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Original Research Article

Association of 24 hour urinary sodium, potassium and $ALDH_2$rs671, MTHFRrs1801133 polymorphisms with blood pressure in isolated Zhangzi Island population

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The purpose of this study is to investigate the association of morning fasting urinary sodium, potassium and genetic background on $ALDH_2$rs671 and MTHFRrs1801133 polymorphisms with blood pressure in Chinese Zhangzi Island population. In this study, we used fasting morning urine to estimate the 24 hour sodium and potassium intake and to test the association with blood pressure in a total of 180 randomly recruited subjects from Zhangzi Island. Beyond the sodium intake, genetic background of $ALDH_2$rs671 and MTHFRrs1801133 polymorphisms was also tested for the association with blood pressure in this population. Zhangzi islanders were randomly recruited for the health checkup in local community hospital, each individual was measured for blood pressure and related metabolic traits (triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), fasting morning urinary sodium, potassium and creatinine. We used the Kawasaki formula to estimate 24h urine sodium and potassium excretion to investigate the association between estimated urine sodium, potassium excretion and blood pressure. According to the adjusted WHO-Monica investigation questionnaire, we obtained the demographic information including sex, age, height, weight, alcohol intake history. Genomic DNA was extracted from whole blood. The $ALDH_2$rs671 and MTHFRrs1801133 polymorphisms were genotyped by the TaqMan real-time polymerase chain reaction assay. After removed the outliers of the estimated 24h urinary sodium and potassium, we found a positive association between Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and estimated 24h urinary sodium (SBP: β=0.157, P<0.05; DBP: β=0.203, P<0.05) with adjustment for age, sex, Body Mass Index (BMI). We found $ALDH_2$rs671 is significant associated with SBP (P<0.05) after adjustment for sex, age, BMI, alcohol intake history and estimated 24h urinary sodium, and $ALDH_2$rs671 is also associated with TC, LDL-C (both P<0.05), but no association was found in MTHFRrs1801133 genotypes in blood pressure or other metabolic traits in these high salt intake islanders. We found that 24h urine sodium excretion is significantly associated with both SBP and DBP; polymorphism of $ALDH_2$rs671 is also associated with SBP, TC and LDL-C in this isolated population.

Key words: urinary sodium, blood pressure, $ALDH_2$rs671, MTHFRrs1801133, urinary potassium

INTRODUCTION

Sodium and potassium intake has been reported to be associated with blood pressure in general population, but measuring sodium intake has been a difficult task, 24 hour urine sodium excretion or spot urine sodium level are often used to estimate sodium intake. Beyond sodium and potassium intake, the dietary influence on blood pressure was also modified by genetic backgrounds, such as $ALDH_2$rs671 and MTHFRrs1801133 polymorphisms through alcohol intake and folate enriched food. But the association of salt intake and genetic backgrounds with blood pressure in the population of isolated Zhangzi Island in China was not clear.

Previous clinical epidemiological studies (Dahl, 1972; Stamler et al., 1991) and animal experiments (Denton et al., 1995) have demonstrated that sodium and potassium intake are associated with blood pressure. However, blood pressure is not only influenced by environmental factors such as dietary sodium intake, but also determined by genetic susceptibility to hypertension. Many epidemiological studies have reported the association between salt intake and blood pressure, but for the different methods leads to the discrepancy, in order to solve this problem, in the 1980s have carried out large scale international cooperative studies.

INTERSALT is an international study of 24 hour urinary electrolyte excretion in relation to blood pressure based on the samples from 52 centers in 39 countries (Elliott et al., 1996), sodium excretion ranged from 0.2 mmol/24h (Yanomamo Indians, Brazil) to 242 mmol/24h (north China) was significantly related to blood pressure, potassium excretion was negatively correlated with blood pressure, the relation of sodium to potassium ratio to blood pressure was similar to that of sodium. But randomized trial found the effect of sodium restriction was very small and restricted largely to systolic blood pressure (Grobbee et al., 1986).

PURE Study which estimates of 24 hour sodium and potassium excretion were made from fasting morning urine (FMU) in 18 countries, indicated that increments of 2.11 mm Hg in SBP and 0.78 mm Hg in DBP for each 1gram increment in estimated sodium excretion (Mente et al., 2014), they also found estimated sodium intake between 3 grams per day and 6 grams per day was associated with a lower risk of death and cardiovascular event than either a higher or lower estimated level of sodium intake (O'Donnell et al., 2014), however, varied types of studies reported that both high and low sodium intakes were associated with increased morality (Graudal et al., 2014). To our knowledge, the issue of salt and blood pressure still remains controversial, the association may vary depends on different population and environmental settings.

GWAS studies have identified $ALDH_2$rs671 (Kato et al., 2011) and MTHFRrs1801133 (Newton-Cheh et al., 2009) that are associated with blood pressure. However, recent replication studies have shown inconsistent results (Wang et al., 2013; Xi et al., 2013), among varied regions and populations, different diets and different sources of sodium, these different results are influenced by multiple environmental and genetic factors.

We investigated these questions in a population from an isolated Zhangzi Island located in the south of Changshan Archipelago, 56 nautical mile away from Dalian (1 nautical equals 1.8 kilometers), China. Our aims were, to investigate the association between 24 h urine sodium and potassium excretion with blood pressure in residents with high salt intake who lived in isolated island). Second, explore the distribution of (Single Nucleotide Polymorphisms (SNPs)) ($ALDH_2$rs671, MTHFRrs1801133) in isolated populations and test their associations with blood pressure.

MATERIALS AND METHODS

A total of 180 Zhangzi islanders were examined from the study, they were randomly recruited for routine health checkup in local community hospital. From these individuals, 9 islanders were excluded from the analysis because of their ages less than 18 years old, the one was excluded for lack of urine specimen. 168 islanders were used in subsequent analysis after removing 2 outliers (the extreme values of estimated 24 h urinary sodium) (A total of 180 subjects in Zhangzi Island were enrolled in our study. Nine subjects were excluded because their ages were under 18 years old; the two were excluded for lack of urine and blood specimens for sodium, TG, TC, H-DLC, LDL-C, FBG; the one subject had estimated 24 h urinary sodium and potassium well over physiological range and was removed from study population as a outlier). The survey was conducted with the adjusted WHO-Monica investigation questionnaire. We obtained the demographic information including sex, age, height, weight, alcohol history by investigation questionnaire. We collected data that related with metabolic traits which including TG, TC, HDL-C, LDL-C, FBG, fasting morning urine (FMU). The blood pressure was measured according to the guidelines for the management of hypertension (Mancia et al., 2013). Written informed consent was obtained from every participant before data collection, and the study was approved by ethics committees of the Affiliated Zhongshan Hospital of Dalian University.

DNA extraction and Genotyping

GWASs have identified a large numbers of SNPs associated with blood pressure (Kato et al., 2011; Newton-Cheh et al., 2009), we selected two SNPs (rs671 in $ALDH_2$, rs1801133 in MTHFR) based on their relevance with dietary habit. Genomic DNA was extracted from whole blood. DNA concentration was measured by using NanoDrop 2000 (Thermo Fisher Scientific Inc.Waltham, MA, USA). All DNA samples were diluted to the concentration of 30 ng/uL before genotyping. The SNPs ($ALDH_2$rs671, MTHFRrs1801133) were genotyped by the TaqMan real-time polymerase chain reaction assay with the ABI PRISM7900HT Sequence Detection System (Applied Biosystems Inc., Foster City, CA,USA).

Table 1. Baseline characteristics of participants in the Zhangzi Island population

	Mean±Std. Deviation
n=168	
Age (years)	52.4±14.3
BMI (kg/㎡)*	25.0±3.8
SBP (mmHg)	126.2±19.8
DBP (mmHg)	82.5±10.8
Fasting Morning Urinary Excretion (mmol/L)	
Urinary Sodium (mmol/L)	100.4±46.5
Urinary Potassium (mmol/L)	31.6±13.6
Urinary Creatinine (mmol/L)	10195.3±4297.8
Estimated Urinary Excretion (g/day)‡	
24h Urinary Sodium (g/day)‡	4.0±1.1
24h Urinary Potassium (g/day)‡	1.7±0.3
Ratio of Sodium to Potassium‡	2.4±0.7
FBG (mmol/L)	6.2±1.7
TG (mmol/L)	1.9±1.0
TC (mmol/L)	4.9±0.9
HDL-C (mmol/L)	1.3±0.3
LDL-C (mmol/L)	2.2±0.6
Sex (female)	118(70.2%)
Alcohol (yes)	19(11.3%)

Abbreviations: BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose. Age, BMI, DBP, SBP, TG, TC, HDL-C, LDL-C values are presented as Mean± Standard Deviation. Gender variables with female and alcohol history with yes are displayed as total numbers and percentages. *The BMI is the weight in kilograms divided by the square of the height in meters.‡ We utilized the Kawasaki formula to estimate 24 h urinary sodium and potassium, from a morning fasting sample (Kawasaki et al., 1993).

Statistical analysis

Quantitative values are presented as Mean and Standard Deviation. Categorical values are expressed as percentiles and were tested by the χ^2 test. Hardy Weinberg Equilibrium (HWE) was assessed by the χ^2 test. We utilized linear regression and logistic regression after adjustment for age, sex, BMI to investigate the association of blood pressure with and urinary sodium, potassium, other metabolic traits. Analysis of covariance was used to calculate mean differences in blood pressure, urinary sodium, potassium, other metabolic traits according to genotypes with age, sex and BMI adjustment. Version 18.0 SPSS (Statistical Product and Service Solutions) IBM (International Business Machines Corporation, Armonk, NY, USA) was used for data analysis. P<0.05 was used to indicate statistical significance.

Methods

We utilized the Kawasaki formula to estimate 24 h urine electrolyte excretion, from a morning fasting sample (Kawasaki et al., 1993), and these estimates as surrogates for sodium and potassium intake. Previous studies have validated Kawasaki formula is the most valid and least biased method of estimating 24h sodium excretion from FMU and is suitable for population studies (Mente et al., 2014).

After removed the extreme values of estimated 24 h urinary sodium and potassium, total 168 Zhangzi islanders with excessive salt intake were assessed the association between blood pressure and estimated urinary sodium, potassium excretion and other metabolic traits through linear regression. The analysis was adjusted by sex, age, BMI, alcohol history.

RESULTS

Association of Systolic Blood Pressure, Diastolic Blood Pressure with Estimated 24 h Urinary Sodium, Potassium, the Ratio of Estimated Sodium to Potassium and SNPs

After removed the outliers of the estimated 24 h urinary sodium and potassium, we found a positive association between estimated 24h urinary sodium with SBP, DBP (SBP: β=0.157, P<0.05; DBP: β=0.203, P<0.05) by linear regression analysis, after adjustment for sex, age, BMI, alcohol history (Table 3). We also found $ALDH_2$rs671 is positively associated with SBP (P<0.05) after adjustment for sex, age, BMI, alcohol history as well as 24h urinary sodium (Table 4) No association were found between BP

Table 2. Distribution of genotypes of $ALDH_2$rs671, MTHFRrs1801133

	$ALDH_2$rs671						**MTHFRrs1801133**					
	Genotype			**HWE**		**MAF**	**Genotype**			**HWE**		**MAF**
	AA	AG	GG	χ^2	p		AA	AG	GG	χ^2	p	
Number of Subjects	1	43	126				41	97	32			
Frequency (%)	0.6	25.3	74.1	1.745	0.186	0.132	24.1	57.1	18.8	3.544	0.06	0.474

Abbreviations: HWE: Hardy–Weinberg equilibrium; MAF: Minor Allele Frequency

Table 3. Association between blood pressure and metabolic traits

	SBP			**DBP**		
	Beta	**T**	**p†**	**Beta**	**t**	**p†**
Fasting Morning Urinary Excretion (mmol/L)						
Urinary Sodium (mmol/L)	0.105	1.504	0.134	0.127	1.739	0.084
Urinary Potassium (mmol/L)	-0.039	-0.537	0.592	-0.056	-0.741	0.459
Urinary Creatinine (mmol/L)	-0.029	-0.382	0.703	-0.122	-1.548	0.124
Estimated Urinary Excretion (g/day)‡						
24h Urinary Sodium (g/day)‡	0.157	2.217	0.028	0.203	2.740	0.007
24h Urinary Potassium (g/day)‡	0.031	0.441	0.660	0.094	1.260	0.210
Ratio of Sodium to Potassium‡	0.111	1.539	0.126	0.117	1.546	0.124
FBG (mmol/L)	0.052	0.712	0.478	0.004	0.046	0.963
TG (mmol/L)	-0.030	-0.393	0.695	0.002	0.019	0.985
TC (mmol/L)	-0.070	-0.928	0.355	-0.119	-1.505	0.134
HDL-C (mmol/L)	-0.029	-0.401	0.689	-0.056	-0.744	0.458
LDL-C (mmol/L)	-0.036	-0.490	0.625	-0.067	-0.869	0.386

Abbreviations: DBP: diastolic blood pressure; SBP: systolic blood pressure; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose. †The P-value was assessed by linear and logistic regression adjusted for sex, age, BMI and alcohol history.‡ We utilized the Kawasaki formula to estimate 24 h urinary sodium and potassium from a morning fasting sample (Kawasaki et al., 1993).

Table 4. Association between blood pressure and SNPs

	SBP				**DBP**			
	Beta	**t**	**p†**	**p‡**	**Beta**	**t**	**p†**	**p‡**
$ALDH_2$rs671#	0.142	2.035	0.043	0.032	0.090	1.219	0.224	0.174
MTHFRrs1801133	-0.003	-0.041	0.968	0.786	0.051	0.683	0.496	0.276

Abbreviations: DBP: diastolic blood pressure; SBP: systolic blood pressure.
†The P-value was assessed by linear and logistic regression after we adjusted for sex, age, BMI and alcohol history.‡ The P-value was assessed by linear and logistic regression after we adjusted for sex, age, BMI, alcohol history and estimated 24 h urinary sodium.# Participant of AA is 1.

and the urinary sodium, potassium, or estimated 24 h urinary potassium, sodium to potassium ratio and other metabolic traits like BMI, lipids in Table 3. There was no association detected for rs1801133 in MTHFR with blood pressure and any metabolic traits.

The Distribution of Genotypes of $ALDH_2$rs671, MTHFRrs1801133, and association with blood pressure

The baseline characteristics of participants in Zhangzi Island are shown in Tables 1. We genotyped $ALDH_2$rs671 and MTHFRrs1801133 in Zhangzi Island population. The SNPs were tested to be in HWE in Table 2. The minor allele frequencies (MAF) of $ALDH_2$rs671 and MTHFRrs1801133 were 0.132 and 0.474 respectively.

We also analyzed the association of $ALDH_2$rs671 and MTHFRrs1801133 different genotypes with blood pressure and metabolic traits including fasting morning urinary excretion (urinary sodium, potassium, fasting morning urinary creatinine), estimated urinary excretion (24h urinary sodium, 24h urinary potassium, ratio of sodium to potassium), TG, TC, HDL-C, DL-C, FBG in Table 5. Our results showed that rs671 in $ALDH_2$ genotypes was significantly different in TC, LDL-C ($P<0.05$), but no statistical significance has been revealed in MTHFRrs1801133 genotypes in blood pressure or other metabolic traits in

Table 5. Association between blood pressure, metabolic traits and SNPs with blood pressure

Gene	$ALDH_2$rs671			MTHFR rs1801133			
Genotype	**AA+AG#**	**GG**	**p**	**AA**	**AG**	**GG**	**p**
Number of Subjects	44	124		40	97	31	
Sex (female)	26(59.1%)	92(74.2%)	0.060	27(67.5%)	67(69.1%)	24(77.4%)	0.620
Age (years)	53.0±12.9	52.2±14.7	0.750	53.2±14.2	52.4±14.4	51.2±14.3	0.846
BMI (kg/㎡)*	25.6±3.4	24.8±3.9	0.196	25.1±3.4	25.3±3.8	23.9±4.2	0.191
Alcohol History (yes)	6(13.6%)	13(10.5%)	0.573	3(7.5%)	11(11.3%)	5(16.1%)	0.528
SBP (mmHg)	122.8±17.0	127.4±20.6	0.184	126.7±21.8	126.4±20.3	124.9±15.8	0.919
DBP (mmHg)	81.5±10.4	83.0±10.9	0.444	82.2±10.7	82.4±10.7	83.3±11.3	0.997
Fasting Morning Urinary Excretion (mmol/L)							
Urinary Sodium (mmol/L)	100.6±50.6	100.4±45.2	0.976	105.7±53.4	101.1±46.7	91.5±35.1	0.436
Urinary Potassium (mmol/L)	29.9±14.1	32.1±13.5	0.363	31.4±14.7	31.4±14.6	31.1±13.3	0.974
Urinary Creatinine (mmol/L)	10008.4±4205.6	10261.6±4345.0	0.738	9925.5±4072.4	10072.2±4229.7	10928.6±4828.4	0.568
Estimated Urinary Excretion (g/day)‡							
24h Urinary Sodium (g/day)‡	4.1±1.2	3.9±1.0	0.307	4.1±1.1	4.0±1.1	3.6±0.9	0.180
24h Urinary Potassium (g/day)‡	1.7±0.3	1.6±0.3	0.642	1.7±0.3	1.7±0.3	1.6±0.3	0.425
Ratio of Sodium to Potassium‡	2.5±0.7	2.4±0.6	0.455	2.5±0.6	2.4±0.7	2.4±0.8	0.455
FBG (mmol/L)	6.3±2.0	6.1±1.6	0.504	6.4±1.7	6.2±1.9	5.8±0.8	0.301
TG (mmol/L)	1.9±1.0	1.9±1.0	0.652	2.1±1.2	1.8±0.9	1.8±0.9	0.255
TC (mmol/L)	5.2±0.8	4.8±0.9	0.023	5.0±0.9	4.9±0.9	4.9±1.0	0.858
HDL-C (mmol/L)	1.3±0.3	1.3±0.3	0.509	13±0.3	1.3±0.3	1.2±0.3	0.407
LDL-C (mmol/L)	2.4±0.5	2.2±0.6	0.010	2.2±0.5	2.2±0.6	2.3±0.6	0.854

Abbreviations: DBP: diastolic blood pressure; SBP: systolic blood pressure; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose. ‡We utilized the Kawasaki formula to estimate 24 h urinary sodium and potassium from a morning fasting sample (Kawasaki et al, 1993).# Participant of AA is 1.

these high salt intake islanders.

DISCUSSION

Previous studies have reported that urinary sodium and potassium (habitual sodium and potassium) associated with blood pressure (Dahl, 1972; Stamler et al, 1991; Denton et al., 1995; Elliott et al., 1996; Mente et al., 2014; Kawasaki et al., 1993; Mente et al., 2014). The randomized trials found blood pressure falls of 3.6 mmHg systolic and 2.0 mmHg diastolic for sodium reduction in primary hypertension (Grobbee et al., 1986). For potassium supplementation, systolic blood pressure reduction of 5.9 mmHg, diastolic blood pressure reduction of 3.4 mmHg (Cappuccio et al., 1991). In present study, we also found association between estimated 24 h urinary sodium and blood pressure in isolated population. Salt intake is best monitored by collecting 24 h urine, 24 h urinary analysis has become the gold standard method in measuring sodium intake in population surveys (World Health Organization, 2014). Yet, in Zhangzi Island, it is impractical to collect 24 h urine, because of their living and working pattern. Our study demonstrated that simple fasting morning urine can be used to access individual's salt intake, and Kawasaki formula can be used in remote area where collecting 24 h urine become obstacle. Our study also demonstrated that Kawasaki formula to estimate 24 h urine sodium and potassium excretion from a fasting morning sample for evaluating salt intake not only can be used in hypertension group, but can be used in general population, or isolated population, the method of estimating 24 h sodium excretion from FMU that we used has been shown the most valid and least biased approach for large epidemiological studies (Mente et al., 2014).

The INTERSALT study, there was a higher median

24h urinary sodium, potassium and the ratio of sodium to potassium in north China than in other geographic regions studied, the median 24h urinary sodium from city of Tianjin was higher than Beijing and Nanning(242.1, 196.4, 158.1 mmol /24h respectively) (Elliott et al., 1996). PURE included 6% population from China older than 59 years old, where the average estimated sodium excretion was higher than in other countries (5.59 grams per day and 4.45 grams per day respectively) (Mente et al., 2014), data from Zhangzi Island showed that the median estimated 24 urinary sodium was 3.9 grams per day (9.6 grams of salt), Dalian and Tianjin are both costal cities in China. Zhangzi islanders would have more salt intake per day, but most participants in our study were female, the islanders eating a variety of fish as their daily food, the total protein they consume were mostly from fish, they used a considerable amount of homemade salty tinned corned fish and pickled fish, high poly unsaturated fatty acids derived from marine fishes, the average level of islanders salt intake, sources of salt in the diet, salt levels of foods in Zhangzi Island could help to explain the salt intake was not very high in Zhangzi Island population. However, most of the salt they consume were hidden in processed foods, most Pacific islanders are likely eating more than the recommender 5 grams of salt per day, so that the salt is the leading risk factor for hypertension, a leading cause of death and disability in Pacific Island countries (World Health Organization, 2014).

Our results are in agreement with the INTERSALT, PURE study, our investigation showed negative trend but no significantly difference between fasting morning urinary potassium excretion and blood pressure (SBP and DBP, P=0.592, β= -0.0 39 vs P=0.459, β= -0.056) (Table 3), these different findings might stem from a smaller sample size in our study, or alternatively, it can be explained through the Dahl's hypothesis that individual variations in susceptibility to blood pressure (DAHL, 1961). Previous population epidemiological studies also revealed an association with blood pressure and salt intake in diverse populations. One study of sodium intake and blood pressure in the populations of the Polynesian Islands Rarotonga and Pukapuka demonstrated that the sodium intake was difference in the similar ethnic (the one was the entire adult population of the isolated coral atoll of Pukapuka in the northern Cook Island; another was the residents in Avarua on Rarotonga in the southern Cook Island for at least 10 years), but no within-population correlation between blood pressure and 24-hour urinary sodium output is demonstrable (Prior et al., 1968). The inconsistency may be explained by the fact that the impact of race, temperature, humidity and habitual dietary sodium and pattern. However, these finding were compatible with Dahl's hypothesis that salt intake affected blood pressure (DAHL, 1961). Our subjects were the residents with high-salt intake who lived in isolated island, if they were on the proportion of subjects susceptible to the influence of salt or sodium excretion, we would find the salt sensitive population responsive to alterations in sodium intake or excretion (Franco et al., 2006). Epidemiological studies with greater sample size, genetic factors, race, diet and lifestyle are needed to confirm the association.

GWAS studies have demonstrated that $ALDH_2$rs671 (Kato et al., 2011) and MTHFRrs1801133 (Newton-Cheh et al., 2009) were associated with blood pressure, our results showed that rs671 in $ALDH_2$ was significantly associated with SBP after adjusted for sex, age, BMI, alcohol history. This association becomes more evident after adjusting estimated 24h urinary sodium, indicating the association of $ALDH_2$rs671 with SBP is independent of 24 h urinary sodium. rs671 in $ALDH_2$ genotypes was significantly different in TC, LDL-C, but no statistical significance has been detected in rs1801133 in MTHFR with blood pressure or MTHFRrs1801133 genotypes in these metabolic traits. Most participants in our study were without hypertension or antihypertensive treatment, although a number of studies on blood pressure and correlated SNPs have been proposed, we detected these associations through our small population size and low migration in this relatively isolated coast Island, our results demonstrated genetic susceptibility to increase blood pressure in this population. Furthermore, different allele frequencies between populations may play an important role in evaluating the association between blood pressure and correlated genes. Our data showed that the MAF of $ALDH_2$rs671 and MTHFRrs1801133 was 0.132 and 0.474, which is slightly lower than the Chinese Han population from HapMap database, indicating that the isolated islander has its own genetic characteristics that may differ from mainland population. In future study, we will extend our population size, provide more habitual dietary records and islanders' background as well as more genetic background of this particular population to gain better understand of blood pressure and sodium, potassium intake.

Conclusion

We found the association of blood pressure with estimated 24 h urinary sodium in the isolated Zhangzi Island, there was no significance association observed in blood pressure and 24 h urinary potassium in coastland populations. Our study also revealed $ALDH_2$rs671 associated with SBP after adjusted for sex, age, BMI, alcohol history and estimated 24 h urinary sodium excretion. There is no association detected of MTHFRrs1801133 with blood pressure, further analysis and greater sample size are needed.

Conflict of interest

No conflict of interest exits in the submission of this manuscript.

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