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Data mining on the medication rules of Chinese medicine for diabetic nephropathy

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Abstract: Objective To investigate the medication patterns of Chinese medicine in treating diabetic nephropathy through data mining analysis. **Methods** A comprehensive collection of medical prescriptions for Chinese medicine treatment of diabetic nephropathy was gathered from databases including CNKI, VIP, Wanfang, and the Chinese Journal of Traditional Chinese Medicine Literature Database from January 2013 to December 2024. An Excel-based database was constructed, and a Chinese medicine data mining system was applied to conduct frequency analysis, medicinal nature and flavor classification, meridian entry, efficacy categorization, hierarchical clustering, association rules, and complex network analysis. The compatibility patterns and significance within the same cluster were also explored. **Results** According to established inclusion and exclusion criteria, 327 articles on Chinese medicine treatment for diabetic nephropathy were selected, involving 327 prescriptions and 205 types of herbs with a cumulative usage frequency of 2 624 times. The top ten most frequently used herbs are *Astragali Radix* (Huangqi), *Poria* (Fuling), *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Dioscoreae Rhizoma* (Shanyao), *Corni Fructus* (Shanzhuyu), *Angelicae Sinensis Radix* (Danggui), *Rhei Radix et Rhizoma* (Dahuang), *Rehmanniae Radix Praeparata* (Shudahuang), *Atractylodis Macrocephalae Rhizoma* (Baizhu) and *Chuanxiong Rhizoma* (Chuanxiong). These herbs predominantly exhibit cold or warm properties and are mainly sweet or bitter in flavor, mostly entering the liver, kidney, and spleen meridian. The 205 herbs can be categorized into 17 classes based on their efficacy, with the highest frequencies being tonifying herbs, blood-activating and stasis-resolving herbs, urine excretion to strain off dampness herbs, heat-clearing herbs, and astringent herbs. The *Apriori algorithm* was used to mine herb pair combinations, and 29 association rules were finally obtained. Among them, the most frequent two-herb combinations were Huangqi-Fuling, Huangqi-Danshen, Huangqi-Danggui, Huangqi-Shanyao, and Huangqi-Shanzhuyu; the most frequent three-herb combinations were Huangqi-Fuling-Shanzhuyu, Huangqi-Fuling-Shanyao, Huangqi-Fuling-Zexie, Huangqi-Shanyao-Danshen, and Huangqi-Shanyao-Zexie. Complex system entropy clustering identified 10 core Chinese medicine combinations for treating diabetic nephropathy, while 5 new formulae were discovered by entropy clustering and improved mutual information method. **Conclusion** *Astragali Radix* (Huangqi), *Poria* (Fuling), *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Dioscoreae Rhizoma* (Shanyao), *Corni Fructus* (Shanzhuyu) are the high-frequency core medications used by modern physicians in the treatment of diabetic nephropathy. Chinese medicine treatments for diabetic nephropathy mainly focus on tonifying drugs, complemented by blood-activating and stasis-resolving drugs, diuretic and dampness-resolving drugs, heat-clearing drugs, and astringent drugs to achieve both symptomatic and radical treatment. The pairing of drugs, core combinations, and new formula combinations further illuminate the common compatibility rules of Chinese medicine in treating diabetic nephropathy, providing new perspectives and methodologies for its treatment.

Keywords: Literature research; Data mining; Chinese medicine; Diabetic nephropathy; Medication rule

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Diabetic kidney disease falls within the categories of "wasting-thirst disorder (xiaoke, 消渴)" "kidney wasting-thirst (shenxiao, 肾消)" and "edema (shuizhong, 水肿)" in traditional Chinese medicine (TCM). According to TCM theory, the disease is located in the kidney and is essentially characterized by deficiency in the root and excess in the manifestation; therefore, treatment should primarily focus on tonifying of qi and yin, activating blood and resolving stasis, and draining dampness to eliminate turbidity [1]. The holistic approach and principle of syndrome differentiation that TCM follows in the treatment of diabetic kidney disease allow for the formulation of individualized regimens based on the patient's constitution and symptoms, thereby alleviating symptoms while regulating the balance of yin and yang to achieve simultaneous treatment of both the root and the branch [2]. However, current studies on TCM treatment of

diabetic kidney disease have concentrated on the efficacy validation of single Chinese herbal medicines or formulas, with relatively little systematic mining of the medication rules derived from massive clinical prescriptions, which is not conducive to the innovation of TCM compound formulas [3]. Moreover, TCM treatment of diabetic kidney disease exhibits multi-target and multi-level characteristics. Integrating TCM theory with data analysis to explore the synergistic effects and mechanisms of action among different drug combinations may also facilitate the discovery of novel therapeutic targets, optimize existing treatment regimens, and thereby improve the therapeutic outcomes for diabetic kidney disease [4]. Data mining techniques have provided new methodological support for TCM research. Algorithms including association rule analysis, complex network clustering, and entropy-based hierarchical clustering can extract core drug combinations from large volumes of medical record data, reveal implicit

compatibility patterns, and infer potential new formulas, thereby providing scientific evidence for the clinical practice of TCM in treating diabetic kidney disease [5]. On this basis, this study aimed to analyze clinical prescriptions for TCM treatment of diabetic kidney disease over the past decade using data mining techniques, to explore the medication rules and underlying mechanisms, so as to assist clinicians in deepening their understanding of TCM treatment for this disease, provide theoretical foundations and technical support for the development of novel therapeutic strategies, and offer methodological references for the inheritance and innovative research of TCM.

1 Subjects and Methods

1.1 Data Sources

Using "diabetic kidney disease", "wasting-thirst disorder (xiaoke, 消渴)", "kidney wasting-thirst (shenxiao, 肾消)" "diabetes complicated by edema", "Chinese medicine treatment" and "Chinese medicine" as search terms, comprehensive searches were conducted in the China National Knowledge Infrastructure (CNKI), VIP Chinese Science and Technology Periodical Database, Wanfang Database, and the Chinese Traditional Medicine Periodical Literature Database. Literature was screened according to inclusion and exclusion criteria, with the retrieval period from January 2013 to December 2024. A total of 327 relevant literature records were collected.

1.2 Inclusion and Exclusion Criteria

1.2.1 Inclusion Criteria

(1) Meeting the TCM and Western medicine diagnostic criteria for diabetic kidney disease [6-7] and definitively diagnosed with diabetic kidney disease;

(2) clinical research literature on TCM treatment of diabetic kidney disease;

(3) using TCM compound formulas as the main treatment regimen;

(4) the prescriptions in the literature included the complete composition of medicinal materials, with clear formula names and dosages;

(5) for clinical observational studies, the difference in treatment efficacy between different groups was statistically significant ($P < 0.05$).

1.2.2 Exclusion Criteria

(1) Animal experimental or cell experimental studies;

(2) review articles or experience summaries;

(3) duplicate publications;

(4) use of external TCM therapies such as acupuncture or Chinese herbal medicinal fumigation and washing;

(5) only describing symptomatic relief without objective indicators.

1.3 Data Standardization

With reference to the *Standard Terminology of Clinical Diagnosis and Treatment in Traditional Chinese Medicine* [8], *Chinese Materia Medica* [9],

Pharmacopoeia of the People's Republic of China [10], and the *Dictionary of Chinese Materia Medica* [11], the names of TCM syndromes and medicinal materials were standardized. For the statistics of properties, flavors, and meridian affinities, the "single primary attribute count" rule was adopted: for each Chinese herbal medicine used in a prescription, only one primary property, one primary flavor, and one primary meridian affinity (as defined in *Chinese Materia Medica* [9] and the *Pharmacopoeia of the People's Republic of China* [10]) were counted per occurrence, with no repeated superposition; within each dimension, the sum of frequencies across all categories equaled the total frequency of Chinese herbal medicine usage.

1.4 Data Analysis

The standardized data on TCM diagnoses, syndrome types, and formula compositions were entered into Excel 2019 software to construct a database. Excel conditional formatting was used to highlight unusual drug dosages, which were then verified and corrected against the original texts. The standardized Excel data were imported into the TCM Data Mining System V2.5 software for further analysis. The "frequency statistics" function was used to calculate the occurrence frequency of each Chinese herbal medicine in the prescriptions, and the results were ranked to identify the most frequently used Chinese herbal medicines. The "property, flavor, and meridian tropism" function was employed to generate the distribution of the four properties, five flavors, and meridian affinities, and to produce visual charts. The "association rule mining," "cluster mining," and "new formula analysis" functions were applied to explore the associations among Chinese herbal medicines, identify high-frequency drug pair combinations, and construct a compatibility network for TCM treatment of diabetic kidney disease, with Chinese herbal medicines as nodes and associations as edges, and to present the compatibility patterns through visual charts. Finally, based on the results of frequency analysis, efficacy statistics, high-frequency drug pairs, and compatibility network analysis, combined with the characteristics of Chinese Chinese herbal medicinal medicine (properties, flavors, efficacy, etc.) and clinical experience, the prescription formulation rules for TCM treatment of diabetic kidney disease were systematically analyzed.

2 Results

2.1 Analysis of Medication Frequencies

Based on the inclusion and exclusion criteria, a total of 327 articles on Chinese medicine treatment of diabetic kidney disease were screened in the present study. The included literature involved 327 TCM prescriptions, comprising 205 distinct medicinal Chinese herbal medicines, with a total medication frequency of 2,624 occurrences. Ranked according to frequency of use, the top 10 Chinese herbal medicines were, in descending order, *Astragali Radix* (Huangqi), *Poria* (Fuling), *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Dioscoreae*

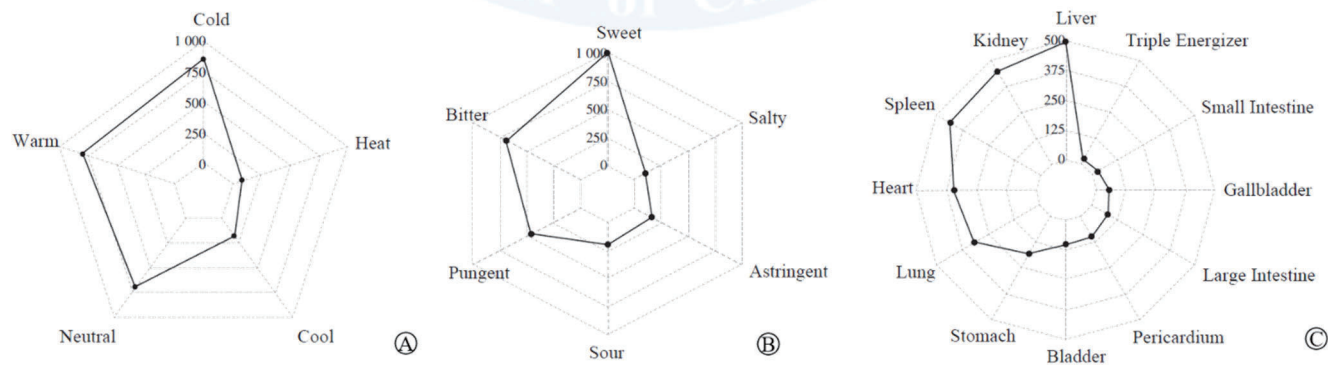
Rhizoma (Shanyao), *Corni Fructus* (Shanzhuyu), *Angelicae Sinensis Radix* (Danggui), *Rhei Radix et Rhizoma* (Dahuang), *Rehmanniae Radix Praeparata* (Shudahuang), *Atractylodis Macrocephalae Rhizoma* (Baizhu) and *Chuanxiong Rhizoma* (Chuanxiong). In terms of medicinal properties, cold and warm properties predominated; in terms of flavors, sweet and bitter were the most common; and the Chinese herbal medicines were most frequently attributed to the liver, kidney, and spleen meridians. See Table 1, Table 2, and Figure 1.

Tab.1 Medication frequency statistics (top 30)

No.	Chinese Name	Pinyin	Latin Name	Frequency (%)	Formula Coverage (%)	No.	Chinese Name	Pinyin	Latin Name	Frequency (%)	Formula Coverage (%)
1	黄芪	Huangqi	<i>Astragali Radix</i>	184(7.01)	56.27	16	太子参	Taizishen	<i>Pseudostellariae Radix</i>	55(2.10)	16.82
2	茯苓	Fuling	<i>Poria</i>	161(6.14)	49.24	17	黄精	Huangjing	<i>Polygonati Rhizoma</i>	55(2.10)	16.82
3	丹参	Danshen	<i>Salviae Miltiorrhizae Radix et Rhizoma</i>	131(4.99)	40.06	18	牛膝	Niuxi	<i>Achyranthis Bidentatae Radix</i>	53(2.02)	16.21
4	山药	Shanyao	<i>Dioscoreae Rhizoma</i>	115(4.38)	35.17	19	地黄	Dihuang	<i>Rehmanniae Radix</i>	53(2.02)	16.21
5	山茱萸	Shanzhuyu	<i>Corni Fructus</i>	97(3.7)	29.66	20	麦冬	Maidong	<i>Ophiopogonis Radix</i>	47(1.79)	14.37
6	当归	Danggui	<i>Angelicae Sinensis Radix</i>	94(3.58)	28.75	21	桃仁	Taoren	<i>Persicae Semen</i>	46(1.75)	14.07
7	大黄	Dahuang	<i>Rhei Radix et Rhizoma</i>	90(3.43)	27.52	22	枸杞子	Gouqizi	<i>Lycii Fructus</i>	44(1.68)	13.46
8	熟地黄	Shudahuang	<i>Rehmanniae Radix Praeparata</i>	88(3.35)	26.91	23	知母	Zhimu	<i>Anemarrhenae Rhizoma</i>	42(1.60)	12.84
9	白术	Baizhu	<i>Atractylodis Macrocephalae Rhizoma</i>	82(3.13)	25.08	24	地龙	Dilong	<i>Pheretima</i>	40(1.52)	12.23
10	川芎	Chuanxiong	<i>Chuanxiong Rhizoma</i>	73(2.78)	22.32	25	五味子	Wuweizi	<i>Schisandrae Chinensis Fructus</i>	38(1.45)	11.62
11	泽泻	Zexie	<i>Alismatis Rhizoma</i>	73(2.78)	22.32	26	红花	Honghua	<i>Carthami Flos</i>	30(1.14)	9.17
12	益母草	Yimucao	<i>Leonuri Herba</i>	72(2.74)	22.02	27	菟丝子	Tusizi	<i>Cuscutae Semen</i>	27(1.03)	8.26
13	甘草	Gancao	<i>Glycyrrhizae Radix et Rhizoma</i>	70(2.67)	21.41	28	水蛭	Shuizhi	<i>Hirudo</i>	24(0.91)	7.34
14	党参	Dangshen	<i>Codonopsis Radix</i>	69(2.63)	21.10	29	赤芍	Chishao	<i>Paeoniae Radix Rubra</i>	24(0.91)	7.34
15	牡丹皮	Mudanpi	<i>Moutan Cortex</i>	64(2.44)	19.57	30	肉桂	Rougui	<i>Cinnamomi Cortex</i>	23(0.88)	7.03

Tab.2 Statistics of main Chinese medicine nature, flavor and meridian tropism

Four Properties			Five Flavors			Meridian Tropism		
Name	Frequency	Percentage	Name	Frequency	Percentage	Name	Frequency	Percentage
Cold	855	32.58	Sweet	998	38.03	Liver Meridian	497	18.94
Warm	793	30.22	Bitter	696	26.52	Kidney Meridian	448	17.07
Neutral	705	26.87	Pungent	458	17.45	Spleen Meridian	440	16.77
Cool	182	6.94	Sour	197	7.51	Heart Meridian	345	13.15
Hot	89	3.39	Astringent	166	6.33	Lung Meridian	318	12.12
			Salty	109	4.16	Stomach Meridian	183	6.97
						Bladder Meridian	102	3.89
						Pericardium Meridian	100	3.81
						Small Intestine Meridian	79	3.01
						Gallbladder Meridian	57	2.17
						Small Intestine Meridian	34	1.30
						Triple energizer Meridian	21	0.80



Note: A, four properties; B, five flavors; C, meridian tropism.

Fig.1 Statistical radar chart of four natures, five flavors and meridian tropism

2.3 Analysis of Herb Association Rules

The 205 Chinese herbal medicines included in this study were analyzed using the Apriori algorithm for mining Chinese herbal medicine-pair combinations. With a support threshold set to ≥ 0.2 , a confidence threshold of ≥ 0.8 , and only association combinations with a lift value >1 considered meaningful, a total of 29 association rules were obtained. See Table 4 and Table 5.

2.4 Analysis of Prescription Formulation Rules

Tab.3 Statistical analysis results of main drugs in various categories of high-frequency medication efficacy

Efficacy	Classification	Main drugs and frequency of use
Tonifying and replenishing medicinal	qi-tonifying	<i>Astragali Radix</i> (Huangqi) (184), <i>Dioscoreae Rhizoma</i> (Shanyao) (115), <i>Atractylodis Macrocephalae Rhizoma</i> (Baizhu) (82), <i>Glycyrrhizae Radix et Rhizoma</i> (Gancao) (70), <i>Codonopsis Radix</i> (Dangshen) (69), <i>Pseudostellariae Radix</i> (Taizishen) (55), <i>Ginseng Radix et Rhizoma</i> (Renshen) (15), <i>Panacis Quinquefolii Radix</i> (Xiyangshen) (7), <i>Jujubae Fructus</i> (Dazao) (2), <i>Rhodiolae Crenulatae Radix et Rhizoma</i> (Hongjingtian) (2), <i>Ginseng Radix et Rhizoma Rubra</i> (Hongshen) (1)
	Blood-tonifying	<i>Angelicae Sinensis Radix</i> (Danggui) (94), <i>Rehmanniae Radix Praeparata</i> (Shudahuang) (88), <i>Paeoniae Radix Alba</i> (Baishao) (12), <i>Asini Corii Colla</i> (Ejiao) (6), <i>Polygoni Multiflori Radix</i> (Heshouwu) (4)
	Yin-tonifying	<i>Polygonati Rhizoma</i> (Huangjing) (55), <i>Ophiopogonis Radix</i> (Maidong) (47), <i>Dendrobii Caulis</i> (Shihu) (15), <i>Ligustri Lucidi Fructus</i> (Nvzhenzi) (10), <i>Adenophorae Radix</i> (Shashen) (5), <i>Mori Fructus</i> (Sangshen) (2), <i>Asparagi Radix</i> (Tiandong) (1)
	Yang-tonifying	<i>Cuscutae Semen</i> (Tusizi) (27), <i>Eucommiae Cortex</i> (Duzhogn) (11), <i>Cordyceps</i> (Dongchongxiacao) (10), <i>Psoraleae Fructus</i> (Buguzhi) (5), <i>Morindae Officinalis Radix</i> (Bajitian) (3), <i>Curculiginis Rhizoma</i> (Xianmao) (1)
Blood-activating and stasis-dispelling medicinal	Blood-activating menstruation-regulating	<i>Salviae Miltiorrhizae Radix et Rhizoma</i> (Danshen) (131), <i>Leonuri Herba</i> (Yimucao) (72), <i>Achyranthis Bidentatae Radix</i> (Niuxi) (53), <i>Persicae Semen</i> (Taoren) (46), <i>Carthami Flos</i> (Honghua) (30), <i>Spatholobi Caulis</i> (Jixueteng) (6)
	Blood-activating analgesic	<i>Chuanxiong Rhizoma</i> (Chuanxiong) (73), <i>Curcumae Longae Rhizoma</i> (Jianghuang) (5), <i>Faeces Trogloteri</i> (Wulingzhi) (2)
	Blood-breaking mass-eliminating	<i>Hirudo</i> (Shuizhi) (24), <i>Ramulus Euonymi</i> (Guijianyu) (2), <i>Sparganii Rhizoma</i> (Sanleng) (1)
Dampness-draining medicinal	Water-draining and swelling-dispersing	<i>Poria</i> (Fuling) (161), <i>Alismatis Rhizoma</i> (Zexie) (73), <i>Coicis Semen</i> (Yiyiren) (22), <i>Stigma Maydis</i> (Yumixu) (16), <i>Benincasae Exocarpium</i> (Dongguapi) (5)
	Strangury-relieving	<i>Plantaginis Semen</i> (Cheqianzi) (18), <i>Dioscoreae Hypoglaucae Rhizoma</i> (Bixie) (10), <i>Plantaginis Herba</i> (Cheqiancao) (6)
	Dampness-draining anti-icteric	<i>Polygoni Cuspidati Rhizoma et Radix</i> (Huzhang) (3)
Heat-clearing medicinal	Heat-clearing blood-cooling	<i>Moutan Cortex</i> (Mudanpi) (64), <i>Rehmanniae Radix</i> (Dihuang) (53), <i>Paeoniae Radix Rubra</i> (Chishao) (24)
	Heat-clearing detoxicating	<i>Forsythiae Fructus</i> (Lianqiao) (5), <i>Galium Aparine L</i> (Baxiancao) (2), <i>Isatidis Radix</i> (Banlangen) (2), <i>Scutellariae Barbatae Herba</i> (Banzhilian) (1), <i>Lonicerae Japonicae Flos</i> (Jinyinhua) (1)
	Heat-clearing fire-purging	<i>Anemarrhenae Rhizoma</i> (Zhimu) (42), <i>Prunellae Spica</i> (Xiakucao) (13), <i>Cassiae Semen</i> (Juemingzi) (4)
	Heat-clearing and dampness-drying	<i>Coptidis Rhizoma</i> (Huanglian) (13), <i>Phellodendri Chinensis Cortex</i> (Huangbai) (6), <i>Centellae Herba</i> (Jixuecao) (2)
	Deficiency heat-clearing	<i>Lycii Cortex</i> (Digupi) (5), <i>Artemisiae Annuae Herba</i> (Qinghao) (1)
Astringent medicinal	Lung-intestine astringent	<i>Schisandrae Chinensis Fructus</i> (Wuweizi) (38)
	Securing essence reducing urination	<i>Corni Fructus</i> (Shanzhuyu) (97), <i>Mantidis Oötheca</i> (Sangpiaoxiao) (12)
	Relieving leukorrhea	<i>Euryales Semen</i> (Qianshi) (15), <i>Rosae Laevigatae Fructus</i> (Jinyingzi) (3)

Tab.4 Statistics of high-frequency 2-Chinese herbal medicine combinations (top 10)

No.	Couplet Medicinals	Support	Lift	Main Efficacy
1	Huangqi-Fuling	0.40	1.26	Tonify qi and induce diuresis
2	Huangqi-Danshen	0.39	1.57	Tonify qi and activate blood
3	Huangqi-Danggui	0.37	1.33	Tonify qi and replenish blood
4	Huangqi-Shanyao	0.35	1.24	Tonify qi and fortify spleen
5	Huangqi-Shanzhuyu	0.33	1.36	Tonify qi and reinforce qi
6	Fuling-Shanyao	0.33	1.30	Fortify spleen and drain dampness
7	Huangqi-Baizhu	0.32	1.27	Fortify spleen and replenish qi
8	Huangqi-Chuanxiong	0.31	1.11	Move qi and tonify qi
9	Shanyao-Danggui	0.30	1.18	Fortify spleen and tonify blood
10	Huangqi-Zexie	0.30	1.08	Induce diuresis to alleviate edema

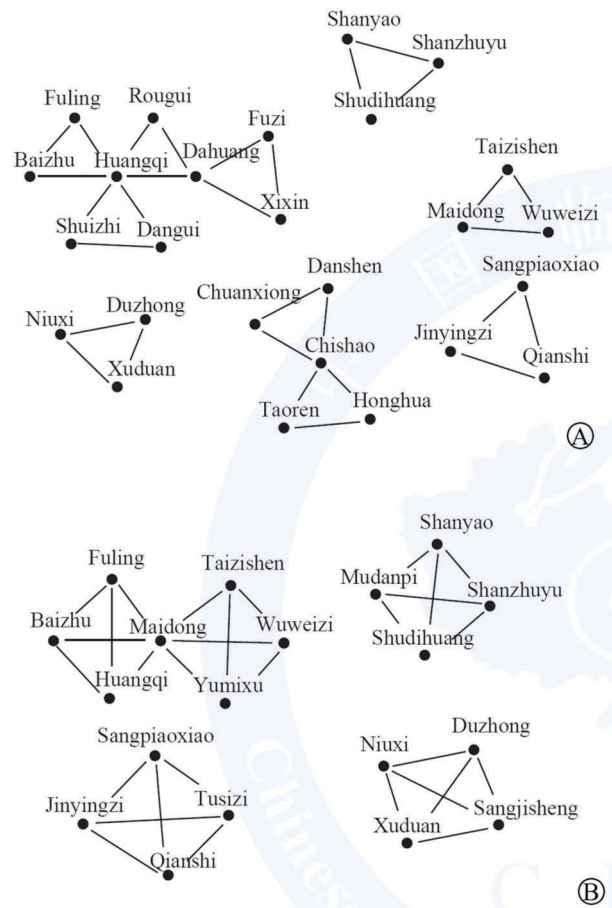
Based on the results presented in Section 2.3, with a correlation coefficient set to 5 and a penalty factor set to 2, the complex system entropy clustering method was applied to analyze core combinations, yielding 10 core Chinese herbal medicine combinations for the treatment of diabetic kidney disease. Using entropy clustering and the improved mutual information method for mining new formula combinations, 5 novel prescription combinations for treating diabetic kidney disease were identified. See Table 6 and Figure 2.

Tab.5 Statistics of high-frequency 3-Chinese herbal medicine combinations (top 10)

No.	Combination Medicinals	Support	Main Efficacy
1	Huangqi-Fuling-Shanzhuyu	0.38	Tonify qi and Yin, reinforce kidney
2	Huangqi-Fuling-Shanyao	0.37	Fortify spleen, tonify qi, reinforce kidney
3	Huangqi-Fuling-Zexie	0.36	Induce diuresis, subside swelling, tonify qi
4	Huangqi-Shanyao-Danshen	0.36	Activate blood, remove blood stasis, tonify qi
5	Huangqi-Shanyao-Zexie	0.34	Tonify qi, drain dampness, reinforce kidney
6	Huangqi-Shanyao-Shanzhuyu	0.34	Replenish yin, tonify the kidney, strength body
7	Huangqi-Shanyao-Danggui	0.34	Tonify qi, replenish blood, regulate menstruation
8	Huangqi-Danshen-Zexie	0.33	Blood-activating, induce diuresis, tonify qi
9	Huangqi-Danggui-Chuanxiong	0.31	Enrich blood, move qi, activate blood
10	Huangqi-Shanzhuyu-Dihuang	0.31	Replenish yin, tonify the kidney, secure essence

Tab.6 Core combinations based on complex system entropy clustering method

No.	Core combination	No.	Core combination
1	Fuling-Baizhu-Huangqi	6	Danshen-Chuanxiong-Chishao
2	Dahuang-Rougui-Huangqi	7	Duzhong-Xuduan-Niuxi
3	Shanzhuyu-Shanyao-Shudihuang	8	Taoren-Honghua-Chishao
4	Taizishen-Maidong-Wuweizi	9	Dahuang-Fuzi-Xixin
5	Shuizhi-Huangqi-Danggui	10	Sangpiao Xiao-Jinyingzi-Qianshi



Note: A, core combination; B, New prescription.

Fig.2 Combination map of Chinese medicine in the treatment of diabetic nephropathy

3 Discussion

Diabetic kidney disease, as the most common complication of diabetes mellitus, has consistently been a research focus among scholars both domestically and internationally. Current Western medical treatment for diabetic kidney disease mainly employs approaches such as glycemic control, blood pressure reduction, and lipid regulation, which are beneficial to a certain extent in improving long-term renal endpoint events. However, Western medical therapies primarily target a single molecular target and are therefore insufficient for comprehensive intervention; moreover, long-term administration of multiple medications may expose patients to the risks of adverse drug reactions and relapse

upon discontinuation [12-14]. TCM possesses unique advantages in ameliorating the clinical symptoms of patients with diabetic kidney disease and delaying disease progression, yet systematic mining of TCM formulas remains inadequate. On the basis of 327 TCM prescriptions, the present study employed data mining techniques to investigate the core medication combinations and potential novel formula combinations for TCM treatment of diabetic kidney disease, with the aim of providing further scientific evidence for the prevention and management of this condition.

According to TCM theory, the pathogenesis of diabetic kidney disease is influenced by the interplay of multiple factors, with deficiency of kidney qi, dysfunction of the spleen and stomach, and impaired liver qi dispersion being important predisposing factors for the development of this disease [15-16]. It is evident that systematic analysis of clinical TCM prescriptions, revealing frequently used Chinese herbal medicines and their combination patterns, can facilitate the formulation of more precise treatment strategies based on individual variability and enable a greater number of patients to understand and benefit from TCM therapy. A total of 327 TCM prescriptions were included in this study, involving 205 distinct medicinal Chinese herbal medicines. The most frequently used Chinese herbal medicines were predominantly *Astragali Radix* (Huangqi), *Poria* (Fuling), *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Dioscoreae Rhizoma* (Shanyao), *Corni Fructus* (Shanzhuyu), among which *Astragali Radix* (Huangqi) ranked first with an overwhelming predominance. This finding is highly consistent with the TCM pathogenesis theory that "spleen-kidney deficiency constitutes the root, while phlegm, stasis, turbidity, and toxin constitute the manifestation" [17]. *Astragali Radix* (Huangqi), as a qi-supplementing Chinese herbal medicine, has the effects of supplementing qi, consolidating the exterior, promoting diuresis, and alleviating edema; its high frequency of use suggests that "tonifying qi" plays a significant role in the treatment of diabetic kidney disease [18]. *Poria* (Fuling) is renowned for its effect of draining dampness and promoting diuresis, while *Dioscoreae Rhizoma* (Shanyao) assists in supplementing qi and nourishing yin, and tonifying the spleen, lung, and kidney. The frequent use of these two Chinese Chinese herbal medicinal medicines reflects the emphasis placed on spleen and kidney function in TCM treatment of diabetic kidney disease [19-20]. Blood stasis constitutes an indispensable component in the disease progression of diabetic kidney disease; the application of *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen) can not only ameliorate symptoms attributable to blood stasis but also alleviate qi and blood deficiency in patients [21]. For patients with diabetic kidney disease, the astringent and securing effects of *Corni Fructus* (Shanzhuyu) can help enhance the body's resistance, prevent the leakage of essential qi, and play a critical role in maintaining internal environmental homeostasis [22]. Analysis of the properties, flavors, and meridian affinities of the Chinese herbal medicines revealed that the majority

of Chinese herbal medicines used in TCM treatment of diabetic kidney disease are cold or warm in property, predominantly sweet and bitter in flavor, and are most frequently attributed to the liver, kidney, and spleen meridians. This reveals a dynamic equilibrium strategy in the treatment of this disease that employs both warm and cold Chinese herbal medicines in combination, uses sweet and bitter flavors in mutual assistance, and attaches equal importance to the liver meridian, spleen meridian, and kidney meridian.

In this study, the 205 Chinese herbal medicines were classified into 17 categories based on therapeutic efficacy, among which tonifying and replenishing medicinal, blood-activating and stasis-dispelling medicinal, dampness-draining medicinal, heat-clearing medicinal and astringent medicinal occupied a relatively large proportion. This distribution pattern reflects the emphasis placed on supplementing the spleen and kidney, draining dampness and promoting diuresis, activating blood and resolving stasis, and clearing heat and purging fire in TCM treatment of diabetic kidney disease. In addition, the extensive application of astringent Chinese herbal medicines reflects the TCM concept of "consolidation and securing" which, in synergy with Chinese herbal medicines of other therapeutic categories, can form a multi-dimensional intervention network. This further validates the composite therapeutic principle of "tonifying deficiency-promoting diuresis-activating blood" for this disease, and also corresponds to the requirement for multi-target intervention in the modern medical pathological axis of "metabolism-inflammation-fibrosis." The synergistic effects of these Chinese herbal medicines are not only manifested in the harmonization of the four properties and five flavors and the multi-directional intervention of meridian tropism, but are also fully demonstrated in high-frequency Chinese herbal medicine-pair combinations and Chinese herbal medicine compatibility patterns. The 29 association rules mined using the Apriori algorithm in the present study provide novel perspectives for TCM treatment of diabetic kidney disease. For example, among two-Chinese herbal medicine combinations, the most frequent pair was Huangqi-Fuling: *Astragali Radix* (Huangqi) supplements qi and raises yang to promote the vaporization of body fluids, while *Poria* (Fuling) strengthens the spleen, permeates dampness, and guides water downward; their combined application—one ascending and one descending—achieves the effects of supplementing qi and promoting diuresis, embodying the concept of "simultaneous treatment of qi and water." Among three-Chinese herbal medicine combinations, the most frequent was Huangqi-Fuling-Shanzhuyu: *Astragali Radix* (Huangqi) tonifies the spleen and supplements qi, *Poria* (Fuling) promotes diuresis and strengthens the spleen, and *Corni Fructus* (Shanzhuyu) tonifies the kidney and consolidates essence; the three Chinese herbal medicines together form a closed-loop regulation characterized by "supplementation without stagnation and diuresis without compromising the healthy qi," which aligns with the theory of "simultaneous regulation of the

spleen and kidney". This study further employed the complex system entropy clustering method to analyze core combinations, yielding 10 core Chinese herbal medicine combinations for the treatment of diabetic kidney disease, which represent relatively mature and effective therapeutic regimens currently used in clinical practice. The five novel formula combinations derived from entropy clustering and the improved mutual information method demonstrate a well-integrated fusion of data mining and TCM theory. These novel combinations break through the fixed framework of traditional formulas and embody the precise treatment thinking of "integrating disease and syndrome with dynamic adjustment," and may possess greater clinical adaptability than single therapeutic approaches. For instance, the core combination of Fuling-Baizhu-Huangqi exerts the core effects of supplementing qi, strengthening the spleen, permeating dampness, and promoting diuresis, and may improve water-sodium retention and proteinuria in patients at the stage of "spleen deficiency with exuberant dampness." The addition of *Ophiopogonis Radix* (Maidong), which has yin-nourishing effects, can achieve the effects of supplementing qi, promoting diuresis, nourishing yin, and generating fluids, making it applicable to a broader range of patients. The combination of Shanzhuyu-Shanyao-Shudihuang can effectively improve clinical manifestations such as fatigue, weakness, and frequent nocturia in patients with spleen-kidney deficiency pattern through tonifying the kidney, nourishing yin, consolidating, and securing essential qi. The addition of *Moutan Cortex* (Mudanpi) can enhance the regulation of blood-level stasis-heat; while the core combination targets "deficiency" and "failure of consolidation," the addition of *Moutan Cortex* (Mudanpi) targets "heat" and "stasis," forming a composite therapeutic approach of "tonifying deficiency-clearing heat-resolving stasis," thereby rendering the novel formulas more comprehensive in addressing complex symptoms. It is evident that the evolutionary pathway from "core combinations" to "novel formula combinations" not only reflects the capability of data mining to reveal implicit patterns but also aligns with the clinical thinking of TCM of "treatment based on syndrome differentiation and modification according to the syndrome".

In summary, *Astragali Radix* (Huangqi), *Poria* (Fuling), *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Dioscoreae Rhizoma* (Shanyao), *Corni Fructus* (Shanzhuyu) are the high-frequency core Chinese herbal medicines employed by contemporary practitioners in the treatment of diabetic kidney disease. TCM treatment of this condition primarily utilizes deficiency-supplementing Chinese herbal medicines, complemented by blood-activating and stasis-resolving Chinese herbal medicines, water-draining and dampness-permeating Chinese herbal medicines, heat-clearing Chinese herbal medicines, and astringent Chinese herbal medicines, in order to achieve simultaneous treatment of both the root and the branch. The Chinese herbal medicine-pair combinations, core combinations, and novel formula combinations further reveal the common compatibility

patterns in TCM treatment of diabetic kidney disease, providing novel ideas and methods for the TCM management of this condition.

Conflict of Interest None

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· 论 著 ·

糖尿病肾病中医药治疗用药规律的数据挖掘

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摘要: **目的** 探讨基于数据挖掘的糖尿病肾病中医药治疗用药规律。**方法** 收集 2013 年 1 月至 2024 年 12 月中国知网(CNKI)、维普中文科技期刊数据库(VIP)、万方数据库、中国中医药期刊文献数据库中关于中医治疗糖尿病肾病的医案药方,使用 Excel 软件构建数据库,应用中医药数据挖掘系统进行用药频次、药性、药味、归经、功效、层次聚类、关联及复杂网络分析,并探究同一聚类药物的配伍规律及意义。**结果** 本研究基于纳入标准和排除标准共筛选 327 篇中医药治疗糖尿病肾病的文献。所纳入的文献涉及中药处方 327 首,205 味中药,用药频次 2 624 次,根据使用频次进行排序,用药频次前 10 位的药物依次为黄芪、茯苓、丹参、山药、山茱萸、当归、大黄、熟地黄、白术、川芎。药物药性以寒性、温性为主,药味以甘、苦为主,多归肝经、肾经、脾经。205 味中药根据功效可分为 17 类,其中频率最高的前五位分别为补虚药、活血化瘀药、利水渗湿药、清热药和收涩药。使用 Apriori 算法挖掘药对组合,最终得到 29 条关联组合,其中频次最高的 2 味药组合为黄芪-茯苓、黄芪-丹参、黄芪-当归、黄芪-山药、黄芪-山茱萸,频次最高的 3 味药组合为黄芪-茯苓-山茱萸、黄芪-茯苓-山药、黄芪-茯苓-泽泻、黄芪-山药-丹参、黄芪-山药-泽泻。使用复杂系统熵聚类法分析核心组合,得到 10 个中药治疗糖尿病肾病的核心组合;使用熵聚类及改进互信法挖掘新方组合,得到 5 个治疗糖尿病肾病的新方组合。**结论** 黄芪、茯苓、丹参、山药、山茱萸等为现代医家治疗糖尿病肾病的高频核心药物,中医治疗糖尿病肾病多以补虚药为主,同时配合活血化瘀药、利水渗湿药、清热药、收涩药等以达到标本兼治的作用,药对组合、核心组合、新方组合进一步揭示了中医药治疗糖尿病肾病的常用配伍规律,为中医药治疗糖尿病肾病提供了新的思路和方法。

关键词: 文献研究; 数据挖掘; 中医药; 糖尿病肾病; 用药规律

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Data mining on the medication rules of Chinese medicine for diabetic nephropathy

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Abstract: **Objective** To investigate the medication patterns of Chinese medicine in treating diabetic nephropathy through data mining analysis. **Methods** A comprehensive collection of medical prescriptions for Chinese medicine treatment of diabetic nephropathy was gathered from databases including CNKI, VIP, Wanfang, and the Chinese Journal of Traditional Chinese Medicine Literature Database from January 2013 to December 2024. An Excel-based database was constructed, and a Chinese medicine data mining system was applied to conduct frequency analysis, medicinal nature and flavor classification, meridian entry, efficacy categorization, hierarchical clustering, association rules, and complex network analysis. The compatibility patterns and significance within the same cluster were also explored. **Results** According to established inclusion and exclusion criteria, 327 articles on Chinese medicine treatment for diabetic nephropathy were selected, involving 327 prescriptions and 205 types of herbs with a cumulative usage frequency of 2 624 times. The top ten most frequently used herbs are *Astragalus*, *Poria*, *Salvia miltiorrhiza*,

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Dioscorea, *Cornus officinalis*, *Angelica sinensis*, *Rheum palmatum*, *Rehmannia glutinosa*, *Attractylodes macrocephala*, and *ligusticum chuanxiong*. These herbs predominantly exhibit cold or warm properties and are mainly sweet or bitter in flavor, mostly entering the liver, kidney, and spleen entry. The 205 herbs can be categorized into 17 classes based on their efficacy, with the highest frequencies being tonifying herbs, blood-activating and stasis-resolving herbs, urine excretion to strain off dampness herbs, heat-clearing herbs, and astringent herbs. The Apriori algorithm was used to mine herb pair combinations, and 29 association rules were finally obtained. Among them, the most frequent two-herb combinations were *Astragalus* - *Poria*, *Astragalus* - *Salvia miltiorrhiza*, *Astragalus* - *Angelica sinensis*, *Astragalus* - *Dioscorea*, and *Astragalus*-*Cornus officinalis*; the most frequent three-herb combinations were *Astragalus*-*Poria*-*Cornus officinalis*, *Astragalus* - *Poria* - *Dioscorea*, *Astragalus* - *Poria* - *Alisma*, *Astragalus* - *Dioscorea* - *Salvia miltiorrhiza*, and *Astragalus*-*Dioscorea*-*Alisma*. Complex system entropy clustering identified 10 core Chinese medicine combinations for treating diabetic nephropathy, while 5 new formulae were discovered by entropy clustering and improved mutual information method. **Conclusion** *Astragalus*, *Poria*, *Salvia miltiorrhiza*, *Dioscorea*, and *Cornus officinalis* are among the high-frequency core medications used by modern physicians in the treatment of diabetic nephropathy. Chinese medicine treatments for diabetic nephropathy mainly focus on tonifying drugs, complemented by blood-activating and stasis-resolving drugs, diuretic and dampness-resolving drugs, heat-clearing drugs, and astringent drugs to achieve both symptomatic and radical treatment. The pairing of drugs, core combinations, and new formula combinations further illuminate the common compatibility rules of Chinese medicine in treating diabetic nephropathy, providing new perspectives and methodologies for its treatment.

Keywords: Literature research; Data mining; Chinese medicine; Diabetic nephropathy; Medication rule

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糖尿病肾病在中医学中归属“消渴”“肾消”“水肿”范畴,中医认为,该病的病位在肾,从本质上来说是本虚标实,治疗时应以益气养阴、活血化瘀、利湿泄浊为主^[1]。中医在治疗糖尿病肾病时所遵循的整体观念和辨证论治原则,可根据患者的体质和症状制定个性化方案,在缓解症状的同时,调整阴阳平衡,达到标本兼治的效果^[2]。然而,目前多数中医药治疗糖尿病肾病的研究都聚焦于单味药或经典方剂的疗效验证,而较少对海量临床处方的用药规律进行系统性挖掘,不利于中药复方创新^[3]。另外,中医药在治疗糖尿病肾病时具有多靶点、多层次的作用特点,将中医药理论与数据分析相结合,探究不同药物组合之间的协同效应及作用机制,也有助于发现新的治疗靶点,优化现有治疗方案,从而提高糖尿病肾病的治疗效果^[4]。数据挖掘技术为中医药研究提供了新的方法论支持,关联规则分析、复杂网络聚类及熵层次聚类算法能够从大量医案数据中提取核心药物组合、揭示隐性配伍规律,并推测潜在新方,为中医药治疗糖尿病肾病的临床实践提供科学依据^[5]。基于此,本研究旨在运用数据挖掘技术对近十年中医药治疗糖尿病肾病的临床处方进行分析,探索其中的用药规律和潜在机制,以帮助医师深化对中医药治疗该病的认知,为开发新型治疗策略提供理论基础和技术支持,同时为中医药传承与创新研

究提供方法学参考。

1 资料与方法

1.1 数据来源 以“糖尿病肾病”“消渴”“肾消”“糖尿病合并水肿”“中医治疗”“中医药”等作为检索词,使用中国知网、维普中文科技期刊数据库、万方数据库、中国中医药期刊文献数据库进行全面检索,根据纳入标准和排除标准筛选文献,检索时间为2013年1月至2024年12月,共收集整理出相关文献记录327篇。

1.2 纳入和排除标准

1.2.1 纳入标准 (1) 符合糖尿病肾病的中西医诊断标准^[6-7],并确诊为糖尿病肾病;(2) 治疗糖尿病肾病的中医临床研究文献;(3) 以中药复方为主治疗方案;(4) 文献中的方剂包括全部药物组成,且有明确的方药名称、用药剂量;(5) 临床观察类文献不同组别之间治疗有效率差异有统计学意义($P<0.05$)。

1.2.2 排除标准 (1) 动物实验或细胞实验类;(2) 综述或经验总结;(3) 重复出现的文献;(4) 使用针灸、中药熏洗等中医外治疗法;(5) 仅描述症状缓解但无客观指标。

1.3 数据规范 参考《中医临床诊疗术语》^[8]、《中药学》^[9]、《中华人民共和国药典》^[10]、《中药大辞典》^[11]等对中医证候名称及药材名称进行规范化处理,如“脾肾阳虚”“脾肾阳衰”统一归为“脾肾阳虚”;“生黄芪”

“炙黄芪”统一归为“黄芪”等。对于方药剂量统一以克(g)为单位,如“一两”应换算为 3 g。性味归经统计采用“单次首要属性计数”规则,每味药每次使用仅取 1 项首要药性、药味及归经(依据《中药学》^[9]、《中华人民共和国药典》^[10]界定),不重复叠加,各维度内各类别频次之和等于用药总频次。

1.4 数据分析 将标准化处理后的中医诊断、中医证型、方药组成录入 Excel 2019 软件中构建数据库,利用 Excel 条件格式高亮显示超常规药物剂量,人工核对原文进行修正。将标准化后的 Excel 数据导入中医药数据挖掘系统 V2.5 软件,进一步进行数据分析。使用“频次统计”功能统计每种药物在方剂中的出现频次,并对统计结果进行排序,明确高频使用的中药;使用“性味归经”功能生成药物四气五味及归经分布情况,并生成可视化图表;使用“关联关系挖掘”、“聚类挖掘”及“新方分析”功能挖掘药物之间的关联关系,确定高频出现的药对组合,以药物为节点,以药物之间的关联关系为边,构建中医药治疗糖尿病肾病的配伍网络,以可视化图表呈现药物之间的配伍情况;最后,根据用药频次、功效统计、高频药对和配伍网络分析结果,结合根据药物的性味、功效等特征和临床经验,分析中医药治疗糖尿病肾病的组方规律。

2 结 果

2.1 用药频次分析 本研究基于纳入标准和排除标准共筛选 327 篇中医药治疗糖尿病肾病的文献。所纳入的文献涉及中药处方 327 首,中药 205 味,用药频次 2 624 次,根据使用频次进行排序,用药频次前 10 位的药物依次为黄芪、茯苓、丹参、山药、山茱萸、当归、大黄、熟地黄、白术、川芎。药物药性以寒性、温性为主,药味以甘、苦为主,多归肝经、肾经、脾经。见表 1、表 2 和图 1、图 2、图 3。

2.2 高频用药功效统计 205 味中药根据功效可分为 17 类,其中频率最高的前五位分别为补虚药(频次 998,频率 38.03%)、活血化瘀药(频次 445,频率 16.96%)、利水渗湿药(频次 314,频率 11.97%)、清热药(频次 238,频率 9.07%)、收涩药(频次 165,频率 6.29%)。见表 3。

2.3 药物关联规律分析 对本研究中的 205 味中药进行分析,使用 Apriori 算法挖掘药对组合,将支持度设置为 ≥ 0.2 ,置信度设置为 ≥ 0.8 ,将提升度 >1 的关联组合认为有意义,最终得到 29 条关联组合,其中频次

表 1 用药频次统计(前 30 位)
Tab.1 Medication frequency statistics (top 30)

序号	药名	频次	频率(%)	处方百分比(%)
1	黄芪	184	7.01	56.27
2	茯苓	161	6.14	49.24
3	丹参	131	4.99	40.06
4	山药	115	4.38	35.17
5	山茱萸	97	3.70	29.66
6	当归	94	3.58	28.75
7	大黄	90	3.43	27.52
8	熟地黄	88	3.35	26.91
9	白术	82	3.13	25.08
10	川芎	73	2.78	22.32
11	泽泻	73	2.78	22.32
12	益母草	72	2.74	22.02
13	甘草	70	2.67	21.41
14	党参	69	2.63	21.10
15	牡丹皮	64	2.44	19.57
16	太子参	55	2.10	16.82
17	黄精	55	2.10	16.82
18	牛膝	53	2.02	16.21
19	地黄	53	2.02	16.21
20	麦冬	47	1.79	14.37
21	桃仁	46	1.75	14.07
22	枸杞子	44	1.68	13.46
23	知母	42	1.60	12.84
24	地龙	40	1.52	12.23
25	五味子	38	1.45	11.62
26	红花	30	1.14	9.17
27	菟丝子	27	1.03	8.26
28	水蛭	24	0.91	7.34
29	赤芍	24	0.91	7.34
30	肉桂	23	0.88	7.03

表 2 主要中药性味归经统计
Tab.2 Statistics of main Chinese medicine nature, flavor and meridian entry

四气			五味			归经		
名称	频次	频率(%)	名称	频次	频率(%)	名称	频次	频率(%)
寒	855	32.58	甘	998	38.03	肝经	497	18.94
温	793	30.22	苦	696	26.52	肾经	448	17.07
平	705	26.87	辛	458	17.45	脾经	440	16.77
凉	182	6.94	酸	197	7.51	心经	345	13.15
热	89	3.39	涩	166	6.33	肺经	318	12.12
			咸	109	4.16	胃经	183	6.97
						膀胱经	102	3.89
						心包经	100	3.81
						大肠经	79	3.01
						胆经	57	2.17
						小肠经	34	1.30
						三焦经	21	0.80

最高的2味药组合为黄芪-茯苓、黄芪-丹参、黄芪-当归、黄芪-山药、黄芪-山茱萸,频次最高的3味药组合为黄芪-茯苓-山茱萸、黄芪-茯苓-山药、黄芪-茯苓-泽泻、黄芪-山药-丹参、黄芪-山药-泽泻。见表4、表5。

2.4 组方规律分析 基于2.3中的结果,设置相关系数为5,惩罚度为2,使用复杂系统熵聚类法分析核心组合,得到10个中药治疗糖尿病肾病的核心组合;使用熵聚类及改进互信法挖掘新方组合,得到5个治疗糖尿病肾病的新方组合,分别为茯苓-白术-

黄芪-麦冬,山茱萸-山药-熟地黄-牡丹皮,太子参-麦冬-五味子-玉米须,杜仲-续断-牛膝-桑寄生,桑螵蛸-金樱子-芡实-菟丝子。见表6和图4、图5。

表3 高频用药功效各类别主要药物统计分析结果

Tab.3 Statistical analysis results of main drugs in various categories of high-frequency drug efficacy

分类	主要药物及使用频次
补虚药	
补气药	黄芪(184)、山药(115)、白术(82)、甘草(70)、党参(69)、太子参(55)、人参(15)、西洋参(7)、大枣(2)、红景天(2)、红参(1)
补血药	当归(94)、熟地黄(88)、白芍(12)、阿胶(6)、何首乌(4)
补阴药	黄精(55)、麦冬(47)、石斛(15)、女贞子(10)、沙参(5)、桑椹(2)、天冬(1)
补阳药	菟丝子(27)、杜仲(11)、冬虫夏草(10)、补骨脂(5)、巴戟天(3)、仙茅(1)
活血化瘀药	
活血调经药	丹参(131)、益母草(72)、牛膝(53)、桃仁(46)、红花(30)、鸡血藤(6)
活血止痛药	川芎(73)、姜黄(5)、五灵脂(2)
破血消癥药	水蛭(24)、鬼箭羽(2)、三棱(1)
利水渗湿药	
利水消肿药	茯苓(161)、泽泻(73)、薏苡仁(22)、玉米须(16)、冬瓜皮(5)
利水通淋药	车前子(18)、草薢(10)、车前草(6)
祛湿退黄药	虎杖(3)
清热药	
清热凉血药	牡丹皮(64)、地黄(53)、赤芍(24)
清热解毒药	连翘(5)、八仙草(2)、板蓝根(2)、半枝莲(1)、金银花(1)
清热泻火药	知母(42)、夏枯草(13)、决明子(4)
清热燥湿药	黄连(13)、黄柏(6)、积雪草(2)
收涩药	
清虚热药	地骨皮(5)、青蒿(1)
敛肺涩肠药	五味子(38)
固精缩尿药	山茱萸(97)、桑螵蛸(12)
止带药	芡实(15)、金樱子(3)

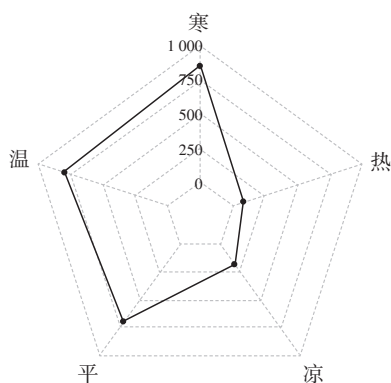


图1 四气频次统计雷达图

Fig.1 Four-gas frequency statistical radar chart

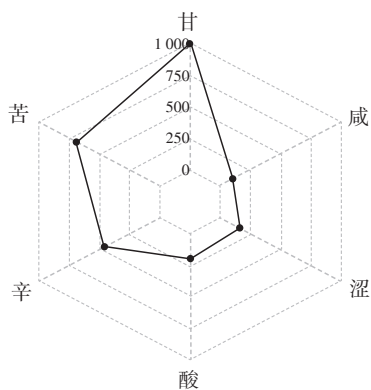


图2 五味频次统计雷达图

Fig.2 Five flavor frequency statistical radar chart

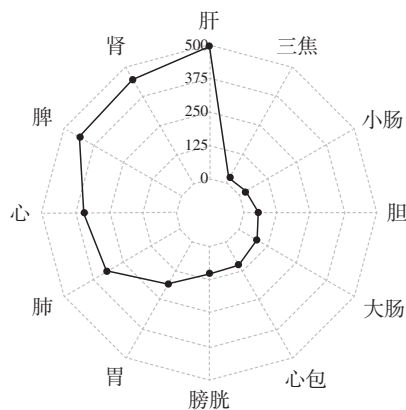


图3 归经频次统计雷达图

Fig.3 Statistical radar chart of meridian frequency

表4 高频2味药组合统计(前10位)

Tab.4 Statistics of high-frequency 2-herb combinations (top 10)

序号	药对组合	支持度	置信度	提升度	主要功效
1	黄芪-茯苓	0.40	0.88	1.26	补气利水
2	黄芪-丹参	0.39	0.90	1.57	补气活血
3	黄芪-当归	0.37	0.86	1.33	益气双补
4	黄芪-山药	0.35	0.77	1.24	补气健脾
5	黄芪-山茱萸	0.33	0.80	1.36	补气益肾
6	茯苓-山药	0.33	0.72	1.30	健脾利湿
7	黄芪-白术	0.32	0.85	1.27	健脾益气
8	黄芪-川芎	0.31	0.82	1.11	行气补气
9	山药-当归	0.30	0.87	1.18	健脾养血
10	黄芪-泽泻	0.30	0.79	1.08	利水消肿

表5 高频3味药组合统计(前10位)
Tab.5 Statistics of high-frequency 3-herb combinations (top 10)

序号	药物组合	支持度	主要功效
1	黄芪-茯苓-山茱萸	0.38	补气养阴固肾
2	黄芪-茯苓-山药	0.37	健脾益气固肾
3	黄芪-茯苓-泽泻	0.36	利水消肿补气
4	黄芪-山药-丹参	0.36	活血化瘀补气
5	黄芪-山药-泽泻	0.34	补气利湿固肾
6	黄芪-山药-山茱萸	0.34	滋阴补肾强体
7	黄芪-山药-当归	0.34	补血调经益气
8	黄芪-丹参-泽泻	0.33	活血利水补气
9	黄芪-当归-川芎	0.31	补血行气活血
10	黄芪-山茱萸-地黄	0.31	滋阴补肾填精

表6 基于复杂系统熵聚类法的核心组合
Tab.6 Core combinations based on complex system entropy clustering method

序号	核心组合	序号	核心组合
1	茯苓-白术-黄芪	6	丹参-川芎-赤芍
2	大黄-肉桂-黄芪	7	杜仲-续断-牛膝
3	山茱萸-山药-熟地黄	8	桃仁-红花-赤芍
4	太子参-麦冬-五味子	9	大黄-附子-细辛
5	水蛭-黄芪-当归	10	桑螵蛸-金樱子-芡实

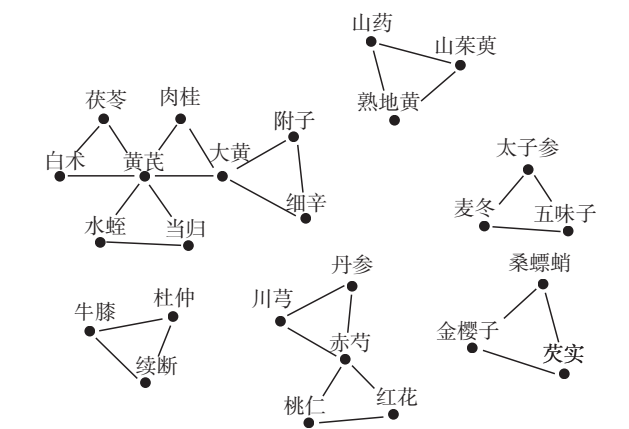


图4 中医药治疗糖尿病肾病的核心组合图谱
Fig.4 The core combination map of Chinese medicine in the treatment of diabetic nephropathy

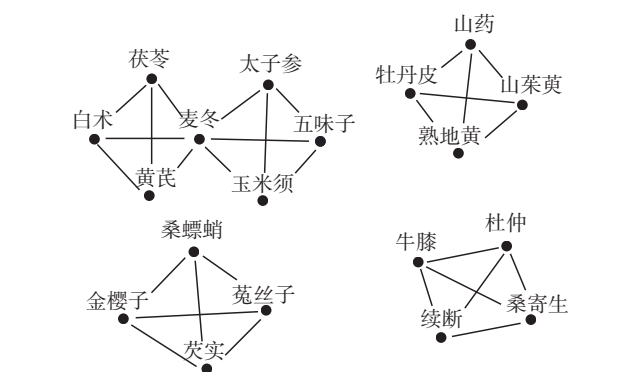


图5 中医药治疗糖尿病肾病的新方组合图谱
Fig.5 New prescription combination map of Chinese medicine in the treatment of diabetic nephropathy

3 讨论

糖尿病肾病作为糖尿病患者最常见的并发症,一直是国内外学者的研究热点。目前西医治疗糖尿病肾病主要采取降糖、降压、调脂等方法,对改善远期肾脏终点事件的发生有一定帮助,但西医治疗主要针对单一靶点,难以进行全面干预,患者长期服用多种药物也会面临药物不良反应和停药后复发的风险^[12-14]。中医药在改善糖尿病肾病患者临床症状、延缓疾病进展方面具有独特优势,但对方剂的系统性挖掘仍显不足。本研究基于327首中药处方,使用数据挖掘技术探究糖尿病肾病的中医药治疗核心用药组合及潜在新方组合,以期为糖尿病肾病的防治提供更多的科学依据。

中医认为,糖尿病肾病发病受到多个方面相互作用的影响,肾气不足、脾胃功能失调、肝气疏泄受阻等均是本病发生的重要诱因^[15-16]。可见系统分析临床中药处方,揭示常用药物及组合模式,有助于更好地制定基于个体差异的精准治疗策略,让更多的患者了解并受益于中医药治疗。本研究共纳入327首中药处方,涉及205味中药,高频药物以黄芪、茯苓、丹参、山药、山茱萸等为主,其中黄芪以绝对优势居于首位。这一结果与中医“脾肾两虚为本,痰瘀浊毒为标”的病机理论高度契合^[17]。黄芪作为补气药,具有补气固表、利水消肿的功效,其高频使用提示“补气”在糖尿病肾病治疗中的作用重大^[18]。茯苓以其利水渗湿的功效著称,山药可帮助益气养阴、补脾肺肾,这两味药物的高频使用体现了中医药治疗糖尿病肾病时对脾肾功能的重视^[19-20]。瘀血是糖尿病肾病疾病发展过程中不可或缺的一环,丹参的应用不仅可以改善本病瘀血所致的症状,还可缓解患者气血亏虚^[21]。对于糖尿病肾病患者来说,山茱萸收涩固脱的功效可帮助增强机体抵抗力,防止精气外泄,在维持体内环境稳定方面具有关键作用^[22]。药物性味归经分析显示,糖尿病肾病中医药治疗的药物大多为寒性或温性,且药味以甘、苦为主,多归于肝、肾、脾三经,揭示了本病治疗时温寒并用、甘苦相佐、肝脾肾三经并重的动态平衡策略。

在本研究中,205味中药按功效可分为17类,其中补虚药、活血化瘀药、利水渗湿药、清热药和收涩药占据了较大的比例,这种分布模式反映了中医药治疗糖尿病肾病时对补益脾肾、利水渗湿、活血化瘀、清热泻火的重视,此外,收涩药的广泛应用也体现了中医“固摄”思想,与其他功效药物协同,可形成

多维度干预网络,进一步验证了本病“补虚-利水-活血”的复合治则,也与现代医学“代谢-炎症-纤维化”病理轴的多靶点干预需求相呼应。这些药物的协同作用不仅体现在四气五味调和与归经导向的多元干预中,也在高频药对组合及药物配伍中得到了充分展示。本研究采用Apriori算法挖掘出的29条关联组合为糖尿病肾病的中医药治疗提供了新视角。如2味药中频次最高的黄芪-茯苓组合:黄芪补气升阳,促进水液气化,茯苓健脾渗湿,导水下行,二者一升一降,共奏益气利水之功,体现了“气水同治”的思想;再如3味药中频次最高的黄芪-茯苓-山茱萸组合:黄芪补脾益气,茯苓利水健脾,山茱萸补肾固精,三者形成“补而不滞、利不伤正”的闭环调节,契合了“脾肾同调”的理论。本研究进一步使用复杂系统熵聚类法分析核心组合,得到10个中药治疗糖尿病肾病的核心组合,这些组合代表了目前临床上较为成熟有效的治疗方案,而通过熵聚类及改进互信息法挖掘的5个新方组合则可良好体现数据挖掘与传统中医理论的融合,这些新方组合突破了传统方剂的固定框架,体现了“病证结合、动态调整”的精准治疗思维,可能较单一治法更具临床适应性。如茯苓-白术-黄芪的核心功效是益气健脾,渗湿利水,可改善处于“脾虚湿盛”阶段患者的水钠潴留及蛋白尿症状,在此基础上加入具有滋阴效果的麦冬,则可实现益气利水、养阴生津的效果,适用于更多类型的患者。山茱萸-山药-熟地黄可通过补肾养阴、固摄精气的方式有效改善脾肾两虚证患者疲劳、乏力、夜尿频多等临床表现,牡丹皮的加入可增强对血分瘀热的调节,核心组合针对“虚”与“失固”,新增牡丹皮则针对“热”与“瘀”,形成“补虚-清热-化瘀”复合治法,这使得新方在应对复杂症状时更为全面。可见,“核心组合-新方组合”的演化路径既体现了数据挖掘对隐性规律的揭示能力,也符合中医“辨证论治,随证加减”的临床思维,为糖尿病肾病的中医药精准治疗提供了范例。

综上所述,黄芪、茯苓、丹参、山药、山茱萸等为现代医家治疗糖尿病肾病的高频核心药物,中医治疗糖尿病肾病多以补虚药为主,同时配合活血化瘀药、利水渗湿药、清热药、收涩药等以达到标本兼治的作用,药对组合、核心组合、新方组合进一步揭示了中医药治疗糖尿病肾病的常用配伍规律,为中医

药治疗糖尿病肾病提供了新的思路和方法。

利益冲突 无

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