Identification of high-risk patients for ADR induced by traditional Chinese medicine injection: a nested case-control study

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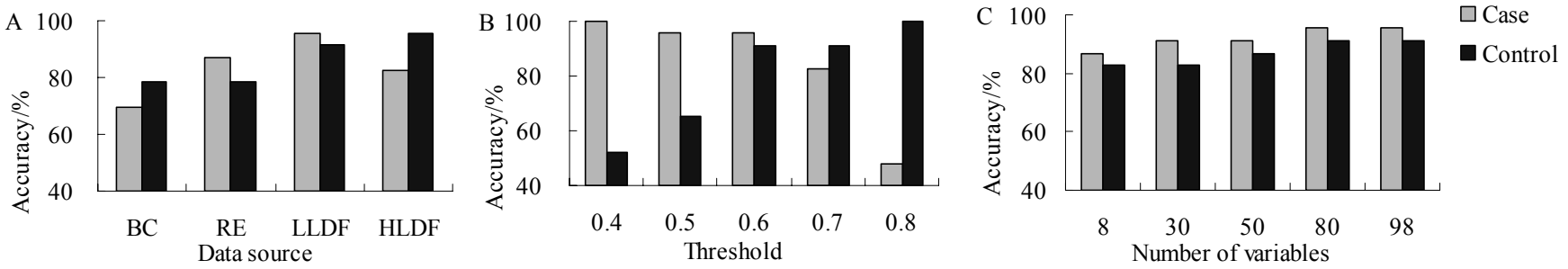

Figure s1. Recognition results of models in validation cohort. **(A)** Models based on different data sources. (BC: Basic characteristic; RE: Routine examination) **(B)** Models with different thresholds. **(C)** Models based on different number of variables.

TCMI names	Number	Herbal species	Major active compounds	References
Shenmai injection	82	*Radix Ginseng Rubra*	Ginsenoside Re, Rg1, Rf, et al.	1-4
		Radix Ophiopogonis	Ophiopogonin D, ophiopogonanone A, 2'-Hydroxyophiopogonone A, et al.	
Kudiezi injection	10	*Ixeridium Sonchifolium*	Sonchifoliasolide M, sonchifoliactone C, ixerisoside C, et al.	5-7
Shuxuening injection	8	*Ginkgo Folium*	Rutin, isoquercitrin, kaempferol, et al.	8-11
Danhong injection	7	*Radix Salviae*	Protocatechuic aldehyde, tanshinol, salvianolic acid A, et al.	12-14
		Carthami Flos	Syringin, quercimeritrin, caffeic acid, et al.	
Xiaoaiping injection	7	*Marsdenia Tenacissima*	Tenacigenin A, B, tenacissoside F, et al.	15
Kangai injection	6	*Hedysarum Multijugum*	Astragaloside IV, calycosin, et al.	16
		Panax Ginseng	Ginsenoside Re, Rg1, Rf, et al.	
		Sophorae Flavescentis Radix	Oxymatrine	
Kanglaite injection	3	*Coicis Semen*	Triolein, coixenolide, coixol, et al.	17

Table s1. Herbal species and major active compounds of each TCMI

Systems / organizations	Total number of cases*	Main manifestations (number of cases*)
Systemic injury	56	Hot flush (35), shiver (11), fever (6), acratia (3), chest pain (1)
Respiratory system damage	54	Chest tightness (33), dyspnea (21)
Skin lesion	37	Erythra(20), pruritus (13), hypethidorosis (4)
Gastrointestinal system damage	21	Sicchasia (11), vomit (8), abdominal pain (2)
Nervous system damage	8	Giddy (5), headache (2), paresthesia (1)
Cardiovascular system damage	5	Hypertension (3), phlebitis (2)

Table s2. Main ADR manifestations in included cases

* There may be several manifestations occurred simultaneously in one ADR case.

Classification of seriousness		Number of cases	Constituent ratio/%
Class I	ADR are deadly or life-threatening.	4	3.25
Class II	Patients have pathologic and physiologic changes.	3	2.44
Class III	Patients cannot endure the ADR and must be given a lower dose or withdrawn from drugs.	20	16.26
Class IV	Patients can endure the ADR.	96	78.05

Table s3. ADR seriousness in included cases

Classification of relevance	Point 1*	Point 2+	Point 3&	Point 4#	Point 5$
Definite	Yes	Yes	Yes	Yes	Yes
Probable	Yes	Yes	Yes	Uncertainty	Yes
Possible	Yes	Yes	Uncertainty	Uncertainty	Uncertainty
Unlikely	No	No	Uncertainty	Uncertainty	Uncertainty
Pending	There are missing contents. The evaluation can be completed when the supplementary specifications are provided.				
Unassessable	Many items are unavailable. The relationship is unassessable since the missing items can not be supplemented.				

Table s4. Relevance evaluation method of the national ADR monitoring center

*: The temporal relation between medication and ADR's occurrence was reasonable;

+: The clinical symptoms were coincided with the known ADR profile;

&: The ADR was relieved or vanished after decreasing dosage or drug withdrawal;

#: The ADR occurred again when drug was re-administered;

$: The probability of ADR caused by concomitant medications, disease progression or other treatment could be excluded.

Variable categories		Variable NO.: variable names (variable descriptions)
Basic characteristic	Demographic Comorbiditie Previous history	1: Gender (male: 1, female: 0); 2: Age (year); 3: Body weight (kg); 4: Height (cm); 5: Hypertension (yes: 1, no: 0); 6: Diabetes (yes: 1, no: 0); 7: Hepatitis (yes: 1, no: 0); 8: Tuberculosis (yes: 1, no: 0); 9: History of trauma surgery (yes: 1, no: 0); 10: History of drug allergy (yes: 1, no: 0); 11: History of food allergy (yes: 1, no: 0); 12: History of blood transfusion (yes: 1, no: 0);
Routine examination	Urine flow analysis	13: Urinary sediment cast (/μL); 14: Urinary sediment conductivity (mS/cm); 15: Urinary sediment epithelial cell (/μL); 16: Urinary sediment mucus (/μL); 17: Urinary sediment path cast (/μL); 18: Urine pH; 19: Urinary sediment red blood cell (/μL); 20: Urinary sediment small round cell (/μL); 21: Urinary sediment white blood cell (/μL); 22: Urinary sediment yeast-like fungi (/μL); 23: Urine white blood cell (negative: 0, +: 1, ++: 2); 24: Urine specific gravity; 25: Urine bilirubin (negative: 0, +: 1, ++: 2); 26: Urine protein (negative: 0, +: 1, ++: 2); 27: Urobilinogen (negative: 0, +: 1, ++: 2); 28: Urine glucose (negative: 0, +: 1, ++: 2); 29: Urine acetone bodies (negative: 0, +: 1, ++: 2); 30: Urine nitrous acid (negative: 0, +: 1, ++: 2); 31: Hematuria (negative: 0, +: 1, ++: 2);
	Blood routine examination	32: White blood cell count (E+09/L); 33: Monocyte count (E+09/L); 34: Monocytes ratio (%); 35: Red blood cell distribution width (%); 36: Red blood cell count (E+12/L); 37: Red blood cell hematocrit (%); 38: Lymphocyte count (E+09/L); 39: Lymphocyte ratio (%); 40: Mean corpuscular volume (fL); 41: Mean corpuscular hemoglobin (pg); 42: Mean corpuscular hemoglobin concentration (g/L); 43: Mean platelet volume (fL); 44: Basophilic granulocyte count (E+09/L); 45: Basophilic granulocyte ratio (%); 46: Eosinophilic granulocyte count (E+09/L); 47: Eosinophilic granulocyte ratio (%); 48: Hemoglobin (g/L); 49: Platelet distribution width (%); 50: Blood platelet count (E+09/L); 51: Thrombocytocrit (%); 52: Neutrophil count (E+09/L); 53: Neutrophil ratio (%);
	Biochemical series examination	54: Aspertate aminotransferase/alanine aminotransferase ; 55: b-hydroxybutyric acid (mmol/L); 56: Albumin (g/L); 57: Albumin/globulin; 58: High-sensitivity C-reactive protein (mg/L); 59: Cholinesterase (U/L); 60: Low density lipoprotein (mmol/L); 61: Amylase (U/L); 62: Glycylproline dipeptidyl aminopeptidase (U/L); 63: Triglyceride (mmol/L); 64: High-density lipoprotein (mmol/L); 65: Glutamyl transpeptidase (U/L); 66: Alanine aminotransferase (U/L); 67: Aspertate aminotransferase (U/L); 68: Serum creatinine (μmol/L); 69: Creatine kinase isoenzyme (U/L); 70: Potassium (mmol/L); 71: Indirect bilirubin (μmol/L); 72: Alkaline phosphatase (U/L); 73: Phosphorus (mmol/L); 74: Creatine phosphate kinase (U/L); 75: Chlorine (mmol/L); 76: Magnesium (mmol/L); 77: Sodium (mmol/L); 78: Urea (mmol/L); 79: Uric acid (μmol/L); 80: Glucose (mmol/L); 81: Hydroxybutyrate dehydrogenase (U/L); 82: Globulin (g/L); 83: Lactic dehydrogenase (U/L); 84: Bicarbonate (mmol/L); 85: Homocysteine (μmol/L); 86: Adenosine deaminase (U/L); 87: Apolipoprotein A (g/L); 88: Apolipoprotein B (g/L); 89: Direct bilirubin (μmol/L); 90: Total cholesterol (mmol/L); 91: Total bilirubin (μmol/L); 92: Total bile acid (μmol/L); 93: Total protein (g/L); 94: Total calcium (mmol/L);
	Coagulation function examination	95: International normalized ratio; 96: Activated partial thromboplastin time (second); 97: Prothrombin time (second); 98: Fibrinogen (g/L)

Table s5. Categories, names and descriptions of clinical information

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