**On-line Supplementary Material**

**Dietary Betaine Intake and Risk of Mortality in Patients with Coronary Artery Disease: The Prospective Guangdong Coronary Artery Disease Cohort**

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**Supplementary Figure 1**. The flow chart of participants through the study.

**Supplementary Table 1**. Associations between dietary betaine intake and plasma concentrations of methionine metabolites and vitamins in patients with CAD.

**Supplementary Table 2**. HRs for mortality according to dietary betaine intake in CAD patients of various subpopulations.

1977 patients underwent coronary angiography were diagnosed with CAD

After excluding 389 participants without enough plasma samples or missing baseline data

1588 patients with CAD in whom we performed baseline measurements of plasma levels of methionine metabolites

After excluding 296 participants with missing baseline FFQ data

A final sample size of 1292 was used to analysis in the present study

After a median follow-up of 9.2 (interquartile range: 8.5–10.2) years

259 patients had died, including 167 deaths from cardiovascular diseases

**Supplementary Figure1**. The flow chart of participants through the study. CAD, coronary artery disease; FFQ, food frequency questionnaire.

**Supplementary Table 1**. Associations between dietary betaine intake and plasma concentrations of methionine metabolites and vitamins in patients with CAD (n=1292)*1*

|  |  |
| --- | --- |
| Variables | Dietary Betaine Intake |
| Univariate | Multivariate |
| r | *P* value | r  | *P* value |
| SAH, nmol/L  | -0.202 | <0.001 | -0.194 | <0.001 |
| SAM, nmol/L | 0.158 | <0.001 | 0.147 | <0.001 |
| SAM/SAH ratio | 0.245 | <0.001 | 0.240 | <0.001 |
| tHcy, μmol/L | -0.174 | <0.001 | -0.167 | <0.001 |
| tCys, μmol/L | 0.028 | 0.307 | 0.034 | 0.220 |
| Folate, nmol/L | 0.023 | 0.418 | 0.023 | 0.416 |
| Vitamin B12, pmol/L | 0.014 | 0.611 | 0.016 | 0.573 |

*1* Multivariate correlation analysis adjusted for age, sex, body mass index, smoking status, alcohol drinker, hypertension, diabetes mellitus, physical activity, family history of coronary artery disease, systolic blood pressure, gensini score, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, use or nonuse of statins, aspirin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and β-blockers, S-adenosylhomocysteine, S-adenosylmethionine, total cysteine; total homocysteine, folate, vitamin B-12, dietary energy intake, dietary protein intake, and dietary choline intake. SAH, S-adenosylhomocysteine; SAM, S-adenosylmethionine; tHcy, total homocysteine; tCys, total cysteine.

**Supplementary Table 2**. HRs for Mortality According to Dietary Betaine Intake in CAD Patients of Various Subpopulations*1*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | No. of Death/No.of Participants | Dietary Betaine Intake  | *P* forTrend | *P* forInteraction |
| Subpopulation | Tertile 1 | Tertile 2 | Tertile 3 |
| All-cause mortality |
| Age groups, y |  |  |  |  |  | 0.157 |
| ≤60 | 68/439 | 1 | 0.99 (0.54, 1.84) | 0.42 (0.20, 0.87) | 0.049 |  |
| >60 | 191/853 | 1 | 0.87 (0.61, 1.22) | 0.83 (0.57, 1.21) | 0.579 |  |
| Sex groups |  |  |  |  |  | 0.513 |
| Men | 178/879 | 1 | 0.92 (0.65, 1.31) | 0.71 (0.47, 1.07) | 0.254 |  |
| Women | 81/413 | 1 | 0.67 (0.37, 1.20) | 0.56 (0.32, 0.99) | 0.114 |  |
| BMI, kg/m2 |  |  |  |  |  | 0.762 |
| <24 | 141/665 | 1 | 0.67 (0.48, 1.08) | 0.55 (0.35, 0.87) | 0.032 |  |
| ≥24 | 118/627 | 1 | 0.86 (0.55, 1.35) | 0.82 (0.51, 1.33) | 0.692 |  |
| Current smoking |  |  |  |  |  | 0.516 |
| Yes | 88/473 | 1 | 0.78 (0.47, 1.29) | 0.56 (0.31, 1.03) | 0.167 |  |
| No | 171/819 | 1 | 0.77 (0.53, 1.11) | 0.75 (0.51, 1.12) | 0.260 |  |
| Alcohol drinker |  |  |  |  |  | 0.092 |
| Yes | 68/334 | 1 | 1.71 (0.92, 3.14) | 0.75 (0.37, 1.51) | 0.061 |  |
| No | 191/958 | 1 | 0.71 (0.48, 1.04) | 0.70 (0.50, 0.98) | 0.074 |  |
| Hypertension |  |  |  |  |  | 0.296 |
| Yes | 148/722 | 1 | 0.73 (0.48, 1.12) | 0.68 (0.45, 1.02) | 0.140 |  |
| No | 111/570 | 1 | 1.02 (0.66, 1.59) | 0.62 (0.36, 1.08) | 0.163 |  |
| Diabetes mellitus |  |  |  |  |  | 0.868 |
| Yes | 75/415 | 1 | 0.69 (0.37, 1.28) | 0.67 (0.37, 1.22) | 0.334 |  |
| No | 184/877 | 1 | 0.89 (0.63, 1.26) | 0.72 (0.49, 1.08) | 0.288 |  |
| Cardiovascular mortality |
| Age groups, y |  |  |  |  |  | 0.279 |
| ≤60 | 47/439 | 1 | 0.71 (0.32, 1.54) | 0.27 (0.10, 0.71) | 0.026 |  |
| >60 | 120/853 | 1 | 0.91 (0.59, 1.38) | 0.68 (0.41, 1.13) | 0.338 |  |
| Sex groups |  |  |  |  |  | 0.990 |
| Men | 115/879 | 1 | 0.74 (0.48, 1.15) | 0.51 (0.29, 0.86) | 0.040 |  |
| Women | 52/413 | 1 | 0.65 (0.33, 1.29) | 0.43 (0.19, 0.99) | 0.124 |  |
| BMI, kg/m2 |  |  |  |  |  | 0.749 |
| <24 | 91/665 | 1 | 0.64 (0.39, 1.05) | 0.42 (0.23, 0.77) | 0.015 |  |
| ≥24 | 76/627 | 1 | 0.91 (0.52, 1.59) | 0.64 (0.34, 1.20) | 0.376 |  |
| Current smoking |  |  |  |  |  | 0.631 |
| Yes | 56/473 | 1 | 0.73 (0.38, 1.36) | 0.38 (0.17, 0.87) | 0.068 |  |
| No | 111/819 | 1 | 0.71 (0.45, 1.09) | 0.58 (0.36, 0.98) | 0.090 |  |
| Alcohol drinker |  |  |  |  |  | 0.273 |
| Yes | 44/334 | 1 | 1.58 (0.69, 3.61) | 0.87 (0.35, 2.16) | 0.404 |  |
| No | 123/958 | 1 | 0.64 (0.42, 0.97) | 0.47 (0.28, 0.78) | 0.008 |  |
| Hypertension |  |  |  |  |  | 0.593 |
| Yes | 94/722 | 1 | 0.58 (0.35, 0.96) | 0.48 (0.27, 0.84) | 0.016 |  |
| No | 73/570 | 1 | 0.93 (0.54, 1.61) | 0.55 (0.27, 1.12) | 0.245 |  |
| Diabetes mellitus |  |  |  |  |  | 0.681 |
| Yes | 49/415 | 1 | 0.78 (0.38, 1.59) | 0.31 (0.12, 0.77) | 0.045 |  |
| No | 118/877 | 1 | 0.80 (0.51, 1.23) | 0.64 (0.38, 1.05) | 0.201 |  |

*1* HRs and 95% CIs were estimated by Cox proportional hazards regression models. BMI, body mass index; CAD, coronary artery disease.

Adjusted for age, sex, body mass index, smoking status, alcohol drinker, hypertension, diabetes mellitus, physical activity, family history of coronary artery disease, systolic blood pressure, gensini score, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, use or nonuse of statins, aspirin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and β-blockers, S-adenosylhomocysteine, S-adenosylmethionine, total cysteine; total homocysteine, folate, vitamin B-12, dietary energy intake, dietary protein intake, and dietary choline intake.