



Different traditional Chinese medicine body constitution in non-Hispanic White and Chinese patients with colorectal polyp

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Worldwide, colorectal cancer remains the third most common cancer in men and the second in women, with 1.8 million new cases diagnosed annually (1). Most colorectal cancer originates from a colorectal polyp. Polyps are common, and most are noncancerous; those, adenomatous polyps, do progress grow and are known precursors of colorectal cancer (1). Identification and removal polyps during cancer screening is the most important colorectal cancer prevention strategy. Meanwhile, interests in applying alternative medicine, such as the traditional Chinese medicine (TCM), in colorectal cancer prevention have been increasing in recent years.

In the TCM constitutions, innate and acquired body characteristics are described from four pairs of dualities including Yin-Yang, exterior-interior, cold-heat, and deficiency-excess, along with Qi, blood, body fluids, and internal organs, which can describe the characteristics of the whole body and different imbalanced states (2). Based on the TCM constitution concept, individuals can be categorized into nine types of body constitutions (BC), which includes Gentleness type, Qi-deficiency type, Yang-deficiency type, Yin-deficiency type, Phlegm-Dampness type, Dampness-Heat type, Blood-Stasis type, Qi-depression type, and Special Diathesis type (3). BC has been clinically used to examine the health status in TCM (3). BC types have been associated with a number of chronic conditions, including obesity, type 2 diabetes and cardiovascular disease (4). However, beside a study including non-Hispanic White

college students who attended universities in Beijing, China, virtually most of existing research on TCM BC types have been conducted within Chinese populations (5).

Recently, one study conducted in the United States (U.S.) firstly showed that the common types of TCM BC in non-Hispanic White participants were different from those among Chinese in China (4). Specifically, the study found that 17.3% and 10.5% US non-Hispanic Whites were Blood-Stasis and Special Diathesis types, respectively; whereas a study conducted in China has reported that Qi-deficient, Dampness-Heat, and Yang-deficient were the top three pathologic BC types among 8,448 Chinese participants (6).

Zhu *et al.* reported in this issue that these differences cannot be fully explained by the different prevalence rates of obesity in the two populations. The study conducted in the American population included participants once diagnosed with colorectal polyp or at high risk of colorectal cancer (4). It is possible that the differences in the distribution of major types of TCM BC may be attributable to the unique BC types specific to colorectal polyp or cancer. In this study, we compared the major types of TCM BC in non-Hispanic White patients with colorectal polyp or at high risk of colorectal cancer and those in Chinese populations with colorectal polyp.

In the current study, we used the TCM BC types reported in a recent paper based on the Personalized Prevention of Colorectal Cancer Trial (PPCCT, NCT01105169 at

ClinicalTrials.gov) conducted in Vanderbilt University Medical Center (TN, USA) between March 2011 and January 2016 (4). Detailed inclusion and exclusion criteria have been reported (4). In brief, 191 non-Hispanic White individuals aged between 40 and 85 years, having a history of colorectal polyp, or at high risk of colorectal cancer were included in the study. The Constitution in Chinese Medicine Questionnaire (CCMQ) was translated to English version (Traditional Chinese Medicine Questionnaire, TCMQ) (3,7), consisting of 60 questions which fall into nine subscales that correspond to one of nine TCM BC types: Gentleness or balanced constitution, Qi-deficiency, Yang-deficiency, Yin-deficiency, Phlegm-wetness or Phlegm-Dampness, Wetness-heat or Damp-heat, Blood-Stasis, Qi-depression or Qi-stagnation, and Special Diathesis or Inherited-special. The detailed methods of generating subscale score and a total transform score have been described (4). According to the diagnosis criteria, a higher score in a specific CCMQ or TCMQ BC subscale indicates a higher likelihood of the corresponding BC type, with a score of 30 as the “threshold” for case definition. To finally categorize an individual within a specific TCM BC type, the following algorithm was used: when (I) the score for the Gentleness subscale was ≥ 60 and other BC type scores were < 30 , the individual was diagnosed as “Gentleness” that was considered the neutral BC; when (II) the score for an imbalanced BC type (all other BCs) was ≥ 40 , then the individual was diagnosed as one or more of eight pathological BC types; when (III) a BC type score was between 30 to 40, then the individual was diagnosed by a well-trained Chinese Medicine Practitioner.

In addition, we searched reviews or original publications within the last 5 years on the distribution of TCM BC types in Chinese population as well as in colorectal polyp patients in China. The studies conducted in China used the original version of the standardized CCMQ (3). Finally, the distribution of TCM BC types in non-Hispanic White participants in the PPCCT was compared with (I) a large-scale study conducted in 108,015 Chinese participants (8); and (II) a meta-analysis of colorectal polyp patients conducted in China (9).

As shown in *Table 1*, patients in PPCCT study had high prevalence of Blood-Stasis (17.3%), and Special Diathesis types (10.5%); whereas in a recent large cross-sectional study with 108,015 participants conducted in China, the corresponding prevalence were 8.0% and 2.6%, respectively (8). In Chinese population, beside the neutral BC type, three most common pathological subtypes

were Yang-deficient (16.4%), Qi-deficiency (13.2%), and Dampness-Heat (10.2%). A proportion of 13.6% of non-Hispanic White participants in PPCCT study had Qi-deficiency subtype, which was similar with the percentage in general Chinese population (8). The study conducted in China included participants aged 15 years and older across the country (8), while participants of PPCCT were non-Hispanic White, aged 40 to 85 years with history of colorectal polyp or at high risk of colorectal cancer. The different characteristics of the study participants might lead to different distributions of BC types in the two populations.

To examine whether the differences in the distribution of BC types are due to the selection bias that the study conducted in the US included only patients with colorectal polyp or at high risk of colorectal cancer, we used a recent meta-analysis of colorectal adenoma patients conducted in China as the second comparison (9) (*Table 1*). The meta-analysis study showed that colorectal adenoma patients in China had large proportion of Dampness-Heat (21%) and Phlegm-Dampness (19%) subtypes, while only 3.1% and 8.4% of non-Hispanic White patients in the US had these two subtypes. Meanwhile, unlike American patients with colorectal polyp or at high risk of colorectal cancer who had high prevalence of Blood-Stasis (17.3%) and Special Diathesis (10.5%) subtypes, the corresponding proportions in Chinese patients with colorectal adenoma were 7% and 1%, respectively.

Table 2 showed the distribution of TCM BC types stratified by age group (< 65 and ≥ 65 years) and gender (male and female). We found that among participants aged < 65 years, 20.3% non-Hispanic White Americans were Blood-Stasis subtype, the corresponding proportion was 7.8% in Chinese. The proportions were 12.0% and 8.8% for Special Diathesis types in non-Hispanic White men and women, respectively. However, the proportions were 2.9% and 2.3% for Special Diathesis types in Chinese men and women, respectively.

In a recent report, Shu *et al.* (4) compared the distribution of BC subtypes in non-Hispanic Whites in the US with that among 8,448 Chinese from a previous study conducted in China (6), and found great variations in the distributions of BC types in the two populations. Consistently, we observed similar results by comparing to a recent study conducted in China with a larger number of participants (i.e., $n=108,015$) recruited all over the country (8). Furthermore, similar results were found through comparing with distributions from a meta-analysis of Chinese colorectal adenoma

Table 1 Comparative distribution of TCM body constitution types among PPCCT population and representative studies in Chinese populations

Characteristics	Non-Hispanic White Americans	Chinese (Bai <i>et al.</i> 2020) (8)								Meta-analysis in Chinese colorectal adenoma (Zhang <i>et al.</i> 2021) (9)
	Total	Total	North	East	Central	South	Southwest	Northwest	Northeast	Total
Sample size, n	191	108,015	4,309	9,497	4,157	2,726	9,800	10,683	1,008	2,981*
Age (years), mean ± SD or range	60.0±7.8					44.7±14.9				16–81
Gender, n (%)										
Female	91 (47.6)					63,957 (59.2)				990 (37.1)**
TCM, % [95% CI]										
Gentleness	29.8	29.0	27.8	28.6	26.5	26.3	27.3	26.6	36.6	9 [6, 12]
Qi-deficient	13.6	13.2	11.4	13.4	11.9	13.5	13.6	12.2	14.2	17 [13, 22]
Yang-deficient	4.7	16.4	22.5	18.0	18.2	17.3	14.8	15.8	11.9	16 [11, 21]
Yin-deficient	6.3	5.2	7.8	7.8	7.0	8.5	8.5	5.2	6.1	7 [5, 10]
Phlegm-Dampness	8.4	6.8	7.6	6.9	7.0	7.3	7.3	8.1	8.1	19 [15, 24]
Dampness-Heat	3.1	10.2	7.5	9.8	11.1	8.3	8.3	10.0	3.8	21 [16, 25]
Blood-Stasis	17.3	8.0	5.7	7.8	9.7	8.6	9.1	12.1	3.8	7 [5, 9]
Qi-depression	6.3	8.7	8.1	7.8	8.7	6.7	8.1	8.1	12.0	9 [7, 11]
Special Diathesis	10.5	2.6	1.8	2.8	8.7	3.4	8.1	2.1	12.0	1 [1, 2]

*, 2,981 participants from 18 cross-sectional studies; **, 2,671 participants from 16 cross-sectional studies with gender information. PPCCT, personalized prevention of colorectal cancer trial; CI, confidence interval; SD, standard deviation; TCM, traditional Chinese medicine.

Table 2 Distribution of TCM body constitution types, stratified by age and gender in different populations

Characteristics	Americans				Chinese (8)			
	<65 years	≥65 years	Male	Female	<65 years	≥65 years	Male	Female
Sample size, n	133	58	100	91	94,718	13,297	44,058	63,957
TCM, %								
Gentleness	27.1	36.2	42.0	16.5	28.8	30.2	34.7	25.1
Qi-deficient	11.3	19.0	16.0	11.0	13.6	10.4	13.1	13.2
Yang-deficient	6.8	0.0	1.0	8.8	16.8	14.0	11.2	20.0
Yin-deficient	7.5	3.4	2.0	11.0	3.9	14.0	4.4	5.7
Phlegm-Dampness	6.8	12.1	6.0	11.0	6.2	10.7	9.2	5.1
Dampness-Heat	3.0	3.4	5.0	1.1	11.3	2.6	14.8	7.1
Blood-Stasis	20.3	10.3	8.0	27.5	7.8	9.2	4.0	10.7
Qi-depression	7.5	3.4	8.0	4.4	9.0	6.8	5.7	10.8
Special Diathesis	9.8	12.1	12.0	8.8	2.6	2.1	2.9	2.3

TCM, traditional Chinese medicine.

patients (9). These findings indicated that the differences in distribution of BC subtypes including Blood-Stasis and Special Diathesis between non-Hispanic White Americans and Chinese are not solely due to the selection bias.

In addition, we found that the observed differences cannot be explained by the differences in the distributions of sex and age in studies conducted in the US and China. In this issue, Zhu *et al.* reported that the observed differences are not caused by the different prevalence rates of obesity. Thus, it is possible that the observed differences in the distribution of BC subtypes are due to the differences in genetic background and environmental factors, including different patterns of smoking, alcohol drinking, and diet between non-Hispanic White American and Chinese populations. The sample size of current study conducted in American patients with colorectal polyp or at high risk of colorectal cancer was small and all participants were non-Hispanic White. Future large-scale studies with diverse racial/ethnic groups conducted in the US are necessary to confirm the findings and understand the underlying mechanisms for the differences.

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Footnote

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aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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