Correlations Between Traditional Chinese Medicine Syndromes and Clinical Indexes in Health Check-Up Population

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Research

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Abstract

Background

Routine health check-up is associated with improved lifespan and reduced medical cost. Traditional Chinese medicine (TCM) serves as a cost-effective modality in healthcare system. We examined the correlations of TCM syndromes with modern medical indicators in health check-up population.

Methods

We studied 5231 subjects undergoing health check-up between January 1st 2008 and December 31, 2016. Physical indexes such as body weight and blood pressure and biomedical indicators like liver function and tumour markers were measured. All subjects underwent colonoscopy. All subjects were classified and differentiated into five different TCM syndromes. An artificial neural network (ANN) was employed to evaluate the predictive value of TCM syndrome differentiation.

Results

Of enrolled subjects, SADH accounted for 85.8% and IDSIBSB was found in 4576 subject (87.5%). YaDSK and YiDLK accounted for 99.5% (5207) and 80.9% (4232) respectively. We found that YiDLK is correlated with abnormality of liver function indexes. The results showed that SADH is correlated with level of cholesterol in health check-up population. The results showed that the predictive ANN model showed a good fitting with an accuracy of 100%.

Conclusion

The results demonstrated that TCM syndromes were closely correlated with clinical laboratory indexes regardless of health status. TCM syndrome differentiation is suggested to contribute to routine health examination as screening measure with its non-invasive nature.

Background

Health check-up on a regular basis is a preventive measure that provides information of health status and awareness of risk factors of diseases. Undergoing health check-ups has been associated with increases in survival or decreases in overall mortality. It is considered as a part of routine healthcare process, which commonly involves physical examination, laboratory testing and medical diagnosis. Modern health check-up requires access to sophisticated facilities and instrumentation and numbers of healthcare providers with skills and techniques to conduct examination. Furthermore, most of health examinations are invasive and uncomfortable leading to fear, anxiety and discomfort. It is of interest to have a medical measure as screening for routine health check-up which is cost effective and well-accepted.

Traditional Chinese medicine (TCM) is a holistic medical system practiced in many Asian countries. TCM has played an essential role in healthcare system as in preventing disease, and promoting quality of life.
TCM fundamentally includes herbal remedies, acupuncture and massages, which is prescribed based on its own diagnosis.

Diagnostic approaches employed in TCM are non-invasive including inspection, auscultation, inquiry and palpation. Through the TCM diagnoses, the conditions of individuals are categorized into different constitution types according to perceived features such as disharmony and functional disturbance. In TCM, syndromes are differentiated according to the eight principles that are yin, yang, exterior, interior, cold, heat, deficiency (xu) and excess (shi). Recent studies have shown that TCM syndrome differentiation is correlated with western medical laboratory indicators in several disorders.\textsuperscript{1-4} Taken well acceptance and feasibility of TCM in practice, TCM syndrome differentiation holds great promise when it is implemented to routine health examination at a screening phase.

In this study, we investigated the association of TCM syndrome differentiation with medical indicators in a health check-up setting. The TCM syndromes used in this study were identified with focus on lower gastrointestinal malignancies. We applied TCM syndrome differentiation to identify physiological indexes that act as predictors for colorectal cancer.

\textbf{Materials And Methods}

\textbf{Data source}

We analysed the data collected from individuals who received self-paid health examinations including undergone colonoscopy at Taiwan Adventist Hospital from January 1st 2008 to December 31, 2016. The study was reviewed and approved by Institutional review board of Taiwan Adventist Hospital. Informed written consent was waived due to a retrospective study design.

\textbf{Differentiation Of Tcm Syndrome}

TCM syndrome differentiations of all cases were performed by TCM doctors according to the Standard of TCM Diagnosis and Curative Effect of Disease-Syndrome. TCM syndromes were identified as follows: (1) syndrome of accumulated dampness-heat (SADH), (2) intermittent dysentery with syndrome of internal blockade of static blood (IDSIBSB), (3) yang deficiency of spleen and kidney (YaDSK), (4) yin deficiency of liver and kidney (YiDLK) and (5) deficiency of both QI and blood (DQB). TCM syndromes were confirmed for each subject in the condition of two main symptoms or one main symptom with two secondary symptoms. If two or more than two kinds of syndromes occur in one subject, the main syndromes were judged by subsequent discussion.

\textbf{Physiological And Biochemical Measurements}
Physiological indexes included (i) physical examination: height, weight, pulse, systolic pressure (SBP), diastolic pressure (DBP), Intraocular pressure (IOP), occult blood (OB), colonoscopy and Body Mass Index (BMI); (ii) biochemical tests: glutamic oxaloacetic transaminase (AST), glutamic-pyruvic transaminase (ALT), cholesterol (choles), triglycerides (TG), γ-glutamyltransferase (γ-GT), hepatitis B Surface Antibody (HBsAb), hepatitis B Surface Antigen (HBsAg) and hepatitis C antibody (iii) tumor markers: carcinoembryonic antigen (CEA), alpha fetoprotein (AFP) and CA-199. Physical symptoms were evaluated on a system basis in accordance with A Guide to Physical Examination and Assessment.

**Artificial Neural Networks Model**

Back-propagation neural (BPN) network used in this study was developed per previous study. The BPN had three layers of neurons, which were input, hidden and output layer. Hidden layer consisted of 10 neurons. The final network output layer consisted of only one neuron for each TCM syndrome. The learning rate was 0.2. The training termination condition was when the root mean square error (RMSE) was lower or equal to 0.0001 or at most 1000 times training repetitions.

**Statistical analysis**

All statistical analyses were performed using SPSS 17.0 software. The Pearson χ² test was used to determine the correlation between TCM syndromes and clinicopathologic indexes, and the data were presented as the frequency and percentage. p < 0.05 was considered statistical significant.

**Results**

A total of 5231 subjects undergoing health check-up were included and assessed in this study. 55.9% (2922) of enrolled subjects were male and the mean age was 47.9 ± 10.7 years. Of the enrolled subjects, 56.7% had BMI values classified as overweight or obesity and 3108 subjects (59.4%) were detected HBsAb positive. Among subjects undergoing colonoscopy examination, haemorrhoid was found in 3000 subjects (57.4%) and 29 subjects (0.6%) were found with cancers. Regarding TCM syndrome differentiation, subjects diagnosed with SADH, IDSIBSB, YaDSK and YiDLK were 4490 (85.8%), 4576 (87.5%), 5207 (99.5%) and 4232 (80.9%) respectively. There were only 30 (0.6%) diagnosed with DQB. The clinical characteristics of the enrolled subjects are summarized in Table 1.
Table 1
Demographic characteristics of participants

| Item          | M ± SD | n   | (%) | Item          | n   | (%) |
|---------------|--------|-----|-----|---------------|-----|-----|
| Sex           |        |     |     | Anti-HCV Ab   |     |     |
| Male          | 2922   | 55.9|     | Negative      | 5161| 98.7|
| Female        | 2309   | 44.1|     | Positive      | 70  | 1.3 |
| Age           | 47.9 ± 10.7 |     |     | OB            |     |     |
| BMI           |        |     |     | Negative      | 5177| 99.0|
| < 18          | 122    | 2.3 |     | Positive      | 54  | 1.0 |
| 18 ~ 24       | 2799   | 53.5|     | AFP           |     |     |
| > 24          | 2310   | 44.2|     | < 20 ng/ml    | 4847| 92.7|
| CA199         |        |     |     | > 21 ng/ml    | 384 | 7.3 |
| < 37 U/ml     | 5008   | 95.7|     | CEA           |     |     |
| > 38 U/ml     | 223    | 4.3 |     | < 5 ng/ml     | 4868| 93.1|
| TG            |        |     |     | > 6 ng/ml     | 363 | 6.9 |
| < 150 mg/dl   | 4000   | 76.5|     | HBsAg         |     |     |
| > 151 mg/dl   | 1231   | 23.5|     | Negative      | 2755| 52.7|
| choles        |        |     |     | Positive      | 2476| 47.3|
| < 200 mg/dl   | 2734   | 52.3|     | IOP           |     |     |
| > 201 mg/dl   | 2497   | 47.7|     | > 22 mmHg     | 441 | 8.4 |
| AST           |        |     |     |             |     |     |
| 8 ~ 31U/L     | 4880   | 93.3|     | Colonoscopy   |     |     |
| < 7, > 32U/L  | 351    | 6.7 |     | Negative      | 179 | 3.4 |
| ALT           |        |     |     | Hemorrhoid    | 3000| 57.4|
| 0 ~ 41U/L     | 4634   | 88.6|     | Polyp         | 308 | 5.9 |
| > 42U/L       | 597    | 11.4|     | Polyp&Hemorrhoid | 1367| 26.1|
| rGT           |        |     |     | Tumor&Ca      | 29  | 0.6 |
| < 60U/L       | 3683   | 70.4|     | colitis       | 95  | 1.8 |
| > 61U/L       | 1548   | 29.6|     | Diverticulosis| 253 | 4.8 |
| Item     | M ± SD | n   | (%) | Item     | n   | (%) |
|----------|--------|-----|-----|----------|-----|-----|
| HBsAb    |        |     |     |          |     |     |
| Negative |        | 2123| 40.6|          |     |     |
| Positive |        | 3108| 59.4|          |     |     |
| SADH     |        | 4490| 85.8|          |     |     |
| IDSIBSB  |        | 4576| 87.5|          |     |     |
| YaDSK    |        | 5207| 99.5|          |     |     |
| YiDLK    |        | 4232| 80.9|          |     |     |
| DQB      |        | 30  | 0.6 |          |     |     |

We next determined the correlation of 5 TCM syndromes with clinical indexes. The results showed that SADH had significant correlations with BMI, the symptoms in following systems including respiratory system, cardiovascular system, abdomen system, neurologic system, skeletomuscular system and colonoscopy (Table 2). We found that IDSIBSB was significantly correlated with tumour markers including CEA, CA199 and AFP. In addition, statistical correlations were found between IDSIBSB and symptoms in many systems (Table 3). YaDSK was found only to have significant correlations with colonoscopy and symptoms in cardiovascular system, abdomen system and skin (Table 4). YiDLK was correlated with the levels of diagnostic markers that were associated with liver including AST, ALT, rGT, AFP, HBsAb and HBsAg. It also had high correlations with the symptoms in following systems including head and neck/lymphatic, respiratory, cardiovascular, abdomen, neurologic, skin and skeletomuscular systems (Table 5). Statistical correlations of DQB with symptoms in several systems was observed, including head and neck/lymphatic, respiratory, cardiovascular, abdomen, neurologic, skin and skeletomuscular systems (Table 6).
Table 2
Correlation of various medical indicators to syndrome of accumulated dampness-heat (SADH) (Pearson Chi-Square Test)

| Variable                      | Pearson Chi-Squared Test | df | p    | Variable                      | Pearson Chi-Squared Test | df | p    |
|-------------------------------|--------------------------|----|------|-------------------------------|--------------------------|----|------|
|                               | Correlation Coefficient  |    |      |                               | Correlation Coefficient  |    |      |
| sex                           | 7.696                    | 1  | 0.006* | choles                        | 7.184                    | 1  | 0.007*|
|                               | 7.695                    | 1  | 0.006* |                               | 7.183                    | 1  | 0.007*|
| age                           | 8.546                    | 4  | 0.074 | AST                           | 0.954                    | 1  | 0.329 |
|                               | 3.233                    | 1  | 0.072 |                               | 0.954                    | 1  | 0.329 |
| BMI                           | 14.732                   | 2  | 0.001*| ALT                           | 0.127                    | 1  | 0.721 |
|                               | 10.539                   | 1  | 0.001*|                               | 0.127                    | 1  | 0.721 |
| Head and neck/Conjunctive/Lymphatic | 205.110                  | 1  | 0.000*| rGT                           | 4.628                    | 1  | 0.031 |
|                               | 205.071                  | 1  | 0.000*|                               | 4.627                    | 1  | 0.031 |
| Respiratory System            | 205.110                  | 1  | 0.000*| AFP                           | 2.931                    | 1  | 0.087 |
|                               | 205.071                  | 1  | 0.000*|                               | 2.931                    | 1  | 0.087 |
| Cardiovascular System         | 8.316                    | 1  | 0.004*| CEA                           | 0.014                    | 1  | 0.907 |
|                               | 8.314                    | 1  | 0.004*|                               | 0.014                    | 1  | 0.907 |
| Digestive System             | 8.316                    | 1  | 0.004*| HBsAb                         | 0.031                    | 1  | 0.861 |
|                               | 8.314                    | 1  | 0.004*|                               | 0.031                    | 1  | 0.861 |
| Neurologic System            | 50.304                   | 1  | 0.000*| hepatitis C antibody         | 1.769                    | 1  | 0.184 |
|                               | 50.294                   | 1  | 0.000*|                               | 1.769                    | 1  | 0.184 |
| Skin                          | 160.842                  | 1  | 0.000*| OB                            | 0.882                    | 1  | 0.348 |
|                               | 160.811                  | 1  | 0.000*|                               | 0.882                    | 1  | 0.348 |
| Skeletomuscular System        | 59.966                   | 1  | 0.000*| I.P                           | 0.307                    | 1  | 0.579 |
|                               | 59.955                   | 1  | 0.000*|                               | 0.307                    | 1  | 0.579 |
| CA199                         | 0.053                    | 1  | 0.818 | HBsAg                         | 0.985                    | 1  | 0.321 |
| Variable | Pearson Chi-Squared Test | df | p   | Variable          | Pearson Chi-Squared Test | df | p   |
|----------|--------------------------|----|-----|-------------------|--------------------------|----|-----|
|          | Correlation Coefficient  |    |     | Correlation Coefficient |                         |    |     |
|          | 0.053                    | 1  | 0.818 | 0.985             | 1  | 0.321 |
| TG       | 2.114                    | 1  | 0.146 | Colonoscopy       | 2081.810                  | 6  | 0.000* |
|          | 2.114                    | 1  | 0.146 |                 | 178.413                  | 1  | 0.000* |

*p < 0.05
| Variable                       | Pearson Chi-Squared Test | df | p    | Variable                         | Pearson Chi-Squared Test | df | p    |
|-------------------------------|--------------------------|----|------|----------------------------------|--------------------------|----|------|
|                               | Correlation Coefficient  |    |      | choles                           | Correlation Coefficient  |    |      |
| Sex                           | 5.090                    | 1  | 0.024*| 8.195                           | 1  | 0.004*|
|                               | 5.089                    | 1  | 0.024*| 8.194                           | 1  | 0.004*|
| age                           | 4.916                    | 4  | 0.296| AST                              | 0.225                    | 1  | 0.635|
|                               | 1.834                    | 1  | 0.176| 0.225                           | 1  | 0.636|
| BMI                           | 15.391                   | 2  | 0.000*| ALT                             | 0.073                    | 1  | 0.786|
|                               | 9.505                    | 1  | 0.002*| 0.073                           | 1  | 0.786|
| Head and neck/Conjunctive/    | 178.334                  | 1  | 0.000*| rGT                             | 2.555                    | 1  | 0.110|
| Lymphatic                     | 178.300                  | 1  | 0.000*| 2.554                           | 1  | 0.110|
| Respiratory System            | 178.334                  | 1  | 0.000*| AFP                             | 15.538                   | 1  | 0.000*|
|                               | 178.300                  | 1  | 0.000*| 15.535                          | 1  | 0.000*|
| Cardiovascular System         | 8.364                    | 1  | 0.004*| CEA                             | 22.393                   | 1  | 0.000*|
|                               | 8.363                    | 1  | 0.004*| 22.389                          | 1  | 0.000*|
| Digestive System              | 8.364                    | 1  | 0.004*| HBsAb                           | 0.079                    | 1  | 0.779|
|                               | 8.363                    | 1  | 0.004*| 0.079                           | 1  | 0.779|
| Neurologic System             | 43.737                   | 1  | 0.000*| hepatitis C antibody            | 0.181                    | 1  | 0.671|
|                               | 43.728                   | 1  | 0.000*| 0.181                           | 1  | 0.671|
| Skin                          | 139.845                  | 1  | 0.000*| OB                              | 3.132                    | 1  | 0.077|
|                               | 139.818                  | 1  | 0.000*| 3.132                           | 1  | 0.077|
| Skeletomuscular System        | 55.833                   | 1  | 0.000*| I.P                             | 0.000                    | 1  | 0.990|
|                               | 55.823                   | 1  | 0.000*| 0.000                           | 1  | 0.990|
| CA199                         | 13.372                   | 1  | 0.000*| HBsAg                           | 0.857                    | 1  | 0.355|
| TG   | 13.370 | 1  | 0.000* | 0.857 | 1  | 0.355 |
|------|--------|----|--------|-------|----|-------|
|      | 2.580  | 1  | 0.108  | Colonoscopy | 1812.090 | 6  | 0.000* |
|      | 2.580  | 1  | 0.108  |      | 151.779 | 1  | 0.000* |
Table 4
Correlation of various medical indicators to yang deficiency of spleen and kidney (YaDSK) (Pearson Chi-Squared Test)

| Variable                      | Pearson Chi-Squared Test | df | p   | Variable                      | Pearson Chi-Squared Test | df | p   |
|-------------------------------|--------------------------|----|-----|-------------------------------|--------------------------|----|-----|
|                               | Correlation Coefficient  |    |     |                               | Correlation Coefficient  |    |     |
| sex                           | 2.532                    | 1  | 0.112 | choles                       | 1.827                    | 1  | 0.176 |
|                               | 2.531                    | 1  | 0.112 |                              |                          |    |     |
| age                           | 2.544                    | 4  | 0.637 | AST                          | 0.144                    | 1  | 0.704 |
|                               | 1.981                    | 1  | 0.159 |                              |                          |    |     |
| BMI                           | 1.738                    | 2  | 0.419 | ALT                          | 0.258                    | 1  | 0.612 |
|                               | 1.207                    | 1  | 0.272 |                              |                          |    |     |
| Head and neck/Conjunctive/    | 1.188                    | 1  | 0.276 | rGT                          | 0.841                    | 1  | 0.359 |
| Lymphatic                     | 1.188                    | 1  | 0.276 |                              |                          |    |     |
| Respiratory System            | 1.188                    | 1  | 0.276 | AFP                          | 0.159                    | 1  | 0.691 |
|                               | 1.188                    | 1  | 0.276 |                              |                          |    |     |
| Cardiovascular System         | 9.577                    | 1  | 0.002*| CEA                          | 0.149                    | 1  | 0.699 |
|                               | 9.575                    | 1  | 0.002*|                              |                          |    |     |
| Digestive System              | 9.577                    | 1  | 0.002*| HBsAb                        | 1.367                    | 1  | 0.242 |
|                               | 9.575                    | 1  | 0.002*|                              |                          |    |     |
| Neurologic System             | 0.291                    | 1  | 0.589 | hepatitis C antibody         | 0.027                    | 1  | 0.869 |
|                               | 0.291                    | 1  | 0.589 |                              |                          |    |     |
| Skin                          | 4.296                    | 1  | 0.038*| OB                           | 0.021                    | 1  | 0.885 |
|                               | 4.296                    | 1  | 0.038*|                              |                          |    |     |
| Skeletomuscular System        | 0.233                    | 1  | 0.630 | I.P                          | 0.184                    | 1  | 0.668 |
|                               | 0.233                    | 1  | 0.630 |                              |                          |    |     |
| CA199                         | 0.089                    | 1  | 0.765 | HBsAg                        | 1.798                    | 1  | 0.180 |
|                               | 0.089                    | 1  | 0.765 |                              |                          |    |     |
| TG                            | 0.616                    | 1  | 0.433 | Colonoscopy                  | 56.469                   | 6  | 0.000*|
| Variable | Pearson Chi-Squared Test | df | p  | Variable | Pearson Chi-Squared Test | df | p  |
|----------|--------------------------|----|----|----------|--------------------------|----|----|
|          | Correlation Coefficient  |    |    |          | Correlation Coefficient  |    |    |
|          | 0.616                    | 1  | 0.433 |          | 3.683                    | 1  | 0.055* |

*p < 0.05
Table 5: Correlation of various medical indicators to yin deficiency of liver and kidney (YiDLK) (Pearson Chi-Squared Test)

| Variable                     | Pearson Chi-Squared Test | df | p     | Variable                     | Pearson Chi-Squared Test | df | p     |
|------------------------------|--------------------------|----|-------|------------------------------|--------------------------|----|-------|
|                              | Correlation Coefficient  |    |       |                              | Correlation Coefficient  |    |       |
| sex                          | 3.869                    | 1  | 0.049*| choles                       | 0.028                    | 1  | 0.867 |
|                              | 3.869                    | 1  | 0.049*|                              | 0.028                    | 1  | 0.867 |
| age                          | 5.005                    | 4  | 0.287 | AST                          | 5.547                    | 1  | 0.019*|
|                              | 0.149                    | 1  | 0.700 |                              | 5.546                    | 1  | 0.019*|
| BMI                          | 10.276                   | 2  | 0.006*| ALT                          | 9.935                    | 1  | 0.002*|
|                              | 10.069                   | 1  | 0.002*|                              | 9.934                    | 1  | 0.002*|
| Head and neck/Conjunctive/   | 45.798                   | 1  | 0.000*| rGT                          | 32.414                   | 1  | 0.000*|
| Lymphatic                    | 45.789                   | 1  | 0.000*|                              | 32.408                   | 1  | 0.000*|
| Respiratory System           | 45.798                   | 1  | 0.000*| AFP                          | 6.110                    | 1  | 0.013*|
|                              | 45.789                   | 1  | 0.000*|                              | 6.109                    | 1  | 0.013*|
| Cardiovascular System        | 369.137                  | 1  | 0.000*| CEA                          | 2.216                    | 1  | 0.137 |
|                              | 369.067                  | 1  | 0.000*|                              | 2.216                    | 1  | 0.137 |
| Digestive System             | 369.137                  | 1  | 0.000*| HBsAb                        | 52.679                   | 1  | 0.000*|
|                              | 369.067                  | 1  | 0.000*|                              | 52.669                   | 1  | 0.000*|
| Neurologic System            | 11.232                   | 1  | 0.001*| hepatitis C antibody         | 1.046                    | 1  | 0.306 |
|                              | 11.230                   | 1  | 0.001*|                              | 1.046                    | 1  | 0.306 |
| Skin                         | 165.609                  | 1  | 0.000*| OB                           | 0.804                    | 1  | 0.370 |
|                              | 165.578                  | 1  | 0.000*|                              | 0.804                    | 1  | 0.370 |
| Skeletomuscular System       | 8.969                    | 1  | 0.003*| I.P                          | 0.342                    | 1  | 0.558 |
|                              | 8.968                    | 1  | 0.003*|                              | 0.342                    | 1  | 0.558 |
| CA199                        | 0.189                    | 1  | 0.664 | HBsAg                        | 69.310                   | 1  | 0.000*|
| Variable      | Pearson Chi-Squared Test | df | p    | Variable      | Pearson Chi-Squared Test | df | p    |
|---------------|--------------------------|----|------|---------------|--------------------------|----|------|
|               | Correlation Coefficient  |    |      |               | Correlation Coefficient  |    |      |
|               | 0.189                    | 1  | 0.664| 69.297        | 1                        | 0.000* |
| TG            | 4.613                    | 1  | 0.032*| 8.434         | 6                        | 0.208 |
|               | 4.612                    | 1  | 0.032*| 4.270         | 1                        | 0.039* |

*p < 0.05
Table 6
Correlation of various medical indicators to deficiency of both Qi and blood (DQB) (Pearson Chi-Squared Test)

| Variable                                      | Pearson Chi-Squared Test | df | p    | Variable          | Pearson Chi-Squared Test | df | p    |
|-----------------------------------------------|--------------------------|----|------|-------------------|--------------------------|----|------|
|                                               | Correlation Coefficient  |    |      |                   | Correlation Coefficient  |    |      |
| sex                                           | 0.691                    | 1  | 0.406| choles            | 1.819                    | 1  | 0.177|
|                                               | 0.691                    | 1  | 0.406|                  | 1.818                    | 1  | 0.178|
| age                                           | 4.664                    | 4  | 0.324| AST               | 0.279                    | 1  | 0.597|
|                                               | 0.340                    | 1  | 0.560|                  | 0.279                    | 1  | 0.597|
| BMI                                           | 2.893                    | 2  | 0.235| ALT               | 4.937                    | 1  | 0.026*|
|                                               | 1.954                    | 1  | 0.162|                  | 4.936                    | 1  | 0.026*|
| Head and neck/Conjunctive/Lymphatic           | 645.524                  | 1  | 0.000*| rGT              | 0.072                    | 1  | 0.789|
| Respiratory System                            | 645.524                  | 1  | 0.000*| AFP               | 2.873                    | 1  | 0.090|
|                                               | 645.400                  | 1  | 0.000*|                  | 2.873                    | 1  | 0.090|
| Cardiovascular System                         | 5203.044                 | 1  | 0.000*| CEA               | 0.866                    | 1  | 0.352|
|                                               | 5202.049                 | 1  | 0.000*|                  | 0.866                    | 1  | 0.352|
| Digestive System                              | 5203.044                 | 1  | 0.000*| ANTISB            | 1.559                    | 1  | 0.212|
|                                               | 5202.049                 | 1  | 0.000*|                  | 1.558                    | 1  | 0.212|
| Neurologic System                             | 158.316                  | 1  | 0.000*| hepatitis C antibody | 0.111                    | 1  | 0.739|
|                                               | 158.286                  | 1  | 0.000*|                  | 0.111                    | 1  | 0.739|
| Skin                                          | 33.037                   | 1  | 0.000*| OB                | 1.422                    | 1  | 0.233|
|                                               | 33.030                   | 1  | 0.000*|                  | 1.422                    | 1  | 0.233|
| Skeletomuscular System                        | 2876.011                 | 1  | 0.000*| I.P               | 1.695                    | 1  | 0.193|
|                                               | 2875.461                 | 1  | 0.000*|                  | 1.695                    | 1  | 0.193|
| CA199                                         | 0.004                    | 1  | 0.947| HBsAg             | 0.000                    | 1  | 1.000|
|                                               | 0.004                    | 1  | 0.947|                  | 0.000                    | 1  | 1.000|
We also evaluated the predictive potential of clinical indexes for 5 TCM syndromes with focus on colorectal malignancies using artificial neural networks approach. The strength of correlation of syndrome and variables was shown as the width of lines. The results showed that the predictive ANN model showed a good fitting with an accuracy of 100%. The three most predictive factors for SADH were colonoscopy, skin and neural system with importance of 0.24, 0.09 and 0.08 respectively. The interrelationships between predictor factor (input layer), hidden factors (hidden layer), and SADH are shown in Fig. 1. For IDSIBSB, the predictive model exhibited an accuracy of 99.7% and the most predictive factors was colonoscopy with importance of 0.24 (Fig. 2). We found that the accuracy of predictive model for YaDSK was 100% and three factors with high importance were colonoscopy (0.24), digestive system (0.13) and CEA (0.05) (Fig. 3). For YiDLK, the prediction accuracy of ANN model was 100%. The factor with highest importance was cardiovascular system (0.16) followed by digestive system (0.08) and age (0.07) (Fig. 4). The data showed that 3 factors with highest importance in the ANN predictive model for DQB were cardiovascular system (0.26), digestive system (0.2) and skeletomuscular system (0.07).

**Discussions**

In the present study, we investigated the correlation of TCM syndrome differentiations with clinical indicators in a setting of health screening examination. The results indicated that 5 TCM syndromes had different degrees of correlations with certain clinical indexes and markers. We found that SADH, IDSIBSB, YaDSK and YiDLK had significant correlation with colonoscopy which is considered as gold standard for colorectal cancer screening.

TCM is practiced theoretically based on syndrome differentiation of which information is obtained through a series of diagnostic procedures. TCM has received tremendous attention as complementary approach in modern medicine practice. The integration of TCM syndrome differentiation and modern clinical diagnosis has been extensively studied. TCM syndromes have been translationally applied and verified in many diseases including irritable bowel syndrome\(^6\), coronary artery disease, hepatitis B cirrhosis\(^7\), purpura nephritis\(^8\), colorectal carcinoma\(^3\) and post-stroke depression\(^9\). Recently, correlations between TCM syndromes and disorders have been explored and validated. Chen et al reported the association of kidney-vacuity syndrome with osteoporosis in postmenopausal women.\(^{10}\) Qi deficiency
and blood stasis syndrome has been reported to have a correlation with the bleeding after receiving percutaneous coronary intervention.\textsuperscript{11} A study has shown that Qi-deficiency is associated with cancer related fatigue.\textsuperscript{12} In addition to the association with disorders, TCM syndrome differentiation has been demonstrated to correlate with many measurable clinical indexes in modern medicine in disease setting. A recent study has reported that the concentration of adiponectin was correlated with TCM deficiency factors in dyslipidaemia patients.\textsuperscript{13} The correlations of TCM syndrome pattern with clinical indexes including renal function, immunologic function, and blood coagulation in patients with Henoch-Schönlein purpura nephritis have been reported.\textsuperscript{8} Blood stasis syndrome has positive correlation with triglyceride and cholesterol in patients with primary glomerular disease.\textsuperscript{14} In our study, we found that syndrome of accumulated dampness-heat (SADH) is correlated with level of cholesterol in the subjects undergoing health check-up. The finding is consistent with the result of Chen's study showing accumulation of dampness in dyslipidaemia patients.\textsuperscript{13} Our data highlight that yin deficiency of liver and kidney (YiDLK) is associated with abnormality of liver function indexes. This is in agreement with recent study in which common TCM syndromes in primary liver cancer are dampness, blood-stasis, heat, Yang deficiency of spleen and kidney, and Yin deficiency of liver and kidney.\textsuperscript{15} Our findings suggest the usefulness of TCM syndrome differentiation for non-invasive screening at routine health examinations.

Colonoscopy is the gold standard of colorectal cancer screening, which allows physician to examine the anatomic structure of colon and rectum. This procedure is invasive and performed commonly in routine health check-up. We evaluated the correlation between TCM syndromes and colonoscopy findings. We found that 4 TCM syndrome had high correlation with colonoscopy in individual having health check-up, which were SADH, IDSIBSB, YaDSK and YiDLK. Our finding is similar to the results of Yang et al study showing that liver and kidney yin deficiency syndrome, spleen deficiency syndrome, spleen deficient qi stagnation syndrome, and damp heat syndrome were main syndromes in colorectal cancer patients.\textsuperscript{16} Li and his colleagues reported that the TCM patterns of patients with colorectal cancer were blood deficiency, Qi deficiency, and Yin deficiency.\textsuperscript{3} In our study, yang deficiency of spleen and kidney and yin deficiency of liver and kidney were correlated with colonoscopy, nevertheless, deficiency of both Qi and blood had no correlation with colonoscopy. A possible explanation for this different observation is the physical status of enrolled individuals in each study. Further studies are necessarily required to explore the TCM syndrome distribution in different health status and to justify the difference among studies.

Conclusions

In conclusion, the results demonstrated that TCM syndromes were closely correlated with clinical laboratory indexes regardless of health status. TCM syndrome differentiation is suggested to contribute to routine health examination as screening measure with its non-invasive nature. TCM syndrome represents a promising diagnostic means for screening in routine health examination process.

Abbreviations
TCM: Traditional Chinese medicine; ANN: artificial neural network; SADH: syndrome of accumulated dampness-heat; IDSIBSB: intermittent dysentery with syndrome of internal blockade of static blood; YaDSK: yang deficiency of spleen and kidney; YiDLK: yin deficiency of liver and kidney; DQB: deficiency of both Qi and blood; BPN: Back-propagation neural; RMSE: root mean square error; SBP: systolic pressure; DBP: diastolic pressure; IOP: Intraocular pressure; OB: occult blood; BMI: Body Mass Index; AST: glutamic oxaloacetic transaminase; ALT: glutamic-pyruvic transaminase; choles: cholesterol; TG: triglycerides; γ-GT: γ-glutamyltransferase; HBsAb: hepatitis B surface antibody; HBsAg: hepatitis B surface antigen; CEA: carcinoembryonic antigen; AFP: alpha fetoprotein

Declarations

- Ethics approval and consent to participate

The study was reviewed and approved by Institutional review board of Taiwan Adventist Hospital. Informed written consent was waived due to a retrospective study design.

- Consent to publish

Not applicable

- Availability of data and materials

Please contact corresponding authors for data requests

- Competing interests

All authors declare no conflict of interest.

- Funding

Not applicable.

- Authors' Contributions

Conception and design: PHL, CLT, and CFL; Collection and assembly of data: PHL, CLT, and CFL; Data analysis and interpretation: PHL and CFL; Manuscript writing: PHL and CFL; Final approval of manuscript: All authors

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