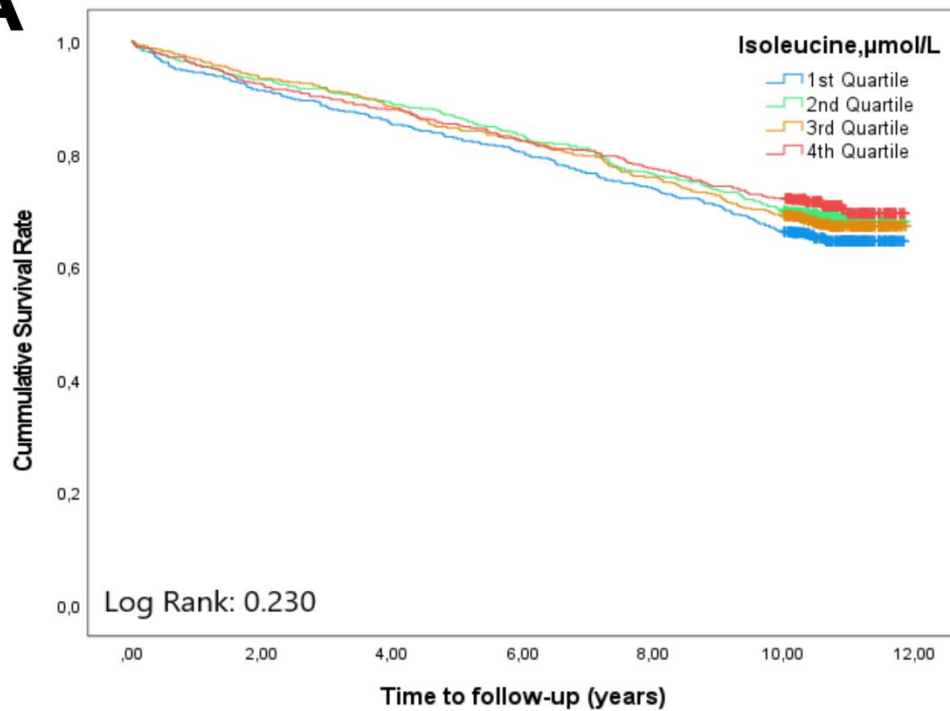
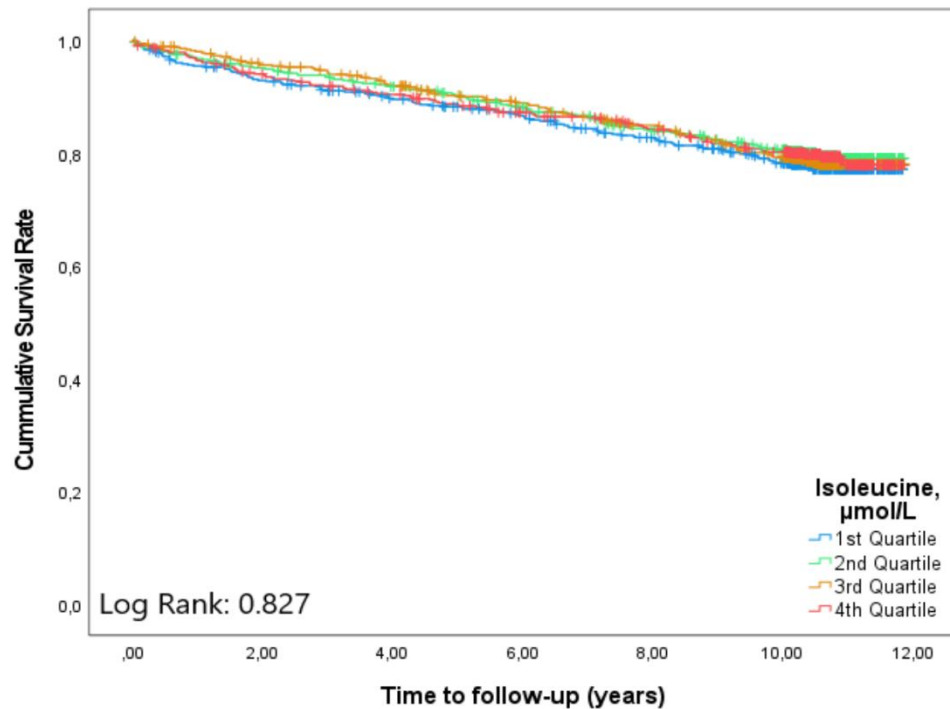


**Supplemental information**

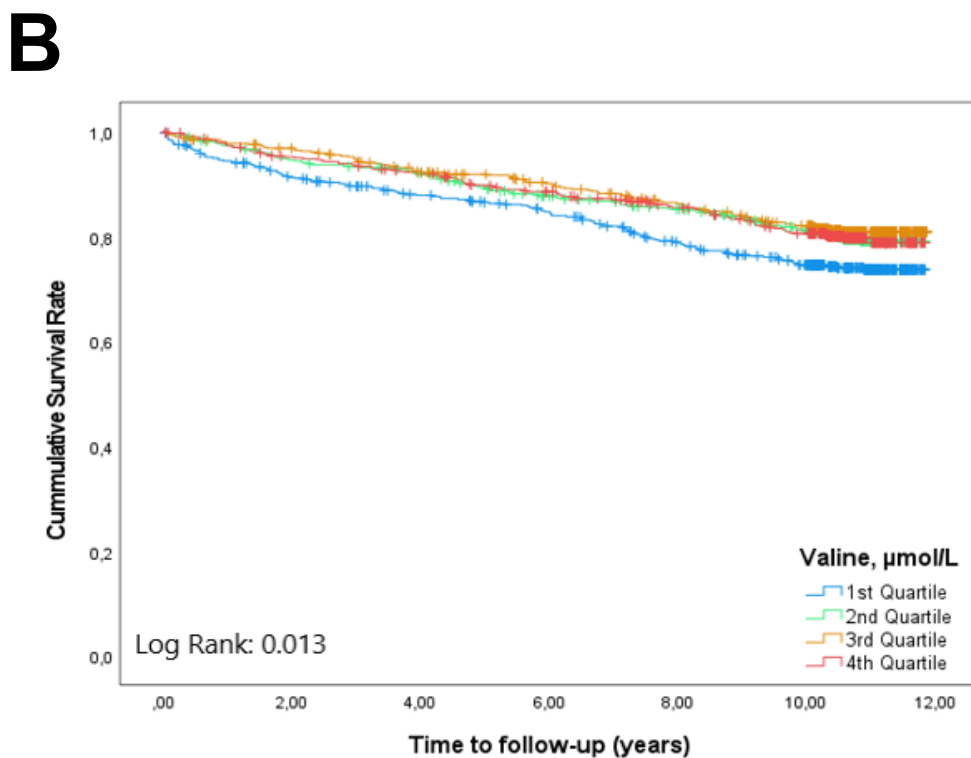
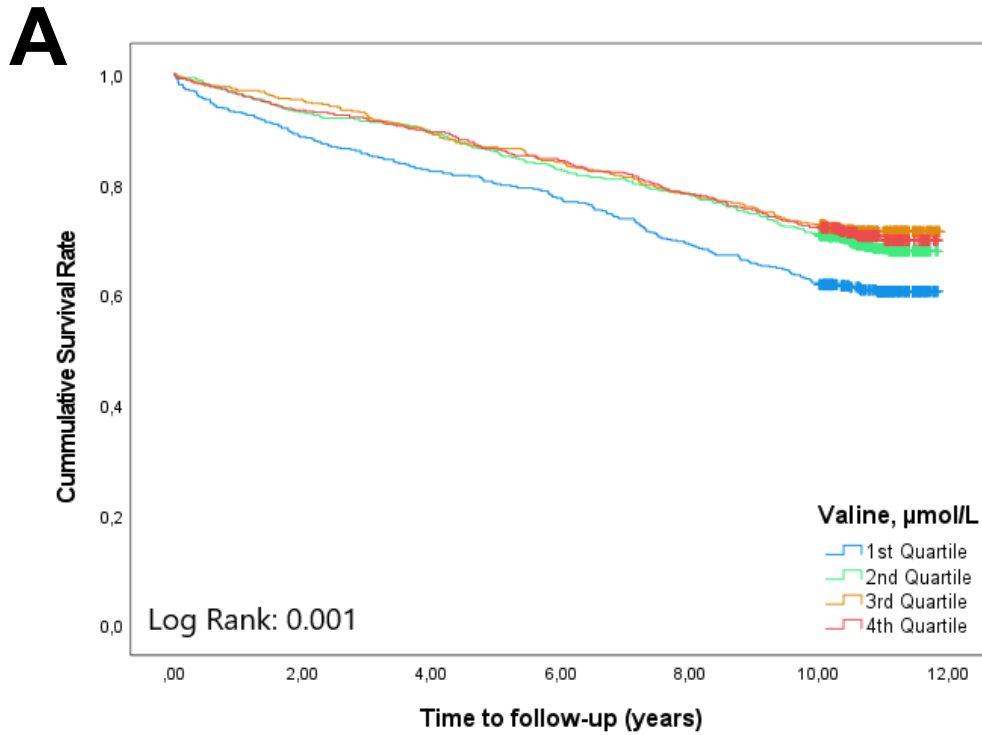
**Association of branched-chain amino acids  
with mortality-the Ludwigshafen Risk  
and Cardiovascular Health (LURIC) study**

**Angela P. Moissl, Stefan Lorkowski, Andreas Meinitzer, Stefan Pilz, Hubert Scharnagl, Graciela E. Delgado, Marcus E. Kleber, Bernhard K. Krämer, Burkert Pieske, Martin R. Grübler, Helmut Brussee, Dirk von Lewinski, Hermann Toplak, Astrid Fahrleitner-Pammer, Winfried März, and Andreas Tomaschitz**

**A****B**

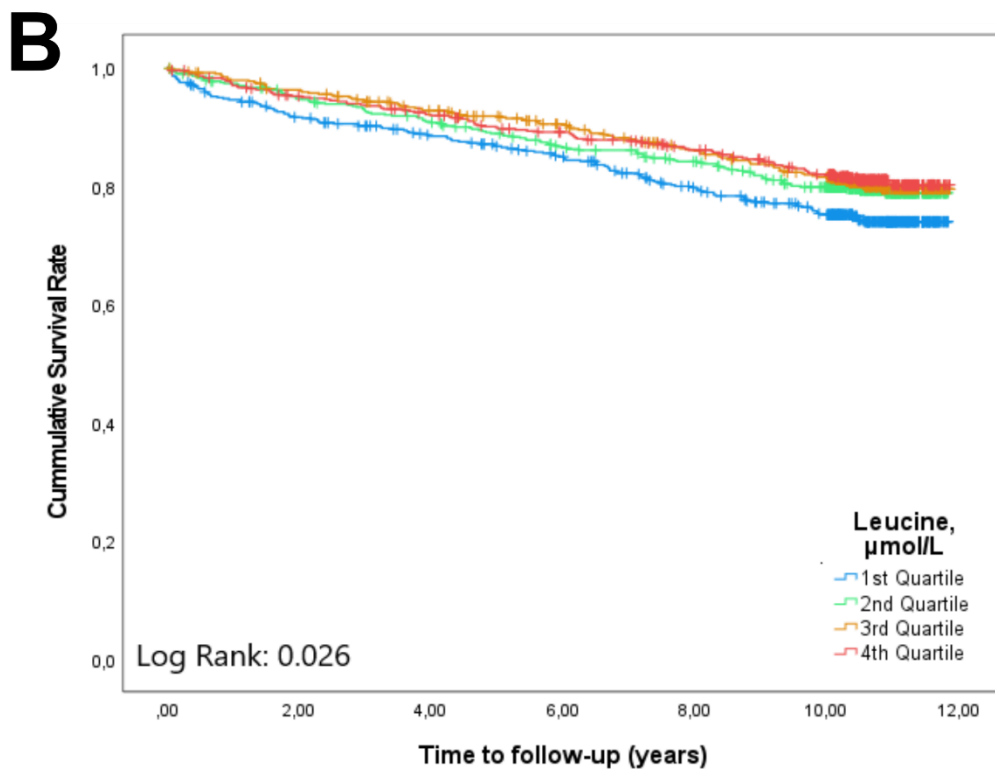
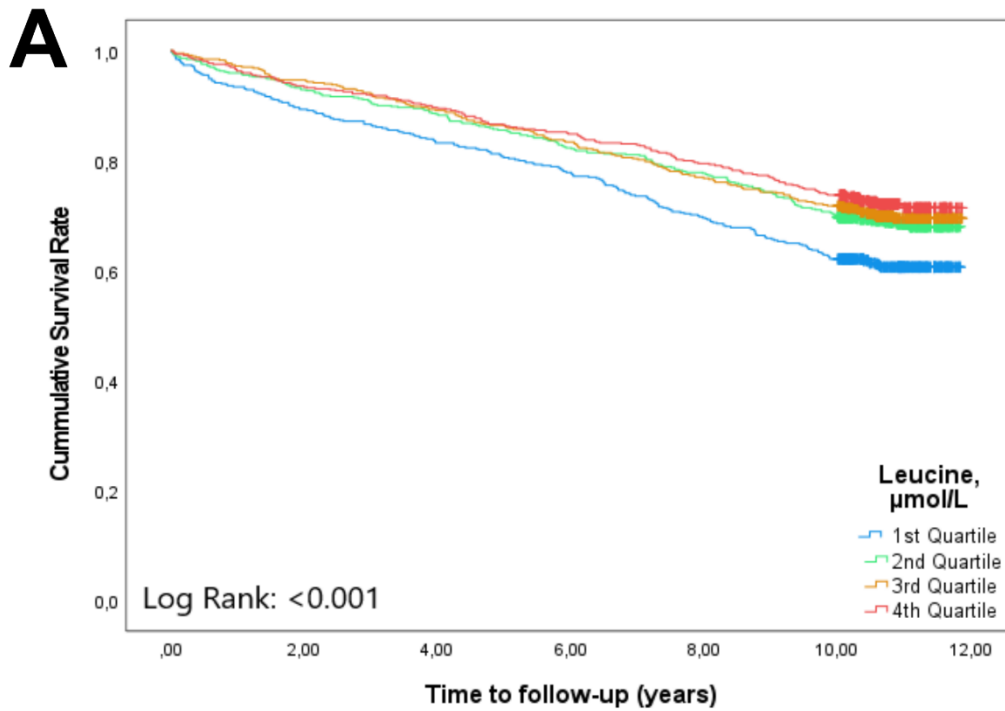
**Supplementary Figure SF1:** Kaplan-Meier curve according to serum isoleucine, related to the results part “Associations between baseline serum BCAA concentrations and outcomes” Figure 1.

**A)** Kaplan-Meier curve for the time to all-cause mortality according to serum Isoleucine concentrations in quartiles at baseline. **B)** Kaplan-Meier curve for the time to cardiovascular mortality according to serum Isoleucine concentrations in quartiles at baseline.



**Supplementary Figure SF2:** Kaplan-Meier curve according to serum valine, related to the results part “Associations between baseline serum BCAA concentrations and outcomes” Figure 1.

**A)** Kaplan-Meier curve for the time to all-cause mortality according to serum Valine concentrations in quartiles at baseline. **B)** Kaplan-Meier curve for the time to cardiovascular mortality according to serum Valine concentrations in quartiles at baseline.



**Supplementary Figure SF3:** Kaplan-Meier curve according to serum leucine, related to the results part “Associations between baseline serum BCAA concentrations and outcomes” Figure 1.

**A)** Kaplan-Meier curve for the time to all-cause mortality according to serum Leucine concentrations in quartiles at baseline. **B)** Kaplan-Meier curve for the time to cardiovascular mortality according to serum Leucine concentrations in quartiles at baseline.

**Supplementary Table S1.** Multivariate hazard ratios for cardiovascular mortality per SD of BCAA stratified by potential moderators, related to the results part “BCAA concentration associated cardiovascular mortality in various subgroups”.

Group	n/Events	Hazard ratio (95% CI)	p-Value	p-Value for interaction
		<i>P</i> <0.001		
All	2142/433 (20.2 %)	0.76 (0.68-0.85)	< 0.001	-
Age, y ( <i>median</i> )				0.314
< 63.5	1081/109 (10.1 %)	0.70 (0.57-0.86)	< 0.001	
≥ 63.5	1061/324 (30.5 %)	0.84 (0.74-0.95)	0.006	
Sex				0.216
Male	1568/326 (20.8 %)	0.78 (0.69-0.89)	< 0.001	
Female	625/117 (18.7 %)	0.70 (0.55-0.87)	0.002	
BMI, kg/m <sup>2</sup>				0.595
< 25.0	635/131 (20.6 %)	0.79 (0.65-0.97)	0.025	
≥ 25.0	1507/302 (20.0 %)	0.75 (0.66-0.85)	< 0.001	
HOMA-IR ( <i>median</i> )				0.506
< 2.2	1047/165 (15.8 %)	0.63 (0.52-0.77)	< 0.001	
≥ 2.2	1021/250 (24.5 %)	0.83 (0.72-0.95)	0.008	
Diabetes				
No	1393/187 (13.4 %)	0.77 (0.64-0.92)	0.004	
Yes	812/256 (31.5 %)	0.76 (0.66-0.87)	< 0.001	
Haemoglobin A <sub>1c</sub> , mmol/mol ( <i>median</i> )				0.223
< 41.0	1107/148 (13.3 %)	0.79 (0.66-0.96)	0.016	
≥ 41.0	1035/285 (27.5 %)	0.80 (0.70-0.91)	< 0.001	
Coronary artery disease				
No	654/69 (10.6 %)	0.77 (0.59-1.02)	0.069	
Yes	1488/364 (24.5 %)	0.77 (0.68-0.87)	< 0.001	
Arterial hypertension				0.973
No	576/85 (14.8 %)	0.77 (0.59-1.00)	0.051	
Yes	1566/348 (22.2 %)	0.76 (0.67-0.86)	< 0.001	
Triglycerides, mmol/l ( <i>median</i> )				0.530
< 1.7	1120/221 (19.7 %)	0.66 (0.56-0.77)	< 0.001	
≥ 1.7	1022/212 (20.7 %)	0.94 (0.81-1.09)	0.395	

LDL-cholesterol, mmol/l (median)				0.832
< 2.9	1064/217 (20.4 %)	0.85 (0.73-0.98)	0.030	
≥ 2.9	1078/216 (20.0 %)	0.75 (0.64-0.88)	< 0.001	
Adiponectin, μM (median)				0.003
< 8.3	1047/176 (16.8 %)	0.90 (0.76-1.06)	0.199	
≥ 8.3	1031/245 (23.8 %)	0.78 (0.67-0.90)	< 0.001	
NYHA				0.015
I/II	1698/291 (17.1 %)	0.82 (0.72-0.94)	0.004	
III/IV	444/142 (32.0 %)	0.67 (0.55-0.81)	< 0.001	
NT-pro-BNP, pg /ml (median)				< 0.001
< 293.5	1062/89 (8.4 %)	0.75 (0.59-0.97)	0.025	
≥ 293.5	1061/339 (32.0 %)	0.86 (0.77-0.97)	0.015	
Galectin-3, ng/ml (median)				0.161
< 13.9	716/118 (16.5 %)	0.86 (0.70-1.05)	0.139	
≥ 13.9	723/174 (24.1 %)	0.76 (0.63-0.91)	< 0.003	
Homoarginine, μmol/l (median)				< 0.001
< 2.4	1013/287 (28.3 %)	0.80 (0.71-0.92)	0.001	
≥ 2.4	1119/144 (12.9 %)	0.92 (0.75-1.10)	0.382	
Smoking status				0.576
No	1741/372 (21.4 %)	0.78 (0.70-0.88)	< 0.001	
Yes	1566/348 (22.2 %)	0.76 (0.67-0.86)	< 0.001	
Haemoglobin, g/dl (median)				0.551
< 13.8	998/240 (24.1 %)	0.73 (0.63-0.85)	< 0.001	
≥ 13.8	1144/193 (16.9 %)	0.78 (0.66-0.91)	0.002	
De Ritis ratio (median)				0.948
< 0.8	1110/202 (18.2 %)	0.79 (0.67-0.93)	0.005	
≥ 0.8	1032/231 (22.4 %)	0.74 (0.64-0.86)	< 0.001	

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**Supplementary Table S2:** Hazard ratios (95% CI) for ten-year specific causes of cardiovascular death, related to STAR Methods”.

<b>Fatal myocardial infarction</b>						
Event rate (%)	3.4 (19/559)	4.8 (27/559)	3.2 (18/559)	2.7 (15/559)	-	-
Crude	1.42 (0.72-2.79)	1.86 (0.99-3.50)	1.21 (0.61-2.39)	1.00 (ref)	0.85 (0.67-1.07)	0.156
Model 1	1.84 (0.92-3.65)	2.12 (1.12-3.97)	1.23 (0.62-2.43)	1.00 (ref)	0.76 (0.60-0.97)	0.028
Model 2	2.74 (1.29-5.81)	2.76 (1.40-5.41)	1.52 (0.76-3.05)	1.00 (ref)	0.65 (0.50-0.85)	0.001
Model 3	2.49 (1.15-5.36)	2.55 (1.29-5.03)	1.49 (0.74-3.01)	1.00 (ref)	0.68 (0.52-0.89)	0.006
<b>Sudden cardiac death</b>						
Event rate (%)	9.3 (52/559)	5.7 (32/559)	7.5 (42/559)	8.6 (48/559)	-	-
Crude	1.20 (0.81-1.78)	0.68 (0.44-1.07)	0.88 (0.58-1.33)	1.00 (ref)	0.92 (0.79-1.08)	0.301
Model 1	1.43 (0.96-2.13)	0.76 (0.48-1.18)	0.86 (0.57-1.31)	1.00 (ref)	0.87 (0.74-1.02)	0.077
Model 2	2.13 (1.37-3.30)	0.94 (0.59-1.51)	0.97 (0.63-1.49)	1.00 (ref)	0.74 (0.62-0.88)	<0.001
Model 3	2.03 (1.30-3.17)	0.94 (0.59-1.51)	1.00 (0.65-1.54)	1.00 (ref)	0.75 (0.63-0.89)	0.001
<b>Death due to congestive heart failure</b>						
Event rate (%)	5.2 (29/559)	5.7 (32/559)	3.6 (20/559)	4.8 (27/559)	-	-
Crude	1.20 (0.71-2.02)	1.22 (0.73-2.04)	0.74 (0.42-1.32)	1.00 (ref)	0.93 (0.76-1.12)	0.414
Model 1	1.36 (0.80-2.32)	1.34 (0.80-2.24)	0.71 (0.40-1.27)	1.00 (ref)	0.88 (0.72-1.08)	0.218
Model 2	2.12 (1.19-3.78)	1.86 (1.09-3.19)	0.89 (0.50-1.60)	1.00 (ref)	0.74 (0.60-0.93)	0.008
Model 3	2.06 (1.14-3.71)	1.89 (1.15-3.71)	0.90 (0.50-1.62)	1.00 (ref)	0.76 (0.61-0.94)	0.013