

**Physical activity attenuates the associations of systemic immune-inflammation index with total and cause-specific mortality among middle-aged and older populations**

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**Table S1. The associations between baseline characteristics and SII level.**

<b>Variables</b>	<b>DFTJ cohort</b>	<b>NHANES 1999-2014</b>
Age	-0.008 (-0.010, -0.007)	-0.001 (-0.002, -0.0003)
Male	-0.019 (-0.043, 0.006)	-0.094 (-0.115, -0.072)
Race		
Non-Hispanic White	-	Ref
Non-Hispanic Black	-	-0.442 (-0.476, -0.409)
Mexican American	-	-0.102 (-0.133, -0.070)
Other	-	-0.144 (-0.188, -0.101)
BMI	0.0004 (-0.002, 0.003)	0.005 (0.003, 0.007)
Smoking	0.116 (0.091, 0.142)	0.053 (0.024, 0.083)
Alcohol drinking	-0.017 (-0.039, 0.006)	-0.013 (-0.042, 0.017)
Physically active	-0.035 (-0.058, -0.013)	-0.090 (-0.114, -0.066)

**Abbreviations:** SII, systemic immune-inflammation index; DFTJ, Dongfeng-Tongji ; NHANES, National Health and Nutrition Examination Survey; BMI, body mass index.

**Note:**  $\beta$  (95%CI)s were calculated by multivariable linear regression models, with adjustment of age, sex, race (only in the NHANES 1999-2014), BMI, smoking status, alcohol drinking status, physical activity and disease history at baseline.

**Table S2. Sensitivity analyses for the associations between the level of SII and mortality risks among the Dongfeng-Tongji cohort.**

SII category	Total mortality		CVD mortality		Cancer mortality		Other causes mortality	
	No of deaths/PYs	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>
<i>Excluded subjects who took drugs two weeks before baseline<sup>b</sup> (n=6755)</i>								
Low SII (<332)	1137/100052	Ref	384	Ref	446	Ref	307	Ref
Middle SII (332-465)	569/47563	1.12 (1.01-1.24)	240	1.41 (1.20-1.66)	180	0.88 (0.74-1.05)	149	1.10 (0.91-1.34)
High SII (>465)	672/471119	1.25 (1.14-1.38)	291	1.60 (1.38-1.87)	209	0.99 (0.84-1.17)	172	1.22 (1.01-1.47)
<i>Excluded subjects who died during the first year of follow-up (n=138)</i>								
Low SII (<332)	1516/127921	Ref	555	Ref	557	Ref	404	Ref
Middle SII (332-465)	766/61131	1.13 (1.03-1.23)	335	1.35 (1.18-1.55)	226	0.88 (0.76-1.03)	205	1.15 (0.97-1.36)
High SII (>465)	891/59882	1.26 (1.16-1.37)	393	1.52 (1.33-1.73)	254	0.97 (0.83-1.13)	244	1.32 (1.12-1.55)
<i>Excluded subjects with baseline history of CVD and cancer (n=5915)</i>								
Low SII (<332)	1011/103778	Ref	351	Ref	382	Ref	278	Ref
Middle SII (332-465)	521/49762	1.11 (1.00-1.23)	215	1.32 (1.11-1.56)	157	0.88 (0.73-1.07)	149	1.16 (0.95-1.41)
High SII (>465)	570/48368	1.22 (1.10-1.36)	245	1.51 (1.29-1.79)	168	0.96 (0.80-1.15)	157	1.23 (1.01-1.49)

**Abbreviations:** SII, systemic immune-inflammation index; CVD, cardiovascular disease; PY, person year.

**Note:** <sup>a</sup> HR (95%CI)s were calculated in the multivariable Cox proportional hazards regression models, with adjustment for age, sex, body mass index, smoking status, alcohol drinking status, physical activity, education, and disease histories.

<sup>b</sup> Drugs included anti-coagulation drugs, thrombolytic drugs, antibiotics and aspirin.

**Table S3. Sensitivity analyses for the associations between the level of SII and mortality risks among the NHANES 1999-2014.**

SII category	Total mortality		CVD mortality		Cancer mortality		Other causes mortality	
	No of deaths/PYs	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>	No of deaths	HR (95%CI) <sup>a</sup>
<i>Excluded subjects who took drugs two weeks before baseline <sup>b</sup> (n=3198)</i>								
Low SII (<498)	1665/88858	Ref	363	Ref	396	Ref	906	Ref
Middle SII (498-691)	879/42847	1.09 (0.99-1.20)	206	1.00 (0.80-1.25)	184	1.03 (0.82-1.29)	489	1.16 (1.00-1.34)
High SII (>691)	1253/42785	1.38 (1.26-1.52)	268	1.26 (1.02-1.55)	279	1.35 (1.12-1.62)	706	1.45 (1.29-1.63)
<i>Excluded subjects who died during the first year of follow-up (n=377)</i>								
Low SII (<498)	1919/98416	Ref	411	Ref	449	Ref	1059	Ref
Middle SII (498-691)	1038/47663	1.07 (0.98-1.17)	247	1.08 (0.87-1.32)	205	0.95 (0.77-1.18)	586	1.12 (0.98-1.28)
High SII (>691)	1507/49459	1.33 (1.22-1.45)	331	1.39 (1.15-1.67)	299	1.15 (0.97-1.37)	877	1.40 (1.25-1.56)
<i>Excluded subjects with baseline history of CVD and cancer (n=6579)</i>								
Low SII (<498)	1167/77816	Ref	231	Ref	296	Ref	640	Ref
Middle SII (498-691)	571/37260	1.05 (0.92-1.20)	130	1.13 (0.84-1.52)	114	0.86 (0.62-1.20)	327	1.13 (0.93-1.36)
High SII (>691)	776/36555	1.29 (1.16-1.43)	153	1.38 (1.06-1.78)	152	1.04 (0.81-1.33)	471	1.38 (1.22-1.57)

**Abbreviations:** NHANES, National Health and Nutrition Examination Survey; SII, systemic immune-inflammation index; CVD, cardiovascular disease; PY, person year.

<sup>a</sup>HR (95%CI)s were calculated in the multivariable Cox proportional hazards regression models, with adjustment for age, sex, race, body mass index, smoking status, alcohol drinking status, physical activity, education, and disease histories.

<sup>b</sup>Drugs included anti-coagulation drugs, antibiotics and aspirin.

**Table S4. The association between SII level and total mortality in subgroups of cohort participants.**

Characteristics	Low SII	Middle SII	High SII	<i>P</i> <sub>int</sub>
<b><i>DFTJ cohort</i></b>				
Sex				0.37
Male	Ref	1.17 (1.05-1.30)	1.29 (1.16-1.42)	
Female	Ref	1.03 (0.89-1.19)	1.19 (1.04-1.37)	
Age				0.56
<65 years	Ref	1.00 (0.86-1.17)	1.15 (0.99-1.33)	
≥65 years	Ref	1.12 (1.02-1.24)	1.27 (1.15-1.39)	
BMI				0.09
<25 kg/m <sup>2</sup>	Ref	1.07 (0.95-1.20)	1.30 (1.17-1.44)	
≥25 kg/m <sup>2</sup>	Ref	1.21 (1.07-1.38)	1.20 (1.05-1.37)	
Smoking status				0.25
Non-smokers	Ref	1.13 (1.01-1.27)	1.19 (1.06-1.34)	
Smokers	Ref	1.12 (0.99-1.28)	1.34 (1.19-1.51)	
Drinking status				0.53
Non-drinkers	Ref	1.14 (1.03-1.27)	1.31 (1.18-1.44)	
Drinkers	Ref	1.08 (0.93-1.25)	1.17 (1.01-1.34)	
Physical activity status				0.36
Inactive	Ref	1.24 (1.04-1.48)	1.25 (1.05-1.48)	
Active	Ref	1.09 (0.99-1.21)	1.27 (1.15-1.39)	
<b><i>NHANES 1999-2014</i></b>				
Sex				0.31
Male	Ref	1.07 (0.93-1.23)	1.31 (1.16-1.47)	
Female	Ref	1.06 (0.94-1.21)	1.43 (1.26-1.63)	
Age				0.07
<65 years	Ref	1.02 (0.83-1.26)	1.27 (1.08-1.50)	
≥65 years	Ref	1.11 (1.01-1.21)	1.45 (1.34-1.57)	
BMI				0.90
<25 kg/m <sup>2</sup>	Ref	1.04 (0.89-1.22)	1.35 (1.15-1.59)	
≥25 kg/m <sup>2</sup>	Ref	1.05 (0.94-1.16)	1.38 (1.25-1.54)	
Smoking status				0.28
Non-smokers	Ref	0.97 (0.85-1.11)	1.29 (1.14-1.46)	
Smokers	Ref	1.14 (0.99-1.30)	1.44 (1.27-1.62)	
Drinking status				0.19
Non-drinkers	Ref	1.07 (0.93-1.24)	1.44 (1.25-1.67)	
Drinkers	Ref	1.08 (0.95-1.23)	1.32 (1.18-1.48)	
Physical activity status				0.04
Inactive	Ref	1.08 (0.97-1.21)	1.43 (1.29-1.58)	
Active	Ref	1.00 (0.78-1.29)	1.14 (0.96-1.37)	

**Abbreviations:** DFTJ, Dongfeng-Tongji cohort; NHANES, National Health and Nutrition Examination Survey; SII, systemic immune-inflammation index; BMI, body mass index. Note: HR(95%CI)s were calculated in the multivariable Cox proportional hazards regression models, with adjustment for age, sex, race (only in the NHANES 1999-2014), BMI, smoking status, alcohol drinking status, physical activity, education, and disease histories, except for the stratification variable.

**Table S5.** The associations of SII level with cause-specific mortality stratified by physical activity in the NHANES 1999-2014.

Physical activity status	Low SII	Middle SII	High SII	<i>P</i> <sub>int</sub>
<b>CVD mortality</b>				<b>0.04</b>
Inactive	Ref	1.03 (0.85-1.24)	1.44 (1.18-1.77)	
Active	Ref	1.01 (0.60-1.69)	0.83 (0.51-1.35)	
<b>Cancer mortality</b>				0.47
Inactive	Ref	0.95 (0.74-1.22)	1.18 (0.99-1.41)	
Active	Ref	1.02 (0.68-1.55)	1.35 (0.92-1.99)	
<b>Other causes mortality</b>				0.06
Inactive	Ref	1.16 (1.00-1.35)	1.54 (1.36-1.74)	
Active	Ref	0.99 (0.73-1.33)	1.17 (0.91-1.49)	

**Abbreviations:** DFTJ, Dongfeng-Tongji cohort; NHANES, National Health and Nutrition Examination Survey; SII, systemic immune-inflammation index.

**Note:** HR (95%CI)s were calculated in the multivariable Cox proportional hazards regression models, with adjustment for age, sex, race (only in the NHANES 1999-2014), body mass index, smoking status, alcohol drinking status, education, and disease histories.