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Consumption of Coffee and Glucose Metabolism in Japanese Men, Cytochrome P450 1A2 Polymorphism

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Coffee consumption has been associated with decreased risk of sort two polygenic disease in several populations. it's conjointly been reportable that low consumption is giving protection related to impaired aldohexose tolerence, as measured by the quality Oral aldohexose Tolerance SSTest (OGTT). low contains a large style of bioactive compounds, as well as caffein, chlorogenic acid, atomic number 12 and trigonelline. Despite the consistent observation between low and kind two polygenic disease, it's unclear what ingredients in low infusion exert a protecting impact on aldohexose metabolism. Since java has conjointly been related to a decreased risk of sort two polygenic disease in many studies, it's instructed that non-caffeine low compounds could also be a lot of vital as protecting part. For a potent inhibitor property and a few helpful effects on aldohexose absorption and metabolism, phenoplast compounds like chlorogenic acid instead of caffein have drawn abundant attention. However, caffein intake itself was shown to be related to a decreased risk of sort two polygenic disease in giant prospective studies of men and girls. during this study, the inverse association with sort two polygenic disease risk was abundant weaker for {decaffeinated low|decaf|coffee|java} as compared with caffeinated coffee. caffein could be a animal starch phosphorylase substance which will lower plasma aldohexose. Moreover, caffein has thermogenic, medication and lipolytic effects, which can be mechanistic explanations for a protecting association between low and kind two polygenic disease. additionally, caffein metabolites are shown to possess AN inhibitor property, suggesting a protecting role of caffein in aldohexose metabolism. caffein is metabolized primarily by hemoprotein P450 1A2 (CYP1A2) within the liver. Of variety of CYP1A2 Single ester Polymorphisms (SNPs), 2 practical SNPs are proverbial. One is CYP1A2 -3860G>A (CYP1A2*1C, rs2069514), that is a lot of common in Asians than in Caucasians. The GG genotype of the CYP1A2*1C is related to exaggerated accelerator activity in smokers. Another practical SNP is CYP1A2 -163C>A (CYP1A2*1F, rs762551), that is common in numerous populations. Smokers with the AA genotype of the CYP1A2*1F polymorphism have higher activity of the accelerator than those with the CA or CC genotype. we tend to theorise that CYP1A2 genotype could modify the association between low consumption and aldohexose tolerance standing if caffein contains a primary impact on aldohexose metabolism. this study aims to research the association of CYP1A2*1C and CYP1A2*1F polymorphisms with aldohexose tolerance standing as determined by OGTT and also the impact modification of the

CYP1A2 polymorphisms on the association between low and impaired aldohexose metabolism in old Japanese men. what is more, as a result of the induction of CYP1A2 by smoking varies with the CYP1A2*1C and CYP1A2*1F polymorphisms, we tend to conjointly examined the impact modifications of those polymorphisms among smokers and nonsmokers severally.

The present study was a cross-sectional study of old Japanese men. Subjects were male officers within the self-defence Forces WHO underwent a pre-retirement health examination between January 1997 and March 2001 at the self-defence Forces urban center and Kumamoto Hospitals. All officers retiring from the self-defence Forces received a pre-retirement health examination as a part of a nationwide program that offered a comprehensive health check. Details of the health examination are delineate elsewhere. additionally to blood samples for routine use within the health examination, a sample of seven metric capacity unit fast blood was obtained for the aim of medical analysis. The study was approved by commission of the Kyushu University college of Medical Sciences. All study subjects gave written consent before their participation within the study. in an exceedingly consecutive series of 2459 men aged 46-59 years, 5 men refused to participate within the survey. We excluded 169 men for the subsequent reasons: past history of operation (n=38), chronic liver disease or liver liver disease (n=49), use of steroids (n=6), use of antidiabetic drug medication (n=43) and undetermined aldohexose tolerance standing (n=36). a number of these men had 2 or additional of the exclusion criteria. what is more, we tend to excluded twenty two men as a result of polymer samples weren't accessible, deed 2263 men within the gift study analysis.

Lifestyle factors as well as low consumption were determined by employing a self-administered form. the topics reported weekly frequency of low drinking, and people drinking low daily reported the quantity of cups consumed per day. styles of low and also the means of drinking low weren't specifically assessed. tea consumption was determined likewise. low and tea intakes calculable from the form were shown to be fairly valid; Spearman rank correlation coefficients for low and tea were zero.75 and 0.64, severally as compared with the 28-diet record [20]. low consumption was classified into null, weekly and daily consumption. tea consumption was classified into

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four teams (0, 1-2, 3-4 and ≥5 cups per day). Smoking habit was classified into womb-to-tomb nonsmoking, past smoking, current lightweight.

Statistical Analysis Odds quantitative relation (OR) and ninety fifth Confidence Interval (CI) were obtained by supplying regression analysis; ninety fifth CI was derived from the quality error for the supplying parametric statistic. applied mathematics adjustment was created for age (continuous variable), hospital, protection Forces rank (low, middle and high), smoke smoking, alcohol intake, tea intake, leisure-time physical activity and BMI. Trend of the association was evaluated with ordinal scores appointed to low classes. In evaluating the result modification of the CYP1A2 polymorphisms, homozygous and heterozygous genotypes of the minor factor were combined as a result of the minor-allele homozygotes were comparatively few. applied mathematics assessment of the interaction was supported the Wald datum for the merchandise term of associate ordinal variable for low consumption and a divided variable for the genotype. Two-sided P-values but zero.05 were thought to be statistically important. All computations in these analyses were meted out victimization Statistically Analysis System (SAS), (SAS Institute, Cary, NC, USA).

Results Characteristics of the study subjects ar summarized in. The mean age of the 2263 men was fifty two.4 years with a spread of four6 to fifty nine years. there have been 139 (6%) prevailing cases of IFG, 421 (19%) of IGT and a hundred and eighty (8%) of sort two polygenic disorder. The remaining 1523 men had traditional aldohexose tolerance. Those with traditional aldohexose tolerance were outlined as controls. As regards -3860G>A (CYP1A2*1C), the frequencies of the GG, GA and AA genotypes among controls were fifty seven, 37% and 6%, severally. The frequencies of the AA, CA and CC genotypes of -163C>A (CYP1A2*1F) among controls were forty third, four hundred and forty yards and thirteen, severally. Frequencies of the minor factor were zero.245 for CYP1A2*1C and zero.349 for CYP1A2*1F. Distribution of the genotypes in controls were compatible with the Hardy-Weinberg equilibrium for each CYP1A2*1C (P=0.83) and CYP1A2*1F (P=0.14). The genotype distribution among sort two polygenic disorder or IFG/IGT cases didn't take issue from that among those with traditional aldohexose tolerance in relevancy either CYP1A2*1C or CYPA2*1F polymorphism (Table 2). Neither of the CYP1A2 polymorphisms showed a measurable association with IFG/IGT or sort two polygenic disorder. low consumption was powerfully reciprocally related to IFG/ IGT and sort two polygenic disorder. The adjusted OR of IFG/IGT for null, weekly and daily consumption of low were one.00 (referent), 0.75 (95% CI zero.54- 1.04) and 0.60 (95% CI zero.45-0.79), severally (trend P=0.0003), and also the corresponding values of sort two polygenic disorder were one.00 (referent), 0.69 (95% CI zero.42-1.13) and 0.44 (0.29-0.68), severally (trend P=0.0001). There was a suggestive effect modification of CYP1A2*1C polymorphism on the association between coffee consumption and type 2 diabetes (interaction P=0.07). The inverse association was highly significant in the GG genotype of CYP1A2*1C, but coffee use was almost unrelated to type 2 diabetes in the GA and AA genotypes combined. The inverse association between coffee consumption and type 2 diabetes did not differ by CYP1A2*1F polymorphism. The prevalence odds of IFG/IGT decreased with increasing consumption of coffee regardless of CYP1A2*1C or CYP1A2*1F genotypes (Supplementary Table 1). The effect modifications of CYP1A2*1C genotype on the association between coffee and type 2 diabetes was statistically significant among current smokers (Table 4). Among nonsmokers, the inverse association between coffee and type 2 diabetes seemed to be more pronounced in the GG genotype of CYP1A2*1C than in the GA and AA genotypes, but the interaction was far from statistical significance. Neither CYP1A2*1C nor CYP1A2*1F polymorphism modified the association between coffee and IFG/IGT among current smokers and nonsmokers each.

The present study first investigated the associations between functional CYP1A2 polymorphisms and impaired glucose metabolism and the effect modification of the CYP1A2 polymorphisms on the association between coffee and impaired glucose metabolism. Overall, neither CYP1A2*1C nor CYP1A2*1F polymorphism was associated with impaired glucose metabolism. While decreased prevalence odds of IFG/IGT associated with coffee consumption did not modified by either of the two polymorphisms, the inverse association between coffee and type 2 diabetes differed by CYP1A2*1C genotype. This effect modification was more evident in current smokers. It is documented that cigarette smoking induces CYP1A2 activity in humans, and both CYP1A2*1C and CYP1A2*1F affect the inducibility of the enzyme. Thus it is of interest whether the interactions between these polymorphisms and coffee on impaired glucose metabolism may differ by smoking status. The present findings on CYP1A2*1C and coffee suggest that caffeine may play a potential role in the coffee-diabetes association. Caffeine metabolites were shown to have an antioxidant potential . Although an in vitro antioxidant effect of caffeine metabolites was lower than that of phenolic compounds of coffee, the antioxidant effect of caffeine metabolites may not be neglected when physiological concentrations of caffeine metabolites are taken into consideration. The GG genotype of the CYP1A2*1C polymorphism is associated with increased enzyme activity among smokers. Thus the stronger inverse association between coffee and type 2 diabetes among current smokers with higher enzyme activities (GG genotype) is compatible with the protective effect of caffeine metabolites. On the other hand, substantial evidence from human studies indicates that caffeine ingestion deteriorates insulin sensitivity acutely. Faster metabolism of caffeine may attenuate the adverse effects of caffeine, and the potential protective effect of coffee

compounds other than caffeine may be more discernible among smokers with CYP1A2*1C GG genotype. It should be noted that CYP1A2*1C polymorphism did not affect the inverse association between coffee and IFG/IGT. A possible protective effect of caffeine metabolites may be more relevant to the progression of impaired glucose metabolism.

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