

The Distribution Pattern of Traditional Chinese Medicine Syndromes in Patients with Hyperlipidemia

Bin Liang, Luyao Wang, Shaoxi Li, Feifei Xue*

School of Traditional Chinese Medicine, Jinan University, Guangzhou, China Email: *feixue1977@126.com

How to cite this paper: Liang, B., Wang, L.Y., Li, S.X. and Xue, F.F. (2024) The Distribution Pattern of Traditional Chinese Medicine Syndromes in Patients with Hyperlipidemia. *Journal of Biosciences and Medicines*, **12**, 173-182. https://doi.org/10.4236/jbm.2024.129017

Received: August 21, 2024 Accepted: September 17, 2024 Published: September 20, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

http://creativecommons.org/licenses/by/4.0/

Abstract

Objective: Hyperlipidemia is a representative nutritional metabolic disease in clinic, which is easy to induce atherosclerotic cardiovascular and cerebrovascular diseases, with complex classification. Traditional Chinese Medicine (TCM) syndrome aims to reflect the characteristics of diseases and is the basic principle of TCM treatment of diseases. This study aimed to summarize the distribution pattern of TCM syndromes in patients with hyperlipidemia. Methods: The frequency, characteristics and distribution of all TCM syndromes of 1012 patients with hyperlipidemia were analyzed. Results: The main disease types determined by frequency of 1012 patients included hypertriglyceridemia combined with hypo high-density lipoprotein cholesterolemia (19.76%), hypo highdensity lipoprotein cholesterolemia (18.58%), hypercholesterolemia (16.50%), mixed hyperlipidemia (16.40%), and hypertriglyceridemia (15.12%). The distribution of TCM syndromes, in order of frequency, was as follows: Qi-deficiency and blood stasis syndrome (23.52%), liver depression and spleen deficiency (9.88%), syndrome of qi stagnation and blood stasis (9.29%), phlegm stasis syndrome (7.41%), and syndrome of yang deficiency of spleen and kidney (6.92%). Conclusion: Qi-deficiency and blood stasis syndrome and liver depression and spleen deficiency are the most common TCM syndromes in patients with hyperlipidemia.

Keywords

Component, Hyperlipidemia, TCM Syndrome Differentiation, Epidemiology, Clinical Symptoms

1. Introduction

Hyperlipidemia is a disease characterized by the decrease of serum cholesterol,

triglyceride and low-density lipoprotein and the increase of high-density lipoprotein, which is one of the factors inducing atherosclerotic cardiovascular and cerebrovascular diseases [1]. With recent lifestyle changes, the incidence of hyperlipidemia—usually a geriatric disease—in the younger population is increasing, endangering public health [2]. At present, the treatment of hyperlipidemia is mainly based on statins and fibrates, combined with diet and exercise intervention [3]. However, existing treatments had limited effects on improving hyperlipidemia symptoms and controlling its complications [4].

Traditional Chinese Medicine (TCM) syndrome is the understanding of the etiology and pathological mechanism of a disease at some stage, reflecting the innate character of the disease and acting as the basis of its clinical treatment [5]. In recent years, TCM, characterized by syndrome differentiation and treatment, plays an increasingly important role in the treatment of hyperlipidemia and its complications [6]. Identifying the different syndrome types of the disease could help doctors identify the main causes and progression of the disease at the current stage, so as to better guide clinical treatment. Therefore, exploring the distribution of the main clinical TCM syndromes and the main cause of hyperlipidemia has a positive effect on the understanding and treatment of the disease. Unfortunately, the present research is deficient in the exploration of diagnosis, differentiation, and classification of the clinical symptoms of hyperlipidemia, which poses limitations on the clinical diagnosis and treatment of the disease. Consequently, investigating the distribution of major clinical TCM syndromes and the primary etiology of hyperlipidemia has become a focal point of current research.

In this study, we analyzed clinical data obtained in an epidemiological survey of 1012 hyperlipidemia patients, explored the distribution pattern of TCM syndromes of hyperlipidemia, and analyzed relevant factors. Therefore, we provide a valuable reference for the standardization of hyperlipidemia syndrome differentiation to effectively direct clinical practice.

2. Methods and Data

2.1. Patients Sample

A total of 1012 outpatients and inpatients (517 men and 495 women) who were admitted to the First Affiliated Hospital of Jinan University between May 2020 and October 2021 met the diagnostic criteria for hyperlipidemia (2016) [7] (Guidelines on Prevention and Treatment of Blood Lipid Abnormality in Chinese Adults). The study was conducted in accordance with the Declaration of Helsinki (2013 revision) [8] and approved by the Ethics Committee of the First Affiliated Hospital of Jinan University. Informed consent was obtained from all patients.

2.2. Inclusion Criteria

Patients were included who: 1) met the diagnostic criteria of hyperlipidemia; 2) were between 15 and 79 years old; 3) had no apparent organ dysfunction; and 4) volunteered to cooperate with the study and signed the informed consent form.

2.3. Exclusion Criteria

Patients were excluded: 1) secondary hyperlipidemia patients; 2) patients who had particular types of diabetes, including gestational diabetes or diabetes with pregnancy; 3) patients who had malignant tumors, immune or blood system diseases, or other diseases; 4) patients who had infectious diseases, stress diseases, or other acute diseases; 5) patients were addicted to alcohol or drugs.

2.4. Dropout Criteria

Dropout occurred where: 1) collection of relevant data in the research process did not meet the requirements for completeness; 2) results could not be analyzed due to incomplete information; or 3) patients were unwilling to continue the study [8].

2.5. Data Collection

2.5.1. TCM Syndrome Diagnostic Criteria

For the patients who met the requirements, two trained professionals collected basic information and TCM symptoms for TCM syndrome differentiation and syndrome analysis using the Basic Information Collection Table of Hyperlipidemia and Information Collection Table of Four Diagnostic Methods of TCM Symptoms. For TCM syndrome differentiation and classification, the patients who met the inclusion criteria were divided into five groups (based on the Clinical Guidelines of New Chinese Medicine). Syndrome-type classification and diagnosis were based on the investigation results of an expert group, who used the Clinic terminology of traditional Chinese medical diagnosis and treatment (2015 edition), as follows:

1) Qi-deficiency and blood stasis syndrome: The main symptoms include emotional irritability or depression, bluish swelling of the body; accompanying symptoms include petechiae or ecchymosis on the tip of the tongue and rough pulse.

2) Liver depression and spleen deficiency: The main symptoms include emotional depression, irritability, dull and distending pain, constipation; accompanying symptoms include pale complexion, the feeling of exhaustion and the taut pulse.

3) Qi stagnation and blood stasis: The main symptoms include chest and hypochondriac distension and stabbing pain in the anterior heart area; accompanying symptoms include upset, petechiae or ecchymosis on the tip of the tongue and rough pulse.

4) Phlegm stasis syndrome: The main symptoms include obesity, chest tightness, and nausea; accompanying symptoms include palpitations, insomnia and loss of appetite.

5) Yang deficiency of spleen and kidney: The main symptoms include chills, feeling cold, dizziness and fatigue; accompanying symptoms include decreased appetite and swollen limbs.

2.5.2. Diagnostic Types of Hyperlipidemia

For the patients who met the requirements, the disease was classified according to the levels of Total Cholesterol (TC), Triglyceride (TG) and High-Density Lipoprotein Cholesterol (HDL-C), as shown in **Table 1**.

Table 1. The diagnostic types of hyperlipidemia.

Туреѕ	TC	TG	HDL-C
Hypercholesterolemia	t		
Hypertriglyceridemia		t	
Mixed hyperlipidemia	t	t	
Hypo high-density lipoprotein cholesterolemia			↓

↑: Elevated expression; \downarrow : Decreased expression.

2.6. Statistical Analysis

SPSS 25.0 software was used to analyze the age, sex, and types of disease of all syndromes in order to investigate the syndrome distribution pattern for hyper-lipidemia.

3. Results

3.1. Age Distribution

Table 2 shows that the 1012 patients with hyperlipidemia were mainly aged 50 - 59 (26.68%), aged 60 - 69 (29.05%) or over 70 (17.79%), these three groups accounting for 73.52% of the sample. However, 11.36% of the patients were under 40 years old.

Age group N		Male		Female		
	IN -	Cases	Percentage (%)	Cases	Percentage (%)	
<20	4	3	0.58	1	0.20	
20 - 29	25	19	3.68	6	1.21	
30 - 39	86	61	11.80	25	5.05	
40 - 49	153	103	19.92	50	10.10	
50 - 59	270	136	26.31	134	27.07	
60 - 69	294	125	24.18	169	34.14	
≥70	180	70	13.54	110	22.22	
Total	1012	517	100.00	495	100.00	

Table 2. Gender proportion of 1012 hyperlipidemia patients in each age group.

3.2. Distribution of TCM Syndromes

Table 3 shows that the most common TCM syndrome among the 1012 patients was Qi-deficiency and blood stasis syndrome (23.52%). This was followed by liver depression and spleen deficiency (9.88%), syndrome of qi stagnation and blood stasis (9.29%), phlegm stasis syndrome (7.41%), and syndrome of yang deficiency of spleen and kidney (6.92%). As two of these syndromes—qi-deficiency and blood stasis syndrome as well as liver depression and spleen deficiency—are subtypes of qi-deficiency, this syndrome accounts for 33.4% of total cases (338 patients).

Table 2 also shows that, of the 238 patients with qi-deficiency and blood stasis syndrome, more were female (133) than male (105). Besides, of the 100 patients with liver depression and spleen deficiency, more were female (62) than male (38).

		Male		Female		Median age
TCM syndromes	Ν	Percentage	Percentage		(interquartile	
			(%)	Cases	(%)	distance)
Liver and kidney yin deficiency syndrome	58 (5.73%)	29	5.61	29	5.86	62.00 (20.00)
Liver depression and spleen deficiency	100 (9.88%)	38	7.35	62	12.53	58.00 (18.00)
Syndrome of yang deficiency of spleen and kidney	70 (6.92%)	26	5.03	44	8.89	63.00 (20.00)
Spleen deficiency and						
dampness excess	20 (1.98%)	14	2.71	6	1.21	56.00 (18.00)
syndrome						
Qi-deficiency and blood stasis	238 (23.52%)	105	20.31	133	26.87	60.00 (18.00)
Syndrome of qi	(2010270)					
stagnation and blood	94 (9.29%)	31	6.00	63	12.73	60.00 (17.00)
stasis						
syndrome of damp-heat obstructing	14 (1.38%)	13	2.51	1	0.20	51.00 (27.00)
in zhong jiqo	11(110070)	10	2101	-	0120	(2,100)
Syndrome of phlegm						
stasis and internal	24 (2.37%)	14	2.71	10	2.02	50.00 (20.75)
obstruction						
Phlegm stasis syndrome	75 (7.41%)	48	9.28	27	5.45	55.00 (18.00)
Other	319 (31.52%)	199	38.49	120	24.24	56.00 (19.00)
Total	1012	517	100.00	495	100.00	58.00 (18.00)

Table 3. General condition of TCM syndromes.

3.3. Frequency of TCM Symptoms

Table 4 shows how frequently different TCM symptoms occurred. The ten most common symptoms were dry eyes, dry mouth and throat (60.47%), tiredness and weakness (53.56%), forgetful (49.41%), excessive abdominal fat (45.35%), feeling painful (42.79%), fear of cold (40.81%), bitter taste (40.52%), sweating easily (37.65%), facial flushing (35.97%), dry skin (35.87%).

Table 4. TCM symptom count table of 1012 hyperlipidemia patients.

Symptoms	Light (cases)	Medium (cases)	Heavy (cases)	Percentage (%)
Tiredness and weakness	348	172	22	53.56
Easy to panic	219	40	5	26.09
Vertigo	270	77	9	35.18
Laziness to speak	168	87	17	26.88
Sweating easily	194	146	41	37.65
Fear of cold	240	122	51	40.81
Susceptible to cold	99	39	5	14.13
Diarrhea	169	94	33	29.25

Continued				
Conscious fever	171	66	9	24.31
Dry skin	263	86	14	35.87
Facial flushing	224	114	26	35.97
Constipation	165	88	24	27.37
Dry eyes, dry mouth and throat	359	208	45	60.47
Chest tightness	278	51	7	33.20
A sense of heaviness	238	99	11	34.39
Excessive abdominal fat	258	137	64	45.35
Oily hair	201	106	27	33.00
Swollen eyes	106	23	12	13.93
Sticky mouth	157	50	6	21.04
Phlegm	122	53	10	18.29
Greasy fur	165	64	11	23.71
Oily skin	204	92	27	31.92
Bitter taste	272	122	16	40.52
Yellow urine	156	33	3	18.98
Sticky feces	147	56	13	21.34
Foul leukorrhea	14	4	1	3.86
Humid scrotum	44	13	4	11.72
Subcutaneous hemorrhage	77	22	2	9.98
Red blood streaks on the cheekbones	45	12	1	5.74
Painful	314	98	21	42.79
Chloasma	195	64	10	26.58
Dark circles	186	50	12	24.51
Forgetful	306	168	26	49.41
Dimly colored lips	187	60	16	25.99
Upset	253	75	3	32.71
Distending pain	84	17	2	10.18
Sigh	153	37	6	19.37
Pharyngeal foreign body sensation	75	22	7	10.27

4. Discussion

Hyperlipidemia, a prevalent metabolic disorder, stands as a pivotal contributor to the development of atherosclerotic cardiovascular and cerebrovascular diseases [9]. It has emerged as a significant public health concern, posing a substantial threat to societal well-being and incurring a heavy economic burden globally [10]. In recent years, Traditional Chinese Medicine (TCM) has demonstrated considerable potential as a therapeutic modality for hyperlipidemia, thereby emerging as a vital clinical intervention strategy in managing this metabolic disorder [11]. For instance, rigorous clinical trials have evidenced that the traditional Chinese medicine compound known as Shanhuang Jiangzhi Tablet effectively diminishes the serum levels of triglycerides, TC, and LDL-C among patients, offering a low-risk therapeutic approach for blood lipid reduction [12]. However, the underlying principle of Traditional Chinese Medicine (TCM) in treating hyperlipidemia is rooted in TCM theory, particularly the establishment of syndrome classification specific to the disease. Consequently, elucidating the distinct characteristics of TCM syndrome classification pertaining to hyperlipidemia holds a pivotal role in directing and optimizing TCM therapeutic interventions for this metabolic disorder.

In the present investigation, we initially conducted an analysis of the age-specific distribution patterns observed within a cohort of 1012 hyperlipidemia cases. Our findings revealed that individuals aged 50 years and above constituted a substantial proportion (73.52%) of the hyperlipidemia patient population, whereas those under 40 years of age comprised merely 11.36% of the total. This distribution underscores the prevalence of hyperlipidemia among middle-aged and elderly individuals, corroborating previous literature [13]. Nevertheless, it is noteworthy that amidst shifts in lifestyle habits and escalating societal pressures, there is a discernible trend towards an escalating incidence of hyperlipidemia among young and middle-aged adults. Consequently, this underscores the paramount importance of early intervention strategies for hyperlipidemia, warranting heightened attention and proactive measures. Furthermore, we conducted an analysis to investigate the gender-specific characteristics of hyperlipidemia. Our findings indicate that the incidence of hyperlipidemia does not exhibit significant gender disparities, underscoring its status as a prevalent metabolic disorder that affects both males and females alike. Contrary to a prior study that proposed a genderspecific prevalence in familial hypercholesterolemia, reporting a higher proportion among women, our current investigation did not uncover significant sex-related characteristics [14]. This discrepancy may potentially stem from the presence of methodological biases or differing demographic and clinical characteristics between the study populations. Furthermore, we concentrated our efforts on elucidating the fundamental syndrome patterns of hyperlipidemia, aiming to provide clinical guidance and insights for therapeutic interventions. Our analysis, encompassing 1012 patients, revealed that the most prevalent Traditional Chinese Medicine (TCM) syndrome was qi-deficiency and blood stasis (23.52%), followed by liver depression and spleen deficiency (9.88%), gi stagnation and blood stasis (9.29%), phlegm stasis syndrome (7.41%), and syndrome of yang deficiency of spleen and kidney (6.92%). Notably, the syndromes of gi-deficiency and blood stasis and liver depression and spleen deficiency, both representing subtypes of qideficiency, collectively accounted for 33.4% (338 cases) of the total patient population. These findings underscore the pivotal role of qi-deficiency as a crucial pathological foundation in hyperlipidemia, suggesting that reinforcing and regulating qi may serve as a fundamental therapeutic principle in the management of this metabolic disorder. Crataegus pinnatifida (CP), a time-honored constituent of traditional Chinese medicine, is renowned for its capacity to harmonize gi flow and facilitate digestion [15]. Additionally, it serves as a functional food that embodies properties conducive to enhancing metabolic well-being. A prior investigation has elucidated the efficacy of CP in ameliorating metabolic disruptions elicited by high-fat diets, specifically addressing impairments such as glucose intolerance, insulin resistance, hyperlipidemia, and hepatic steatosis. This underscores the promising therapeutic potential of qi-regulating herbal remedies in the management of hyperlipidemia [16]. Furthermore, we conducted a thorough analysis of the gender-specific characteristics pertaining to Traditional Chinese Medicine (TCM) syndrome classifications of hyperlipidemia. Our findings revealed a notable preponderance of female patients (133 cases) over male patients (105 cases) among the 238 individuals diagnosed with gi-deficiency and blood stasis syndrome. Similarly, in the cohort of 100 patients suffering from liver depression and spleen deficiency, there was a distinct gender disparity, with 62 females and 38 males. These observations imply that women may be more susceptible to the manifestation of hyperlipidemia-related pathological alterations, potentially mediated by their heightened response to social pressures or lifestyle disruptions, which in turn could disrupt the harmonious flow of qi, a fundamental concept in TCM. This underscores the need for gender-sensitive approaches to understanding and managing hyperlipidemia.

In addition, our study also analyzed the common symptoms of hyperlipidemia. Our results suggest that the ten most common symptoms were dry eyes, dry mouth and throat (60.47%), tiredness and weakness (53.56%), forgetful (49.41%), excessive abdominal fat (45.35%), feeling painful (42.79%), fear of cold (40.81%), bitter taste (40.52%), sweating easily (37.65%), facial flushing (35.97%), dry skin (35.87%). Intriguingly, this observation deviates from the canonical clinical presentations of hyperlipidemia [17], suggesting that in the clinical application of Traditional Chinese Medicine for managing hyperlipidemia, the categorization of syndrome types is grounded primarily in symptomatic manifestations, rather than the pathological biomarkers specific to hyperlipidemia. Besides, the limitation of this study is its reliance primarily on retrospective data, without delving into the biological diagnostic markers of syndromes. Future research could involve collecting clinical serum and plasma samples for molecular biological analysis to screen and identify relevant biomarkers for the diagnosis of disease syndromes.

5. Conclusion

In the TCM syndrome distribution in patients with hyperlipidemia, qi-deficiency and blood stasis syndrome and liver depression and spleen deficiency are the most common TCM syndromes in patients with hyperlipidemia. Furthermore, there exist gender disparities in the distribution of hyperlipidemia syndromes, with a preponderance observed among female patients. In the clinical management of hyperlipidemia, the utilization of TCM that embodies the therapeutic principles of "supplementing qi" and "regulating qi to alleviate depression" has gained increasing prominence, indicating that the latter principle could potentially emerge as a cornerstone in the clinical treatment of hyperlipidemia.

Funding

This work was supported by the National Natural Science Foundation of China (No. 82074331).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- Alloubani, A., Nimer, R. and Samara, R. (2021) Relationship between Hyperlipidemia, Cardiovascular Disease and Stroke: A Systematic Review. *Current Cardiology Reviews*, 17, e051121189015. <u>https://doi.org/10.2174/1573403x16999201210200342</u>
- He, N. and Ye, H. (2020) Exercise and Hyperlipidemia. In: Xiao, J., Ed., *Physical Exercise for Human Health*, Springer, 79-90. https://doi.org/10.1007/978-981-15-1792-1_5
- [3] Aguilar-Salinas, C.A., Gómez-Díaz, R.A. and Corral, P. (2021) New Therapies for Primary Hyperlipidemia. *The Journal of Clinical Endocrinology & Metabolism*, 107, 1216-1224. <u>https://doi.org/10.1210/clinem/dgab876</u>
- Parhofer, K.G. and Laufs, U. (2019) The Diagnosis and Treatment of Hypertriglyceridemia. *Deutsches Ärzteblatt International*, **116**, 825-832. <u>https://doi.org/10.3238/arztebl.2019.0825</u>
- [5] Wei, J., Wu, R. and Zhao, D. (2013) Analysis of TCM Syndrome Elements and Relevant Factors for Senile Diabetes. *Journal of Traditional Chinese Medicine*, **33**, 473-478. <u>https://doi.org/10.1016/s0254-6272(13)60151-x</u>
- [6] Li, G., Han, R., Lin, M., Wen, Z. and Chen, X. (2022) Developing a Core Outcome Set for Clinical Trials of Chinese Medicine for Hyperlipidemia. *Frontiers in Pharmacology*, **13**, Article 847101. <u>https://doi.org/10.3389/fphar.2022.847101</u>
- [7] Song, Q., Liu, X., Zhou, W., Wu, S. and Wang, X. (2020) Night Sleep Duration and Risk of Each Lipid Profile Abnormality in a Chinese Population: A Prospective Cohort Study. *Lipids in Health and Disease*, **19**, Article No. 185. https://doi.org/10.1186/s12944-020-01363-y
- [8] Zhang, G., Liu, X., Liang, J. and Hu, Q. (2021) The Distribution Pattern of Traditional Chinese Medicine Syndromes in 549 Patients with Type 2 Diabetes. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, 14, 2209-2216. https://doi.org/10.2147/dmso.s295351
- [9] Wright, J. and Subramanian, S. (2024) Therapy for Hyperlipidemia. *Medical Clinics of* North America, 108, 881-894. <u>https://doi.org/10.1016/j.mcna.2024.03.005</u>
- [10] Zubirán, R., Cruz-Bautista, I. and Aguilar-Salinas, C.A. (2024) Interaction between Primary Hyperlipidemias and Type 2 Diabetes: Therapeutic Implications. *Diabetes Therapy*, **15**, 1979-2000. <u>https://doi.org/10.1007/s13300-024-01626-2</u>
- [11] Yu, L., Zhao, Y. and Zhao, Y. (2023) Advances in the Pharmacological Effects and Molecular Mechanisms of Emodin in the Treatment of Metabolic Diseases. *Frontiers in Pharmacology*, 14, Article 1240820. <u>https://doi.org/10.3389/fphar.2023.1240820</u>

- [12] Sun, G. and Liang, X. (2023) Comparison of the Efficacy and Safety of Shanhuang Jiangzhi Tablets and Atorvastatin in the Treatment of Patients with Hyperlipidaemia. *Journal of Health, Population and Nutrition*, **42**, Article No. 143. <u>https://doi.org/10.1186/s41043-023-00482-3</u>
- [13] Pan, Y., Liang, J., Zhang, W., Gao, D., Li, C., Xie, W., et al. (2024) Association between Age at Diagnosis of Hyperlipidemia and Subsequent Risk of Dementia. *Journal of the American Medical Directors Association*, 25, Article ID: 104960. https://doi.org/10.1016/j.jamda.2024.01.029
- [14] Schreuder, M.M., Hamkour, S., Siegers, K.E., Holven, K.B., Johansen, A.K., van de Ree, M.A., *et al.* (2023) LDL Cholesterol Targets Rarely Achieved in Familial Hypercholesterolemia Patients: A Sex and Gender-Specific Analysis. *Atherosclerosis*, **384**, Article ID: 117117. <u>https://doi.org/10.1016/j.atherosclerosis.2023.03.022</u>
- [15] Li, R., Luan, F., Zhao, Y., Wu, M., Lu, Y., Tao, C., *et al.* (2023) *Crataegus pinnatifida*: A Botanical, Ethnopharmacological, Phytochemical, and Pharmacological Overview. *Journal of Ethnopharmacology*, **301**, Article ID: 115819. <u>https://doi.org/10.1016/j.jep.2022.115819</u>
- [16] Yuan, J., Hu, Y., Yang, D., Zhou, A., Luo, S., Xu, N., *et al.* (2024) The Effects of *Cra-taegus pinnatifida* and *Wolfiporia extensa* Combination on Diet-Induced Obesity and Gut Microbiota. *Foods*, **13**, Article 1633. <u>https://doi.org/10.3390/foods13111633</u>
- [17] Athar, M. (2024) Potentials of Artificial Intelligence in Familial Hypercholesterolemia: Advances in Screening, Diagnosis, and Risk Stratification for Early Intervention and Treatment. *International Journal of Cardiology*, **412**, Article ID: 132315. <u>https://doi.org/10.1016/j.ijcard.2024.132315</u>