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Diagnosis and treatment of diabetic cardiovascular autonomic neuropathy with Chinese medicine and Western medicine

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Abstract: Diabetic cardiac autonomic neuropathy (DCAN) is one of the common complications of diabetes, significantly increasing the risk of various adverse cardiovascular events. However, DCAN has an insidious onset and severe consequences, and there are currently no effective medications to delay or reverse the progression of the disease. Therefore, early prevention and control of DCAN are crucial. This paper focuses on the recent advance in the diagnosis and treatment of DCAN in Chinese medicine and Western medicine, to provide insights for early prevention and control, new drug development, and the formulation of integrated treatment strategies combining both approaches for DCAN .

Keywords: Diabetes mellitus; Cardiac autonomic neuropathy; Chinese medicine and Western medicine; Treatment based on syndrome differentiation; Metabolic disorder; Nerve nutrition; Sodium-glucose cotransporter 2 inhibitor

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Diabetic cardiovascular autonomic neuropathy (DCAN) is a common complication of diabetes mellitus, characterized by impairment of cardiovascular autonomic function, and the diagnosis can only be established after the exclusion of other possible etiologies [1-2]. DCAN exhibits an insidious onset, with clinical manifestations that progress gradually. In the early stage of the disease, it primarily presents with symptoms of autonomic dysfunction, including reduced heart rate variability (HRV), increased resting heart rate, and decreased exercise tolerance. As the disease advances, it may progressively develop into severe complications such as orthostatic hypotension and silent myocardial infarction, and may ultimately lead to sudden cardiac death. This series of pathophysiological alterations constitutes a significant mortality risk factor for patients with diabetes mellitus [3].

From the perspective of traditional Chinese medicine (TCM), DCAN is approached based on its etiology and pathogenesis, adhering to the preventive philosophy of "preventing disease before it occurs, preventing progression when it has already occurred, and preventing recurrence after recovery," with treatment administered according to syndrome differentiation following the pattern of syndrome evolution. Western medicine, on the other hand, primarily manages DCAN through glycemic control, neurotrophic support, and alleviation of cardiovascular clinical symptoms. The present article aims to analyze the pathogenesis and therapeutic advances of DCAN from both TCM and Western medicine perspectives, thereby providing an important theoretical basis for its clinical prevention and treatment.

1 Understanding and Treatment of DCAN from the TCM Perspective

1.1 TCM Understanding of the Etiology and Pathogenesis of DCAN

In TCM, DCAN does not have a specific disease name; based on its clinical manifestations, it is classified under the category of "palpitations" (Zhengchong, 怔忡). The Jingyue Quanshu (Complete Works of Jingyue, 景岳全书) states: "The disease of palpitations... this syndrome is seen only in patients with yin deficiency and consumptive damage, for when yin is deficient below, the ancestral qi lacks root, and qi fails to return to its source." TCM holds that the disease location of DCAN is in the heart, involving the three viscera of the heart, spleen, and kidney. The pathogenesis of palpitations is mainly related to deficiency of healthy qi in the body, and its causes can be summarized as congenital insufficiency, emotional disturbance, or prolonged illness leading to depletion, resulting in imbalance of qi, blood, yin, and yang, which gives rise to palpitations.

National Master of TCM Lyu Renhe recognized DCAN from the perspective of "collaterals-capillaries," and considered that deficiency of the heart collaterals constitutes its basic pathogenesis, while stasis in the collateral vessels is the key factor in disease progression. In terms of treatment, according to the characteristic that "collaterals function through patency," he advocated the methods of supplementing deficiency, activating blood, and unblocking collaterals, combining supplementation and unblocking [4]. Based on the statement in the Nanjing·Fourteen Difficulties that "when the heart is damaged, regulate the nutritive and defensive qi," some scholars have proposed a treatment regimen with "regulating the nutritive and defensive qi" as the fundamental principle: supplementing for those with

deficiency of nutritive and defensive qi, promoting patency for those with stagnation, and harmonizing for those with disharmony, with the emphasis on restoring the balance of qi, blood, yin, and yang in the body, so that when the nutritive and defensive qi are harmonized, the disease will resolve naturally [5]. The Suwen·Yinyang Yingxiang Dalun records: "Pungent and sweet, dispersing and emitting, pertain to yang; sour and bitter, purging and draining, pertain to yin" [6]. Accordingly, Sun Xuemei et al. [7] proposed the therapeutic principle of combining sour and bitter flavors to eliminate heart fire and treat palpitations. Guo Lizhong *et al*. [8], based on Professor Zhou Zhongying's "three-heat theory," suggested that the treatment of DCAN should follow the principles of simultaneously clearing all three types of heat, concurrently treating qi and blood, and addressing both the root and the branch, with clearing and moistening-drying approaches advanced together, and resolving dampness and eliminating stasis combined with generating fluids and cooling-moistening.

1.2 TCM Treatment of DCAN

1.2.1 Chinese Herbal Medicine Treatment

Yu Jinlian et al. [9] found that Mudan Granules possess the effects of activating blood, resolving stasis, and supplementing primordial qi, and can restore the elasticity of the vascular wall, increase blood flow, improve nerve conduction velocity, and alleviate diabetic symptoms. Gao Qian et al. [10] also found that the combination of Mudan Granules and mecobalamin was superior to mecobalamin alone in improving electrocardiographic parameters in patients with DCAN, as it significantly enhanced parameters including QT dispersion (QTd), the Tpeak-to-Tend interval (Tp-e), and the Tp-e/QT ratio, demonstrating potential clinical value for the prevention of arrhythmias. Additionally, Cai Huijuan et al. [11] treated DCAN patients with qi-yin deficiency pattern using Shensong Yangxin Capsules combined with mecobalamin, and found that after 12 weeks, the treatment group showed lower scores on the Scales for Outcomes in Parkinson's Disease-Autonomic Dysfunction (SCOPA-AUT) and the Composite Autonomic Symptom Score-31 (COMPASS-31) compared with the control group, while QTd and the Valsalva ratio were higher. Yu Donglei [12] treated DCAN patients with heart-spleen deficiency pattern using Guipi Decoction, and patients with heart-yin-blood deficiency pattern using Xuefu Zhuyu Decoction, with a treatment course of 2 months, and found that parameters including respiratory difference, the ratio of cardiac intervals, and recumbent heart rate were significantly improved after treatment. Chinese herbal medicines primarily improve DCAN symptoms and clinical parameters by enhancing blood circulation and neural function, and the combined TCM-Western medicine treatment regimens have demonstrated superior efficacy.

1.2.2 Acupuncture Treatment

Acupuncture has certain therapeutic effects on diabetic neurological complications, with advantages including low cost and few adverse reactions. Potential mechanisms may include improvement of pancreatic islet function, reduction of blood glucose, regulation of relevant hormones, and restoration of the balance between sympathetic and parasympathetic nerves [13-14]. A domestic clinical study demonstrated that alpha-lipoic acid combined with acupuncture at Neiguan (PC6), Pishu (BL20), Zusanli (ST36), and Taixi (KI3) yielded better therapeutic effects on HRV parameters compared with alpha-lipoic acid alone [15]. Xu Min et al. [16] found that after acupuncture at Lingtai (GV10) and Shendao (GV11), the frequency-domain HRV parameter low-frequency (LF)/high-frequency (HF) ratio in DCAN patients decreased significantly, suggesting that acupuncture at these points may be associated with improved balance between sympathetic and vagal function. Yan Liu et al. [17] conducted a randomized controlled study comparing the effects of acupuncture at different acupoints on DCAN patients, and the results showed that compared with the Xuanzhong (GB39) group, the Neiguan (PC6) group had a significantly higher HF, indicating that acupuncture at Neiguan can effectively enhance cardiac vagal activity. Currently, acupuncture treatment for DCAN remains predominantly based on clinical observational studies, and further basic research is required to elucidate its specific molecular mechanisms.

2 Understanding and Treatment of DCAN from the Western Medicine Perspective

2.1 Western Medicine Understanding of the Pathogenesis of DCAN

2.1.1 Glucose and Lipid Metabolic Disorders

Chronic hyperglycemia can lead to metabolic disturbances in nerve cells, increase oxidative stress, and result in neuronal damage. Under hyperglycemic conditions, the activation of the polyol pathway is enhanced, leading to intracellular accumulation of sorbitol, which in turn triggers intracellular oxidative stress responses and damages nerve cells [18]. Patients with diabetes mellitus often present with lipid metabolic disorders, such as elevated triglyceride and cholesterol levels. An animal study has demonstrated that lipid metabolic disturbances can alter the lipid composition of neuronal cell membranes, affecting the function and structure of nerve cells [19]. Jang et al. [20] showed that the triglyceride-to-high-density lipoprotein cholesterol ratio and the mean particle size of low-density lipoprotein cholesterol were positively correlated with the prevalence of DCAN in female patients with type 2 diabetes mellitus. These studies collectively indicate that glucose and lipid metabolic disorders are among the pathogenic mechanisms of DCAN.

2.1.2 Oxidative Stress

Oxidative stress is an important factor in the pathogenesis of diabetic neuropathy, involving both increased formation of free radicals and defective antioxidant defenses [21]. Hyperglycemia leads to

excessive production of reactive oxygen species, which can damage nerve cells and result in autonomic dysfunction [22]. Oxidative stress not only affects neurons but also impacts the neurovascular system, thereby exacerbating the progression of DCAN [23]. An international study suggested that oxidative stress primarily triggers autonomic dysfunction through oxidative-mediated inactivation of neuronal nicotinic acetylcholine receptors (nAChRs), affecting synaptic transmission in sympathetic ganglia and leading to autonomic failure [24].

2.1.3 Inflammation

Studies have indicated that inflammatory cytokines play a dual role in the development and progression of DCAN, being both closely associated with its pathogenesis and directly involved in the pathophysiological processes of disease progression [25]. Another study demonstrated that glomus cells related to the autonomic nervous system can specifically sense oxygen, glucose, and other metabolites. Interleukin (IL)-1 binds to glomus cells, activates Toll-like receptors, and leads to increased expression of nuclear factor kappa-B (NF-κB) and subsequent release of inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and IL-6, and these inflammatory changes are associated with abnormalities in the sympathetic-parasympathetic balance [26]. A cross-sectional study showed that plasma levels of leukotriene B4 (LTB4) in patients with type 2 diabetes mellitus may be associated with cardiovascular autonomic neuropathy, independent of the degree of glycemic control [27]. The above studies indicate a certain relationship between DCAN and inflammation, but further research is still needed to elucidate the specific roles and mechanisms of inflammation in DCAN.

2.1.4 Genetic Factors

The genetic predisposition to DCAN involves multiple genes and genetic markers. Tang et al. [28] found that in patients with type 2 diabetes, the genetic locus rs779142 located on chromosome 1p36 was significantly associated with the development of DCAN, with this variant increasing the risk of DCAN by 35%. In addition, the human leukocyte antigen (HLA)-DR3/4 phenotype has also been closely associated with the development of DCAN in patients with type 1 diabetes, indicating that genetic factors play an important role in the development of DCAN [29]. Further studies have shown that polymorphisms of the HLA-DQB1 gene are also associated with susceptibility and resistance to type 1 diabetes, which may indirectly affect the development of DCAN [30]. These findings provide important clues for understanding the genetic basis of DCAN and may offer potential targets for future therapeutic strategies.

2.2 Western Medicine Treatment of DCAN

2.2.1 Lifestyle Modification

Studies have shown that Mediterranean diet, aerobic exercise, smoking cessation, glycemic control, blood pressure lowering, lipid regulation, and health education can effectively prevent DCAN [31]. An international study demonstrated that lifestyle intervention (including yoga practice and restriction of dietary fat intake) in patients with prediabetes significantly improved cardiac function indices [32]. Furthermore, Ziegler et al. [33] showed that after 12 weeks of combined aerobic exercise and resistance training, HRV indices in both time-domain and frequency-domain parameters decreased significantly compared with baseline in both the control and exercise groups. Compared with the control group, combined exercise significantly increased time-domain indices [standard deviation of normal-to-normal intervals (SDNN) and root mean square of successive differences (RMSSD)] and frequency-domain indices (LF/HF) in DCAN patients, suggesting that combined aerobic and resistance training is beneficial for the prevention and control of DCAN.

2.2.2 Correction of Metabolic Disorders

Chronic hyperglycemia is a major risk factor for the development of DCAN in patients with diabetes mellitus [34]. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) confirmed that intensive glycemic control strategies can effectively reduce the incidence of both peripheral neuropathy and DCAN in diabetic patients [35]. Tang et al. [36] found in the ACCORD study that during a median follow-up of 5 years, intensive glycemic and blood pressure interventions exerted significant protective effects against DCAN in patients with type 2 diabetes. The Steno-2 study on multifactorial intervention and cardiovascular outcomes in type 2 diabetic patients demonstrated that combined control of blood pressure, glycated hemoglobin, triglycerides, and total cholesterol significantly reduced the risk of developing autonomic neuropathy [37].

2.2.3 Neurotrophic Therapy

Alpha-lipoic acid is a natural antioxidant and is widely used in the treatment of diabetic peripheral neuropathy, with multiple effects including improvement of glucose homeostasis and lipid profiles, anti-inflammatory activity, and reduction of oxidative stress [38-39]. A 4-year study of alpha-lipoic acid treatment for diabetic peripheral neuropathy showed that alpha-lipoic acid significantly improved the deep breathing test results in patients with diabetic peripheral neuropathy who were receiving angiotensin-converting enzyme inhibitor (ACEI) therapy, suggesting that the combination of alpha-lipoic acid and ACEI may confer additional DCAN protective effects [40]. In addition, Tankova et al. [41] included 46 patients with type 1 diabetes in their study; the patients first received intravenous alpha-lipoic acid at 600 mg for 10 days, followed by oral alpha-lipoic acid at 600 mg for 50 days, and the results showed that the Cardiovascular Autonomic Reflex Tests (CARTs) score improved significantly. However, these findings remain primarily based on clinical studies, and further basic research is needed to elucidate the underlying mechanisms.

2.2.4 Treatment of Orthostatic Hypotension

Orthostatic hypotension caused by severe DCAN can

be managed through pharmacological and non-pharmacological approaches [42-43]. Non-pharmacological treatment mainly consists of lifestyle adjustments, including adequate fluid intake, appropriate high-sodium diet, and prolonged standing time [43-44]. Commonly used pharmacological interventions encompass multiple mechanisms of action, including α-receptor agonists (midodrine), mineralocorticoids (fludrocortisone), norepinephrine precursors (droxidopa), hematopoietic stimulants (erythropoietin), antidiuretic hormones (desmopressin), gastrointestinal hormones (somatostatin analogues), and β-receptor blockers [45-48]. Approved by the U.S. Food and Drug Administration, droxidopa and midodrine are the two standard therapeutic agents for neurogenic orthostatic hypotension [48]. As a mineralocorticoid, fludrocortisone exerts its therapeutic effects by promoting sodium and water retention and enhancing vascular sensitivity to catecholamines, but its clinical application may be associated with adverse effects such as orthostatic hypertension and electrolyte disturbances [45-48]. Selective β-blockers (e.g., ivabradine) can be used for the treatment of postural tachycardia syndrome [49].

2.2.5 Other Pharmacological Treatments

Sodium-glucose linked transporter-2 (SGLT-2) inhibitors, as a novel class of oral hypoglycemic agents, have important clinical therapeutic value. They lower blood glucose by inhibiting glucose reabsorption in the proximal renal tubules, with representative drugs including dapagliflozin and empagliflozin. Clinical data have demonstrated that dapagliflozin (10 mg/d) administered to DCAN patients for 24 weeks significantly improved HRV [50]. An animal study indicated that sympathetic denervation in obese type 2 diabetic mice was associated with inhibition of SGLT-2 overexpression [51]. Moreover, in a high-fat diet-induced C57BL6/J mouse model, dapagliflozin significantly suppressed the expression of tyrosine hydroxylase in cardiac and renal tissues, thereby reducing norepinephrine biosynthesis [52], whereas in an alloxan-induced diabetic rabbit model, empagliflozin restored renal sympathetic reflexes [53]. These findings suggest that the sympathetic nervous system is closely related to SGLT-2 levels, and that SGLT-2 inhibitors can effectively improve cardiovascular autonomic function; however, more comprehensive studies are still needed to identify the optimal therapeutic regimen for DCAN.

3 Conclusion

The present article has reviewed the pathogenesis and therapeutic advances of DCAN from both traditional Chinese medicine and Western medicine perspectives. As a serious complication of diabetes mellitus, DCAN is characterized by high prevalence, concealed clinical manifestations, and poor prognosis. Recent studies have revealed that traditional Chinese medicine has certain therapeutic efficacy against DCAN. How to fully integrate it with Western medical therapies and leverage the respective advantages for the treatment of DCAN warrants further consideration and investigation. Future research should further utilize integrated traditional Chinese and Western medicine approaches, conduct prospective high-quality clinical studies and related basic research, provide a theoretical foundation for the pathogenesis and treatment strategies of DCAN, and offer clinical evidence for new drug development and the formulation of integrated TCM-Western medicine diagnostic and therapeutic protocols.

Conflict of Interest None

References

[1] Eleftheriadou A, Spallone V, Tahrani A A, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management[J]. Diabetologia, 2024, 67(12): 2611-2625.
[2] Branch Group of Neurological Complications. National guidelines for the diagnosis and treatment of diabetic neuropathy in primary care (2024 edition) [J]. Chin J Diabetes Mellitus,2024,16(5): 496-511 .
[3] Agashe S, Petak S. Cardiac autonomic neuropathy in diabetes mellitus[J]. Methodist Debakey Cardiovasc J, 2018, 14(4): 251-256. **[In Chinese]**
[4] WANG Shiyao, WANG Shidong, FU Qiang, et al. Origin and development of LYU Ren-he's pathological hypothesis of 'micro-Zhengjia' theory[J]. China J Tradit Chin Med Pharm, 2022, 37(8): : 4555-4559. **[In Chinese]**
[5] Tang Rumeng, Wang Shan, Yuan Ruyue, et al. Based on "those who damage their heart, adjust their health", the differentiation and treatment of diabetic cardiac autonomic neuropathy are analyzed[J]. Glob Tradit Chin Med, 2023, 16(11): 2323-2326. **[In Chinese]**
[6] Huang Zuozhen. Guo Aichun's exegetic achievement in "collation, annotation and translation of yellow emperor's canon of internal medicine - plain questions"[J]. J Beijing Univ Tradit Chin Med, 2005, 28(6): 22-25. **[In Chinese]**
[7] Sun Xuemei, Zhang Meng, Mao Chenhan, et al. Syndrome identification and treatment of diabetic cardiac autonomic neuropathy by the method of regulating astringency with sour and bitter flavors[J]. J Nanjing Univ Tradit Chin Med, 2021, 37(4): 570-573. **[In Chinese]**
[8] Guo Lizhong, Wu Mianhua, Zhou Xueping, et al. Summary of professor ZHOU Zhong-Ying's academic thoughts[J]. J Nanjing Univ Tradit Chin Med Nat Sci, 2008, 24(6): 361-365. **[In Chinese]**
[9] Yu Jinlian, Zhong Qiurun, Yu Yufeng, et al. Meta analysis of clinical efficacy of Mudan Granule combined with mecobalamin in the treatment of diabetic peripheral neuropathy[J]. Diabetes New World, 2022, 25(2): 33-38. **[In Chinese]**
[10] Gao Qian, Jia Rongmei, Yang Limei, et al. Effect of Mudan Granule combined with Mecobalamin on the end of ECG T peak in patients with diabetic cardiovascular autonomic neuropathy[J]. Beijing Med J, 2020, 42(4): 352-354. **[In Chinese]**
[12] Yu Donglei. Clinical effect of TCM syndrome differentiation on diabetic cardiovascular autonomic neuropathy[J]. Guide China Med, 2019, 17(6): : 146-147. **[In Chinese]**
[13] Wang Lin, Wang Limin. Perspective on acupuncture treatment for diabetic peripheral neuropathy: a perspective[J]. Medicine, 2025, 104(23): e42646.
[14] Wang Chunliang, Fan Yuzhu, Liang Guiting, et al. Acupuncture for the treatment of painful diabetic peripheral neuropathy: a systematic review and meta-analysis[J]. Complement Ther Clin Pract, 2024, 57: 101889.
[15] Li Xiaoshan. Clinical observation on lipoic acid combined with acupuncture in the treatment of diabetic cardiovascular autonomic neuropathy[J]. J Pract Tradit Chin Med, 2019, 35(1): : 61-62. **[In Chinese]**
[16] Xu Min, Guo Li, Cui Huafeng, et al. Effect of acupuncture at Lingtai(GV10) and Shendao(GV11) on heart rate variability in patients with diabetic cardiac autonomous neuropathy[J]. Shanghai J Acupunct Moxibustion, 2019, 38(6): 588-591. **[In Chinese]**
[17] Yan Liu, Sun Wei, Wang Changchun, et al. Effect of needling PC6 on HRV of DCAN patients[J]. J Clin Acupunct Moxibustion, 2019, 35(5): 34-36. **[In Chinese]**
[18] Liu Hailin, Zhou Lian, Wang Xifeng, et al. PIEZO1 as a new target for hyperglycemic stress-induced neuropathic injury: The potential therapeutic role of bezafibrate[J]. Biomed Pharmacother, 2024, 176: 116837.
[19] Kotredes K P, Pandey R S, Persohn S, et al. Characterizing molecular and synaptic signatures in mouse models of late-onset Alzheimer's disease independent of amyloid and tau pathology[J]. Alzheimers Dement, 2024, 20(6): 4126-4146.
[20] Jang E H, Park Y M, Hur J, et al. Higher levels of small dense low-density

lipoprotein (LDL) are associated with cardiac autonomic neuropathy in patients with type 2 diabetes[J]. Diabet Med, 2013, 30(6): 694-701.
[21] Sharan L, Pal A, Babu S S, et al. Bay 11-7082 mitigates oxidative stress and mitochondrial dysfunction via NLRP3 inhibition in experimental diabetic neuropathy[J]. Life Sci, 2024, 359: 123203.
[22] Khodaie S A, Razavi R, Nikkhah H, et al. Nigella sativa L. and its bioactive and nutraceutical components in the management of diabetic peripheral neuropathy[J]. Inflammopharmacology, 2024, 32(5): 2897-2920.
[23] Stoian A, Muntean C, Babă D F, et al. Update on biomarkers of chronic inflammatory processes underlying diabetic neuropathy[J]. Int J Mol Sci, 2024, 25(19): 10395.
[24] Chandna A R, Nair M, Chang C, et al. RAGE mediates the inactivation of nAChRs in sympathetic neurons under high glucose conditions[J]. Eur J Neurosci, 2015, 41(3): 341-351.
[25] Wang Zhaoxiang, Zhang Li, Lu Bing, et al. Causal relationships between circulating inflammatory cytokines and diabetic neuropathy: a Mendelian Randomization study[J]. Cytokine, 2024, 177: 156548.
[26] Hansen M K, O'Connor K A, Goehler L E, et al. The contribution of the vagus nerve in interleukin-1beta-induced fever is dependent on dose[J]. Am J Physiol Regul Integr Comp Physiol, 2001, 280(4): R929-R934.
[27] Neves J A J, De Matos M R, Ramalho T, et al. Increased leukotriene B4 plasma concentration in type 2 diabetes individuals with cardiovascular autonomic neuropathy[J]. Diabetol Metab Syndr, 2020, 12(1): 99.
[28] Tang Yaling, Shah H, Sun Xiuqin, et al. 321-OR: a genetic locus on chromosome 1p36 associated with cardiovascular autonomic neuropathy in type 2 diabetes[J]. Diabetes, 2019, 68(Supplement_1): 321-3OR.
[29] Barzilay J, Warram J H, Rand L I, et al. Risk for cardiovascular autonomic neuropathy is associated with the HLA-DR3/4 phenotype in type I diabetes mellitus[J]. Ann Intern Med, 1992, 116(7): 544-549.
[30] Zamani M, Pociot F, Raeymaekers P, et al. Linkage of type I diabetes to 15q26 (IDDM3) in the Danish population[J]. Hum Genet, 1996, 98(4): 491-496.
[31] Eleftheriadou A, Spallone V, Tahrani A A, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management[J]. Diabetologia, 2024, 67(12): 2611-2625.
[32] Saboo N, Kacker S. A study on Yoga-based lifestyle intervention versus dietary intervention alone on cardiometabolic risk factors among people with prediabetes[J]. Ann Afr Med, 2024, 23(2): 202-212.
[31] Eleftheriadou A, Spallone V, Tahrani A A, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management[J]. Diabetologia, 2024, 67(12): 2611-2625.
[33] Ziegler D, Sohr C G, Nourooz-Zadeh J. Oxidative stress and antioxidant defense in relation to the severity of diabetic polyneuropathy and cardiovascular autonomic neuropathy[J]. Diabetes Care, 2004, 27(9): 2178-2183.
[34] Siam N H, Snigdha N N, Tabasumma N, et al. Diabetes mellitus and cardiovascular disease: exploring epidemiology, pathophysiology, and treatment strategies[J]. Rev Cardiovasc Med, 2024, 25(12): 436.
[35] Martin C L, Albers J W, Pop-Busui R, et al. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study[J]. Diabetes Care, 2014, 37(1): 31-38.
[36] Tang Yaling, Shah H, Bueno Junior C R, et al. Intensive risk factor management and cardiovascular autonomic neuropathy in type 2 diabetes: the ACCORD trial[J]. Diabetes Care, 2021, 44(1): 164-173.
[37] Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes[J]. N Engl J Med, 2003, 348(5): 383-393.
[38] Tanbek K, Ozerol E, Yilmaz U, et al. Alpha lipoic acid decreases neuronal damage on brain tissue of STZ-induced diabetic rats[J]. Physiol Behav, 2022, 248: 113727.
[39] Baicus C, Purcarea A, von Elm E, et al. Alpha-lipoic acid for diabetic peripheral neuropathy[J]. Cochrane Database Syst Rev, 2024, 1(1): CD012967.
[40] Ziegler D, Low P A, Freeman R, et al. Predictors of improvement and progression of diabetic polyneuropathy following treatment with α-lipoic acid for 4 years in the NATHAN 1 trial[J]. J Diabetes Complications, 2016, 30(2): 350-356.
[41] Tankova T, Koev D, Dakovska L. Alpha-lipoic acid in the treatment of autonomic diabetic neuropathy (controlled, randomized, open-label study)[J]. Rom J Intern Med, 2004, 42(2): 457-464.
[42] Juraschek S P, Hu J R, Cluett J L, et al. Orthostatic hypotension, hypertension treatment, and cardiovascular disease: an individual participant meta-analysis[J]. JAMA, 2023, 330(15): 1459-1471.
[43] Kulkarni S, Jenkins D, Dhar A, et al. Treating lows: management of orthostatic hypotension[J]. J Cardiovasc Pharmacol, 2024, 84(3): 303-315.
[44] Kempler P, Körei A. Diabetic cardiovascular autonomic neuropathy: clinical significance, diagnosis and therapy[J]. Orv Hetil, 2024, 165(16): 602-612.
[45] Dimitropoulos G. Cardiac autonomic neuropathy in patients with diabetes mellitus[J]. WJD, 2014, 5(1): 17.
[46] Balcıoğlu A S, Müderrisoğlu H. Diabetes and cardiac autonomic neuropathy: Clinical manifestations, cardiovascular consequences, diagnosis and treatment[J]. World J Diabetes, 2015, 6(1): 80-91.
[47] Tesfaye S, Boulton A J, Dyck P J, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments[J]. Diabetes Care, 2010, 33(10): 2285-2293.
[48] Park J W, Okamoto L E, Shibao C A, et al. Pharmacologic treatment of orthostatic hypotension[J]. Auton Neurosci, 2020, 229: 102721.
[49] Pierson B C, Apilado K, Franzos M A, et al. Oral medications for the treatment of postural orthostatic tachycardia syndrome; a systematic review of studies before and during the COVID-19 pandemic[J]. Front Neurol, 2024, 15: 1515486.
[50] Balcıoğlu A S, Çelik E, Şahin M, et al. Dapagliflozin improves cardiac autonomic function measures in type 2 diabetic patients with cardiac autonomic neuropathy[J]. Anatol J Cardiol, 2022, 26(11): 832-840.
[51] Herat L Y, Matthews J, Azzam O, et al. Targeting features of the metabolic syndrome through sympatholytic effects of SGLT2 inhibition[J]. Curr Hypertens Rep, 2022, 24(3): 67-74.
[52] Matthews V B, Elliot R H, Rudnicka C, et al. Role of the sympathetic nervous system in regulation of the sodium glucose cotransporter 2[J]. J Hypertens, 2017, 35(10): 2059-2068.
[53] Gueguen C, Burke S L, Barzel B, et al. Empagliflozin modulates renal sympathetic and heart rate baroreflexes in a rabbit model of diabetes[J]. Diabetologia, 2020, 63(7): 1424-1434.

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·研究进展·

糖尿病心血管自主神经病变的中西医诊治

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摘要：糖尿病心血管自主神经病变（DCAN）是糖尿病常见的并发症之一，会显著增加各种心血管不良事件的发病风险。但DCAN起病隐匿、危害严重，目前尚缺乏有效延缓和逆转疾病进程的治疗药物。因此，对DCAN的早期防控至关重要。本文着重阐述近年来DCAN在中西医领域的诊治研究进展，为糖尿病心血管自主神经病变的早期防控、新药研发及中西医联合诊疗方案的制定提供思路。

关键词：糖尿病；心血管自主神经病变；中西医；辨证论治；代谢紊乱；营养神经；钠-葡萄糖协同转运蛋白2抑制剂

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Diagnosis and treatment of diabetic cardiovascular autonomic neuropathy with Chinese medicine and Western medicine

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Abstract: Diabetic cardiac autonomic neuropathy (DCAN) is one of the common complications of diabetes, significantly increasing the risk of various adverse cardiovascular events. However, DCAN has an insidious onset and severe consequences, and there are currently no effective medications to delay or reverse the progression of the disease. Therefore, early prevention and control of DCAN are crucial. This paper focuses on the recent advance in the diagnosis and treatment of DCAN in Chinese medicine and Western medicine, to provide insights for early prevention and control, new drug development, and the formulation of integrated treatment strategies combining both approaches for DCAN.

Keywords: Diabetes mellitus; Cardiac autonomic neuropathy; Chinese medicine and Western medicine; Treatment based on syndrome differentiation; Metabolic disorder; Nerve nutrition; Sodium-glucose cotransporter 2 inhibitor

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糖尿病心血管自主神经病变（diabetic cardiovascular autonomic neuropathy，DCAN）是糖尿病常见的并发症，其特征为心血管自主神经功能受损，且需排除其他可能病因后方可确诊[1-2]。DCAN具有隐匿性发病特征，其临床表现呈渐进性发展。疾病早期主要表现为心率变异性（heart rate variability，HRV）降低、静息心率增快及运动耐力下降等自主神经功能失调症状，随病程进展可逐步发展为体位性低血压、无症状性心肌梗死等严重并发症，最终可能引发心源性猝死，这一系列病理生理改变构成了糖尿病患者的重要死亡风险因素[3]。中医从DCAN的病因病机出发，秉承“未病先防，既病防变，瘥

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后防复”的治未病理念，依其证候演变规律辩证施治。西医则主要通过控制血糖、营养神经、缓解心血管临床症状等方面治疗DCAN。本文拟分别从中西医角度剖析DCAN的发病机制及治疗进展，进而为其临床防治提供重要理论依据。

1　中医角度对DCAN的认识与治疗

1.1　中医对DCAN病因病机的认识　在中医学中，DCAN并无专属病名，根据其临床症状，将其归属于“怔忡”范畴。《景岳全书》曰：“怔忡之病……此证惟阴虚劳损之人乃有之，盖阴虚于下，则宗气无根，而气不归源。”中医学认为DCAN病位在心，涉及心、脾、肾三脏。心悸的发病机制主要与机体正气亏虚相关，其成因可归纳为先天禀赋不足、情志失调或久病耗损等，致气血阴阳失衡而发心悸。

国医大师吕仁和从“孙络-微血管”视角认识DCAN，认为心络亏虚为其基本病机，疾病进展的关键因素是络脉瘀滞，治疗上当根据“络以通为用”的特点，采用补虚活血通络之法，通补结合[4]。根据《难经·十四难》所言“损其心者，调其营卫”，有学者提出了以“调营卫”为基本大法的治疗方案，营卫亏虚者治以补养，营卫壅滞者治以畅通，营卫不偕者治以调和，重在恢复机体气血阴阳之平衡，使营卫调，则病自消[5]。《素问·阴阳应象大论》中载“辛甘发散为阳，酸苦涌泄为阴”[6]，据此孙雪梅等[7]提出酸苦相合以去除心火而治心悸的治疗原则。郭立中等[8]根据周仲瑛教授提出的“三热论”，认为治疗DCAN应以“三热”并清、气血同治、标本兼顾为原则，清化与润燥并进，化湿祛瘀与生津凉润并举。

1.2　中医对DCAN的治疗

1.2.1　中药治疗　余金莲等[9]研究发现，木丹颗粒具有活血化瘀、增补元气的功效，可恢复血管壁弹性，增加血流量，提高神经传导速度，改善糖尿病症状。高倩等[10]的研究亦发现，木丹颗粒联合甲钴胺治疗方案在改善DCAN患者心电指标方面优于单用甲钴胺，其可显著提升QT离散度（QT dispersion，QTd）、T波峰末间期（T_{peak} to T_{end} interval，T_{p-e}）及T_{p-e}/QT比值等参数，对预防心律失常具有潜在临床价值。此外，蔡晖娟等[11]运用参松养心胶囊联合甲钴胺治疗气阴两虚型DCAN患者，发现12周后治疗组患者的帕金森病自主神经功能障碍量表（Scales for Outcomes in Parkinson's Disease-Autonomic Dysfunction，SCOPA-AUT）、复合自主神经症状评分-31（Composite Autonomic Symptom Score-31，COMPASS-31）评分低于对照组，而QTd和Valsalva动作指数高于对照组。于东雷[12]采用归脾汤治疗心脾两虚型DCAN患者，采用血府逐瘀汤治疗心阴血虚型DCAN患者，治疗周期为2个月，发现患者治疗后的呼吸差、心搏间期比值、卧位心率等指标均较前明显改善。中药主要通过改善血液循环、增强神经功能来改善DCAN症状和临床指标，中西医联合治疗方案显示出了更佳的疗效。

1.2.2　针灸治疗　针灸治疗糖尿病神经并发症具有一定的疗效，且有花费低、不良反应少等优势，可能的相关机制包括改善胰岛功能、降低血糖、调节相关激素、恢复交感神经和副交感神经的平衡等[13-14]。国内一项临床研究表明硫辛酸联合针灸内关穴、脾俞穴、足三里穴及太溪穴较单用硫辛酸对心率变异指标治疗效果更佳[15]。徐敏等[16]发现针刺灵台、神道穴后，DCAN患者HRV频域指标低频（low frequency，LF）/高频（high frequency，HF）显著降低，提示针刺灵台、神道穴可能与交感神经与迷走神经功能的平衡性提高有关。闫鏐等[17]一项随机对照研究比较了不同穴位针刺对DCAN患者的影响，结果显示，与悬钟穴组相比，内关穴组患者HF显著提升，提示内关穴针刺可有效增强心脏迷走神经活性。目前针灸治疗DCAN仍以临床观察性研究为主，未来需要更多的基础研究来阐述其具体的分子机制。

2　西医角度对DCAN的认识与治疗

2.1　西医对DCAN发病机制的认识

2.1.1　糖脂代谢紊乱　长期高血糖可导致神经细胞的代谢紊乱，增加氧化应激，导致神经细胞损伤。高血糖状态下，多元醇途径的激活增加，导致细胞内山梨醇积累，进而引发细胞内氧化应激反应，损害神经细胞[18]。糖尿病患者常伴有脂代谢紊乱，如三酰甘油和胆固醇水平升高。一项动物研究表明脂代谢紊乱可导致神经细胞膜的脂质成分改变，影响神经细胞的功能和结构[19]。Jang等[20]研究显示三酰甘油/高密度胆固醇比值和低密度胆固醇的平均粒径与2型糖尿病女性患者的DCAN的患病率呈正相关。以上研究均表明糖脂代谢紊乱是DCAN的发病机制之一。

2.1.2　氧化应激　氧化应激是糖尿病神经病变发病机制中的一个重要因素，包括自由基形成增多和抗氧化防御缺陷[21]。高血糖导致过量的氧自由基产生，可以损伤神经细胞，导致自主神经功能障碍[22]。氧化应激不仅影响神经细胞，还影响神经血管系统，从而加剧DCAN的进展[23]。一项国外研究表明，氧化应激主要通过氧化介导的神经尼古丁型乙酰胆碱受体（nicotinic acetylcholine receptors，nAChRs）失活，触发自主神经功能障碍，影响交感神经节的突触传递，导致自主功能衰竭[24]。

2.1.3　炎症　研究表明，炎症因子在DCAN的发生发展中具有双重作用，既与其发病机制密切相关，又直接参与疾病进展的病理生理过程[25]。另外一项研究表明，与自主神经系统相关的血管球细胞可特定感知氧气、葡萄糖和其他代谢物。白细胞介素（interleukin，IL）-1与血管球细胞结合，激活Toll样受体并导致核因子κB（nuclear factor kappa-B，NF-κB）的表达增加以及随后释放炎性细胞因子，例如肿瘤坏死因子-α（tumor necrosis factor-α，TNF-α）和IL-6，并且炎症变化与交感-副交感神经平衡的异常相关联[26]。一项横断面研究显示，2型糖尿病患者血浆中白三烯B4（leukotriene B4，LTB4）水平可能与心血管自主神经病变有关，而与血糖控制程度无关[27]。上述研究显示DCAN与炎症之间存在一定的联系，但仍需更多的研究来阐明炎症在DCAN中的具体作用和机制。

2.1.4　遗传因素　DCAN的遗传倾向涉及多个基因和遗传标记。Tang等[28]研究发现，在2型糖尿病患者中，位于染色体1p36的遗传位点rs779142与DCAN的发展有显著关联，该位点的变异增加了35%的DCAN发病风险。此外，人类白细胞

抗原(angiotensin-converting enzyme inhibitor, HLA)-DR3/4表型也与1型糖尿病患者中DCAN的发展密切相关,表明遗传因素在DCAN的发展中起着重要作用[29]。进一步的研究表明,*HLA-DQB1*基因的多态性也与1型糖尿病的易感性和抵抗力有关,这可能间接影响到DCAN的发展[30]。这些发现为理解DCAN的遗传基础提供了重要线索,并可能为未来的治疗策略提供潜在的靶点。

2.2　西医对DCAN的治疗

2.2.1　改善生活方式　研究表明,地中海饮食、有氧运动、戒烟、降糖、降压、降脂及健康教育等可以有效预防DCAN[31]。一项国际研究表明,针对糖尿病前期患者实施生活方式干预(包括瑜伽锻炼和限制膳食脂肪摄入)可显著改善心脏功能指标[32]。此外,Ziegler等[33]研究显示,在进行为期12周的有氧运动结合抗阻训练后,对照组和运动组的HRV指标在时域和频域均较运动前显著降低。与对照组相比,联合运动方式可显著提高DCAN患者的时域指标[正常窦性心搏间期标准差(standard deviation of normal to normal intervals,SDNN)及相邻正常窦性心搏间期差值的均方根(root mean square of successive differences,RMSSD)]和频域指标(LF/HF),提示有氧运动联合抗阻训练有助于预防和控制DCAN。

2.2.2　纠正代谢紊乱　长期高血糖是糖尿病患者发生DCAN的主要危险因素[34]。糖尿病控制与并发症试验研究(Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications, DCCT/EDIC)证实,强化血糖控制策略可有效降低糖尿病患者并发周围神经病变及DCAN的发病率[35]。Tang等[36]在ACCORD研究中发现,在中位随访5年期间,强化血糖和血压干预对2型糖尿病合并DCAN具有显著的保护作用。2型糖尿病患者的多因素干预和心血管结局研究(Steno-2)表明联合控制血压、糖化血红蛋白、三酰甘油和总胆固醇可显著降低自主神经病变发病风险[37]。

2.2.3　营养神经治疗　α-硫辛酸是一种天然的抗氧化剂,并被广泛用于糖尿病周围神经病变的治疗,具有改善葡萄糖稳态和脂质分布,抗炎、减少氧化应激等多种作用[38-39]。一项为期4年的α-硫辛酸治疗糖尿病周围神经病变的研究显示,α-硫辛酸显著改善了接受血管紧张素转换酶抑制剂(angiotensin converting enzyme inhibitor, ACEI)治疗的DPN患者深吸气试验结果,这表明α-硫辛酸联合ACEI可能产生额外的DCAN保护作用[40]。此外,Tankova等[41]在研究中纳入了46例1型糖尿病患者,患者先接受静脉注射600 mg α-硫辛酸10天,随后口服600 mg α-硫辛酸50天,结果显示患者的心血管自主神经反射试验评分(Cardiovascular Autonomic Reflex Tests score, CARTs评分)显著改善。然而这些发现仍以临床研究为主,需要更多的基础研究阐述其中的机制。

2.2.4　针对直立性低血压的治疗　严重DCAN所引起直立性低血压可通过药物治疗及非药物治疗[42-43]。非药物治疗主要为生活方式的调整,包括充分饮水、适当高钠饮食、延长站立时间等[43-44]。临床常用药物干预方案涵盖多种作用机制,主要包括α受体激动剂(米多君)、盐皮质激素(氟氢可的松)、去甲肾上腺素前体(屈昔多巴)、造血刺激剂(促红细胞生成素)、抗利尿激素(去氨加压素)、胃肠激素(生长抑素类似物)以及β受体阻滞剂等[45-48]。经美国食品药品监督管理局认证,屈昔多巴与米多君是神经源性体位性低血压的两种标准治疗药物[48]。作为一种盐皮质激素类药物,氟氢可的松通过促进钠水潴留和增强血管对儿茶酚胺的敏感性发挥治疗作用,但其临床应用可能引发体位性高血压及电解质紊乱等不良反应[45-48]。选择性β受体阻滞剂(如依伐布雷定)可用于治疗体位性心动过速综合征[49]。

2.2.5　其他药物治疗　钠-葡萄糖协同转运蛋白2(sodium-glucose linked transporter inhibitor, SGLT-2)抑制剂作为新型口服降糖药物,在临床治疗中具有重要应用价值,通过抑制肾近端小管葡萄糖重吸收达到降糖效果,代表药物包括达格列净和恩格列净等。临床研究数据显示,采用达格列净(10 mg/d)对DCAN患者进行为期24周的干预治疗,可显著改善患者的HRV[50]。一项动物研究表明,肥胖2型糖尿病小鼠的交感神经去神经与*SGLT-2*过表达的抑制相关[51]。此外,在高脂饮食诱导的C57BL6/J小鼠模型中,达格列净可显著抑制心脏和肾脏组织中酪氨酸羟化酶的表达水平,进而降低去甲肾上腺素的生物合成[52],而在四氧嘧啶诱导的糖尿病家兔模型中,恩格列净可恢复肾交感神经反射[53]。这些发现表明交感神经系统与SGLT-2水平密切相关,并且SGLT-2抑制剂可有效改善心血管自主神经功能,但仍需更全面的研究以寻找DCAN的最佳治疗方案。

3　结　语

本文从中医和西医角度,对DCAN的发病机制及治疗进展进行了综述。DCAN作为糖尿病中一种严重的并发症,具有发病率高、临床表现隐匿、预后不佳等特点。近年来研究发现中医药对DCAN具有一定的疗效,如何将其与西医疗法充分结合,发挥各自优势去治疗DCAN,值得思考和研究。未来可进一步利用中西医结合治疗的方法,开展前瞻性高质量临床研究及相关基础研究,为DCAN的发病机制和治疗方案提供理论基础,也为新药研发和中西医协同诊疗方案的制定提供临床依据。

利益冲突　无

参考文献

[1] Eleftheriadou A, Spallone V, Tahrani AA, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management[J]. Diabetologia, 2024, 67(12): 2611-2625.

[2] 中华医学会糖尿病学分会神经并发症学组. 国家基层糖尿病神经病变诊治指南(2024版)[J]. 中华糖尿病杂志, 2024, 16(5): 496-511.

[3] Agashe S, Petak S. Cardiac autonomic neuropathy in diabetes mellitus[J]. Methodist Debakey Cardiovasc J, 2018, 14(4): 251-256.

[4] 王诗尧, 王世东, 傅强, 等. 国医大师吕仁和"微型癥瘕"病理假说的源流及发展[J]. 中华中医药杂志, 2022, 37(8): 4555-4559.

[5] 唐茹梦, 王姗, 袁如月, 等. 基于"损其心者,调其营卫"探析糖

尿病心脏自主神经病变的辨治[J]. 环球中医药, 2023, 16(11): 2323-2326.
[6] 黄作阵. 郭霭春《黄帝内经素问校注语译》的训诂成就[J]. 北京中医药大学学报, 2005, 28(6): 22-25.
[7] 孙雪梅, 张蒙, 毛晨晗, 等. 酸苦调敛法辨治糖尿病心脏自主神经病变[J]. 南京中医药大学学报, 2021, 37(4): 570-573.
[8] 郭立中, 吴勉华, 周学平, 等. 周仲瑛教授学术思想简介(一)[J]. 南京中医药大学学报(自然科学版), 2008, 24(6): 361-365.
[9] 余金莲, 钟秋润, 余雨枫, 等. 木丹颗粒联合甲钴胺治疗糖尿病周围神经病变临床疗效的Meta分析[J]. 糖尿病新世界, 2022, 25(2): 33-38.
[10] 高倩, 贾荣梅, 杨丽梅, 等. 木丹颗粒联合甲钴胺对糖尿病心血管自主神经病变患者心电图T波峰末期的影响[J]. 北京医学, 2020, 42(4): 352-354
[11] 蔡晖娟, 谢海洋, 黄兰蕙. 参松养心胶囊对气阴两虚型糖尿病心血管自主神经病变患者血液流变学和心血管功能的影响[J]. 中国医院用药评价与分析, 2022, 22(11): 1349-1352, 1356.
[12] 于东雷. 中医辨证治疗糖尿病心血管自主神经病变的临床疗效[J]. 中国医药指南, 2019, 17(6): 146-147.
[13] Wang L, Wang LM. Perspective on acupuncture treatment for diabetic peripheral neuropathy: a perspective[J]. Medicine, 2025, 104(23): e42646.
[14] Wang CL, Fan YZ, Liang GT, et al. Acupuncture for the treatment of painful diabetic peripheral neuropathy: a systematic review and meta-analysis[J]. Complement Ther Clin Pract, 2024, 57: 101889.
[15] 李晓珊. 硫辛酸结合针灸治疗糖尿病心血管自主神经病变临床观察[J]. 实用中医药杂志, 2019, 35(1): 61-62.
[16] 徐敏, 郭丽, 崔华峰, 等. 针刺灵台、神道穴对糖尿病心脏自主神经病变患者心率变异性的影响[J]. 上海针灸杂志, 2019, 38(6): 588-591.
[17] 闫缪, 孙炜, 王长春, 等. 针刺内关穴对糖尿病性心脏自主神经病变患者心率变异性的影响[J]. 针灸临床杂志, 2019, 35(5): 34-36.
[18] Liu HL, Zhou L, Wang XF, et al. PIEZO1 as a new target for hyperglycemic stress-induced neuropathic injury: the potential therapeutic role of bezafibrate[J]. Biomed Pharmacother, 2024, 176: 116837.
[19] Kotredes KP, Pandey RS, Persohn S, et al. Characterizing molecular and synaptic signatures in mouse models of late-onset Alzheimer's disease independent of amyloid and tau pathology[J]. Alzheimers Dement, 2024, 20(6): 4126-4146.
[20] Jang EH, Park YM, Hur J, et al. Higher levels of small dense low-density lipoprotein (LDL) are associated with cardiac autonomic neuropathy in patients with type 2 diabetes[J]. Diabet Med, 2013, 30(6): 694-701.
[21] Sharan L, Pal A, Babu SS, et al. Bay 11-7082 mitigates oxidative stress and mitochondrial dysfunction *via* NLRP3 inhibition in experimental diabetic neuropathy[J]. Life Sci, 2024, 359: 123203.
[22] Khodaie SA, Razavi R, Nikkhah H, et al. *Nigella sativa* L. and its bioactive and nutraceutical components in the management of diabetic peripheral neuropathy[J]. Inflammopharmacology, 2024, 32(5): 2897-2920.
[23] Stoian A, Muntean C, Babă DF, et al. Update on biomarkers of chronic inflammatory processes underlying diabetic neuropathy[J]. Int J Mol Sci, 2024, 25(19): 10395.
[24] Chandna AR, Nair M, Chang C, et al. RAGE mediates the inactivation of nAChRs in sympathetic neurons under high glucose conditions[J]. Eur J Neurosci, 2015, 41(3): 341-351.
[25] Wang Z, Zhang L, Lu B, et al. Causal relationships between circulating inflammatory cytokines and diabetic neuropathy: a Mendelian randomization study[J]. Cytokine, 2024, 177: 156548.
[26] Hansen MK, O'Connor KA, Goehler LE, et al. The contribution of the vagus nerve in interleukin-1beta-induced fever is dependent on dose[J]. Am J Physiol Regul Integr Comp Physiol, 2001, 280(4): R929-R934.
[27] Neves JAJ, De Matos MR, Ramalho T, et al. Increased leukotriene B4 plasma concentration in type 2 diabetes individuals with cardiovascular autonomic neuropathy[J]. Diabetol Metab Syndr, 2020, 12(1): 99.
[28] Tang YL, Shah H, Sun XQ, et al. A genetic locus on chromosome 1p36 associated with cardiovascular autonomic neuropathy in type 2 diabetes[J]. Diabetes, 2019, 68(Supplement_1): 321-3OR.
[29] Barzilay J, Warram JH, Rand LI, et al. Risk for cardiovascular autonomic neuropathy is associated with the HLA-DR3/4 phenotype in type 1 diabetes mellitus[J]. Ann Intern Med, 1992, 116(7): 544-549.
[30] Zamani M, Pociot F, Raeymaekers P, et al. Linkage of type Ⅰ diabetes to 15q26 (IDDM3) in the Danish population[J]. Hum Genet, 1996, 98(4): 491-496.
[31] Eleftheriadou A, Spallone V, Tahrani AA, et al. Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management[J]. Diabetologia, 2024, 67(12): 2611-2625.
[32] Saboo N, Kacker S. A study on Yoga-based lifestyle intervention versus dietary intervention alone on cardiometabolic risk factors among people with prediabetes[J]. Ann Afr Med, 2024, 23(2): 202-212.
[33] Ziegler D, Sohr CGH, Nourooz-Zadeh J. Oxidative stress and antioxidant defense in relation to the severity of diabetic polyneuropathy and cardiovascular autonomic neuropathy[J]. Diabetes Care, 2004, 27(9): 2178-2183.
[34] Siam NH, Snigdha NN, Tabasumma N, et al. Diabetes mellitus and cardiovascular disease: exploring epidemiology, pathophysiology, and treatment strategies[J]. Rev Cardiovasc Med, 2024, 25(12): 436.
[35] Martin CL, Albers JW, Pop-Busui R. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study[J]. Diabetes Care, 2014, 37(1): 31-38.
[36] Tang YL, Shah H, Bueno Junior CR, et al. Intensive risk factor management and cardiovascular autonomic neuropathy in type 2 diabetes: the ACCORD trial[J]. Diabetes Care, 2021, 44(1): 164-173.
[37] Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes[J]. N Engl J Med, 2003, 348(5): 383-393.
[38] Tanbek K, Ozerol E, Yilmaz U, et al. Alpha lipoic acid decreases neuronal damage on brain tissue of STZ-induced diabetic rats[J]. Physiol Behav, 2022, 248: 113727.
[39] Baicus C, Purcarea A, von Elm E, et al. Alpha-lipoic acid for diabetic peripheral neuropathy[J]. Cochrane Database Syst Rev, 2024, 1(1): CD012967.
[40] Ziegler D, Low PA, Freeman R, et al. Predictors of improvement and progression of diabetic polyneuropathy following treatment with α-lipoic acid for 4 years in the NATHAN 1 trial[J]. J Diabetes Complications, 2016, 30(2): 350-356.
[41] Tankova T, Koev D, Dakovska L. Alpha-lipoic acid in the treatment of autonomic diabetic neuropathy (controlled, randomized, open-label study)[J]. Rom J Intern Med, 2004, 42(2): 457-464.
[42] Juraschek SP, Hu JR, Cluett JL, et al. Orthostatic hypotension, hypertension treatment, and cardiovascular disease: an individual participant meta-analysis[J]. JAMA, 2023, 330(15): 1459-1471.
[43] Kulkarni S, Jenkins D, Dhar A, et al. Treating lows: management of orthostatic hypotension[J]. J Cardiovasc Pharmacol, 2024, 84(3): 303-315.

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robiol Aging, 2011, 32(5): 763-777.
[31] Sluiman AJ, McLachlan S, Forster RB, et al. Higher baseline inflammatory marker levels predict greater cognitive decline in older people with type 2 diabetes: year 10 follow-up of the Edinburgh Type 2 Diabetes Study[J]. Diabetologia, 2022, 65(3): 467-476.
[32] Dybjer E, Engström G, Helmer C, et al. Incretin hormones, insulin, glucagon and advanced glycation end products in relation to cognitive function in older people with and without diabetes, a population-based study[J]. Diabet Med, 2020, 37(7): 1157-1166.
[33] 吴锦景, 卫哲, 刘子荷. 小胶质细胞介导的炎性反应在阿尔茨海默病中的研究进展[J]. 中国老年学杂志, 2025, 45(4): 996-1001.
[34] Shabab T, Khanabdali R, Moghadamtousi SZ, et al. Neuroinflammation pathways: a general review[J]. Int J Neurosci, 2017, 127(7): 624-633.
[35] Shih RH, Wang CY, Yang CM. NF-kappaB signaling pathways in neurological inflammation: a mini review[J]. Front Mol Neurosci, 2015, 8: 77.
[36] De La Monte SM. Insulin resistance and Alzheimer's disease[J]. BMB Rep, 2009, 42(8): 475-481.
[37] Rosenberg PB. Clinical aspects of inflammation in Alzheimer's disease[J]. Int Rev Psychiatry, 2005, 17(6): 503-514.
[38] Zhang LQ, Zhang W, Li T, et al. GLP-1R activation ameliorated novel-object recognition memory dysfunction *via* regulating hippocampal AMPK/NF-κB pathway in neuropathic pain mice[J]. Neurobiol Learn Mem, 2021, 182: 107463.
[39] Bhalla S, Mehan S, Khan A, et al. Protective role of IGF-1 and GLP-1 signaling activation in neurological dysfunctions[J]. Neurosci Biobehav Rev, 2022, 142: 104896.
[40] Wang LX, Tang L, Wang YP, et al. Exendin-4 protects HUVECs from t-BHP-induced apoptosis *via* PI3K/Akt-Bcl-2-caspase-3 signaling[J]. Endocr Res, 2016, 41(3): 229-235.
[41] McClean PL, Hölscher C. Liraglutide can reverse memory impairment, synaptic loss and reduce plaque load in aged APP/PS1 mice, a model of Alzheimer's disease[J]. Neuropharmacology, 2014, 76: 57-67.
[42] Meca AD, Boboc IKS, Mititelu-Tartau L, et al. Unlocking the potential: semaglutide's impact on Alzheimer's and Parkinson's disease in animal models[J]. Curr Issues Mol Biol, 2024, 46(6): 5929-5949.
[43] 张晨虹, 杨鑫. 微生物组与人体健康研究策略及方法[J]. 诊断学理论与实践, 2019, 18(3): 250-257.
[44] Guo XH, Okpara ES, Hu WT, et al. Interactive relationships between intestinal flora and bile acids[J]. Int J Mol Sci, 2022, 23(15): 8343.
[45] de Paiva IHR, da Silva RS, Mendonça IP, et al. Semaglutide attenuates anxious and depressive-like behaviors and reverses the cognitive impairment in a type 2 diabetes mellitus mouse model *via* the microbiota-gut-brain axis[J]. J Neuroimmune Pharmacol, 2024, 19(1): 36.

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[44] Kempler P, Körei A. Diabetic cardiovascular autonomic neuropathy: clinical significance, diagnosis and therapy[J]. Orv Hetil, 2024, 165(16): 602-612.
[45] Dimitropoulos G, Tahrani AA, Stevens MJ. Cardiac autonomic neuropathy in patients with diabetes mellitus[J]. World J Diabetes, 2014, 5(1): 17-39.
[46] Balcıoğlu AS, Müderrisoğlu H. Diabetes and cardiac autonomic neuropathy: clinical manifestations, cardiovascular consequences, diagnosis and treatment[J]. World J Diabetes, 2015, 6(1): 80-91.
[47] Tesfaye S, Boulton AJM, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments[J]. Diabetes Care, 2010, 33(10): 2285-2293.
[48] Park JW, Okamoto LE, Shibao CA, et al. Pharmacologic treatment of orthostatic hypotension[J]. Auton Neurosci, 2020, 229: 102721.
[49] Pierson BC, Apilado K, Franzos MA, et al. Oral medications for the treatment of postural orthostatic tachycardia syndrome; a systematic review of studies before and during the COVID-19 pandemic[J]. Front Neurol, 2025, 15: 1515486.
[50] Balcıoğlu AS, Çelik E, Şahin M, et al. Dapagliflozin improves cardiac autonomic function measures in type 2 diabetic patients with cardiac autonomic neuropathy[J]. Anatol J Cardiol, 2022, 26(11): 832-840.
[51] Herat LY, Matthews J, Azzam O, et al. Targeting features of the metabolic syndrome through sympatholytic effects of SGLT2 inhibition[J]. Curr Hypertens Rep, 2022, 24(3): 67-74.
[52] Matthews VB, Elliot RH, Rudnicka C, et al. Role of the sympathetic nervous system in regulation of the sodium glucose cotransporter 2[J]. J Hypertens, 2017, 35(10): 2059-2068.
[53] Gueguen C, Burke SL, Barzel B, et al. Empagliflozin modulates renal sympathetic and heart rate baroreflexes in a rabbit model of diabetes[J]. Diabetologia, 2020, 63(7): 1424-1434.

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