ± 1.2 | - | 5.6 ± 1.7 |
| Creatinine (mmol·L-1) | 68.2 ± 28.9 | - | 66.0 ± 19.9 | 73.0 ± 4.5 | - | 74.6 ± 12.2 | 70.6 ± 14.5 | - | 70.3 ± 15.1 |
| Bilirubin (μmol·L-1) | 13.2 ± 3.8 | 11.0 ± 2.9 | 13.4 ± 5.2 | 12.8 ± 5.5 | 13.0 ± 6.1 | 11.8 ± 6.3 | 13.0 ± 4.4 | 12.0 ± 4.6 | 12.6 ± 5.5 |
| ALT (IU·L-1) | 38.2 ± 19.1 | 35.0 ± 15.9 | 28.6 ± 6.2 | 31.0 ± 12.1 | 36.2 ± 13.6 | 28.6 ± 6.2 | 34.6 ± 15.5 | 35.6 ± 14.0 | 28.3 ± 6.8 |
| ALP (IU·L-1) | 79.0 ± 19.2 | 84.0 ± 20.8 | 87.6 ± 16.3 | 84.0 ± 42.6 | 80.8 ± 39.9 | 96.0 ± 41.0\* | 81.5 ± 31.3 | 82.4 ± 30.1 | 91.8 ± 29.8\* |
| Gamma GT (IU·L-1) | 36.2 ± 16.9 | 31.8 ± 11.8 | 32.4 ± 12.3 | 48.6 ± 30.0 | 31.0 ± 17.4 | 38.6 ± 16.3 | 42.4 ± 23.9 | 31.4 ± 14.0 | 35.5 ± 14.0 |
| Total protein (g·L-1) | 70.0 ± 4.3 | 71.2 ± 2.5 | 68.4 ± 3.6 | 71.8 ± 3.6 | 72.8 ± 3.2 | 75.0 ± 3.4\*† | 70.9 ± 3.8 | 72.0 ± 2.8 | 71.7 ± 4.8 |
| Albumin (g·L-1) | 41 (38 - 45) | 40 (38 - 44) | 43 (36 - 45) | 40 (40 - 43) | 42 (40 - 43) | 42 (37 - 44) | 41.4 ± 2.1 | 41.1 ± 1.9 | 41.1 ± 3.6 |
| Globulin (g·L-1) | 28 (25 - 33) | 30 (27 - 35) | 28 (20 - 35) | 29 (29 - 34) | 29 (29 - 35) | 36 (30 - 36)\*† | 29.3 ± 2.8 | 30.9 ± 3.0 | 30.6 ± 5.4 |
| Cholesterol (mmol·L-1) | 4.6 ± 0.74 | 4.1 ± 0.97 | 3.9 ± 0.85 | 4.0 ± 0.26 | 3.5 ± 0.93 | 3.9 ± 0.41 | 4.3 ± 0.63 | 3.8 ± 0.95 | 3.9 ± 0.63 |
| Triacylglycerols (mmol·L-1) | 1.0 (0.8 - 1.4) | 0.9 (0.6 - 2.3) | 1.0 (0.8 - 2.1) | 1.7 (0.9 - 2.6) | 1.0 (0.6 - 1.9) | 0.9 (0.7 - 2.3) | 1.1 (0.8; 2.6) | 1.0 (0.6; 2.3) | 0.95 (0.7; 2.3) |
| HDL (mmol·L-1) | 1.4 (1.1 - 1.5) | 1.4 (1.0 - 1.6) | 1.4 (1.0 - 1.7) | 1.3 (1.1 - 1.8) | 1.4 (1.1 - 1.4) | 1.3 (1.2 - 1.7) | 1.4 ± 0.23 | 1.3 ± 0.18 | 1.4 ± 0.22 |
| LDL (mmol·L-1) | 2.8 ± 0.57 | 2.2 ± 0.63 | 2.2 ± 0.73 | 1.8 ± 0.35 | 1.6 ± 0.63 | 1.9 ± 0.52 | 2.3 ± 0.67 | 1.9 ± 0.68 | 2.0 ± 0.62 |
| Cholesterol / HDL ratio | 3.29 (3.13 - 3.80) | 2.73 (2.60 - 3.79) | 2.67 (2.53 - 3.85) | 3.15 (2.00 - 3.91) | 2.71 (2.00 - 3.29) | 3.00 (1.88 - 3.33) | 3.1 ± 0.59 | 2.8 ± 0.50 | 2.9 ± 0.58 |
| CRP (mg·L-1) | 1.0 (1 - 4) | - | 1.0 (1 - 2) | 2.5 (1 - 5) | - | 2.5 (1 - 3) | 1 (1; 5) | - | 1 (1; 3) |
| Ketones (mmol·L-1) | 0.2 (0.1 - 0.2) | - | 0.2 (0.2 - 0.6) | 0.1 (0.1 - 0.2) | - | 0.2 (0.1 - 0.3) | 0.15 (0.1; 0.2) | - | 0.2 (0.1; 0.6) |
| eGFR (ml·min-1) | 90 (72 - 90) | - | 90 (77 - 90) | 90 (63 - 90) | - | 86.9 (51 - 90) | 90 (63; 90) | - | 88 (51; 90) |
| HbA1c (mmol·mol-1) | 50.4 ± 7.9 | 48.0 ± 6.7 | 47.4 ± 7.1 | 48.4 ± 11.9 | 42.8 ± 6.3‡ | 43.8 ± 5.1 | 49.4 ± 9.6 | 45.7 ± 6.7‡\* | 45.6 ± 6.1 |
| Insulin (pmol·L-1) | 76.2 ± 34.7 | - | 55.2 ± 27.3 | 82.6 ± 65.0 | - | 87.6 ± 44.2 | 79.4 ± 49.2 | - | 71.4 ± 38.6 |
| Glucose (mmol·L-1) | 7.2 (5.5 - 8.3) | 6.9 (4.6 - 7.8) | 7.1 (4.4 - 7.2) | 5.9 (5.6 - 11.4) | 5.8 (5.2 - 6.7) | 6.7 (5.8 - 8.2) | 6.5 (5.5 - 11.4) | 6.5 (4.6 - 7.8) | 6.9 (4.4 - 8.2) |
| HOMA-IR | 4.20 (1.15 - 6.09) | - | 1.91 (1.14 - 4.63) | 2.25 (1.09 - 15.71) | - | 4.91 (2.18 - 7.58) | 3.52 (1.09 - 15.71) | - | 3.34 (1.14 - 7.58) |
| vWF (IU·mL-1) | 0.90 (0.42 - 1.44) | - | 1.20 (0.92 - 1.20) | 0.84 (0.33 - 1.06) | - | 0.62 (0.58 - 1.13)† | 0.83 ± 0.33 | - | 0.93 ± 0.25 |
| sE-selectin (ng·mL-1) | 12.0 ± 8.5 | - | 15.0 ± 10.2 | 26.1 ± 12.7 | - | 20.0 ± 14.1 | 19.1 ± 12.6 | - | 17.5 ± 11.9 |

Values are expressed as mean ± SD, or median (range)

ALP, Alkaline phosphatase; ALT, alanine transaminase; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; GT, glutamyl transferase; HbA1c, glycosylated haemoglobin; HDL, high density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment – insulin resistance; vWF, von Willebrand factor

- Indicates parameter were not measured at time point; \* Significant difference from baseline, p < 0.05; † Significant difference between groups at time point, p < 0.05; ‡ one value missing

Secondary outcome measures

Anthropometry and physiological measures at baseline, 4 weeks and 8 weeks following a low carbohydrate, high protein (LC) or conventional energy restricted (ER) diet

|  |  |  |  |
| --- | --- | --- | --- |
|  | ER (n = 5) | LC (n = 5) | Combined (n = 10) |
|  | Baseline | 4 weeks | 8 weeks | Baseline | 4 weeks | 8 weeks | Baseline | 4 weeks | 8 weeks |
| Weight (kg) | 92.4 ± 12.8 | 90.7 ± 12.2 | 89.4 ± 11.6 | 89.4 ± 7.4 | 85.7 ± 5.6\* | 85.6 ± 6.2 | 90.9 ± 10.0 | 88.2 ± 9.3\* | 87.5 ± 9.0\* |
| BMI (kg·m-2) | 32.7 ± 3.5 | 32.1 ± 3.3 | 31.7 ± 3.6 | 32.4 ± 3.1 | 31.2 ± 3.1\* | 31.1 ± 2.5 | 32.6 ± 3.1 | 31.6 ± 3.1\* | 31.4 ± 2.9\* |
| Waist circumference (cm) | 113.6 ± 6.3 | 110.1 ± 6.3 | 106.7 ± 7.0† | 112.6 ± 8.2 | 109.4 ± 11.5 | 111.2 ± 9.3 | 113 ± 6.9 | 110 ± 8.8 | 109 ± 8.1\* |
| Waist to hip ratio | 0.98 ± 0.06 | 0.98 ± 0.05 | 0.94 ± 0.06\*† | 0.96 ± 0.04 | 0.97 ± 0.05 | 0.98 ± 0.02 | 0.97 ± 0.05 | 0.98 ± 0.05 | 0.96 ± 0.05 |
| Body fat (%) | 36.4 ± 6.5 | 34.9 ± 8.3 | 34.3 ± 8.6 | 35.6 ± 10.2 | 35.1 ± 11.0 | 34.3 ± 10.0 | 33.1 (25.4 - 48.2) | 33.5 (23.0 - 48.5) | 34.3 (26.4 - 49.7) |
| Systolic blood pressure (mmHg) | 134 ± 12.5 | 123 ± 12.4 | 127 ± 13.7 | 142 ± 10.7 | 116 ± 9.4\* | 126 ± 12.3\*† | 138 (119 - 155) | 117 (108 - 142)\* | 130 (109 - 140)\* |
| Diastolic blood pressure (mmHg) | 83 ± 13.6 | 78 ± 5.3 | 74 ± 8.9 | 75 ± 5.1 | 70 ± 5.1‡ | 69 ± 4.9 | 79.3 ± 10.5 | 73.7 ± 6.4 | 71.2 ± 7.2 |

Values are expressed as mean ± SD or median (range)
\* Significant difference from baseline p < 0.05
† Significant difference from 4 weeks p < 0.05
‡ Significant difference between groups at time point

**Adverse events**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **LC group** | **ER group** | **Total** |
| **Constipation (no. of events)** | 3 | 1 | 4 |
| **Diarrhoea (no. of events)** | 0 | 3 | 3 |
| **Dizziness (no. of events)** | 2 | 1 | 3 |
| **Headaches (no. of events)** | 2 | 0 | 2 |
| **Dermatitis (no. of events)** | 1 | 0 | 1 |
| **Halitosis (no. of events)** | 1 | 0 | 1 |