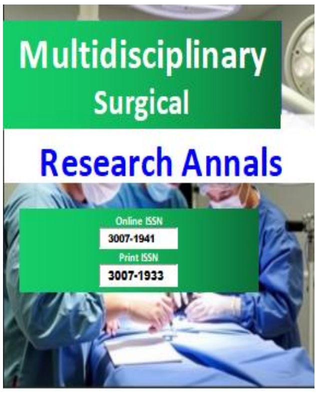

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Exploring the Role of Non-Coding RNAs in Cardiovascular Disease and its Determinants-A Comprehensive Study

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Abstract

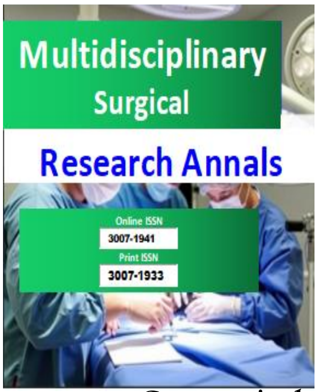
Background: Globally, cardiovascular illnesses are vital source of morbidity and mortality, and RNA that don't code protein have been corresponding the pathology of Cardiovascular disease and has emerged as important mediators of expression of genes. Objectives: The purpose of present research was to explore the potential of non-coding RNAs as prognostic and diagnostic biomarkers through investigating their levels of expression in both healthy controls and patients with cardiovascular disease. Methodology: In this study, 26 cardiovascular diseases patients and other healthy controls were enrolled. Quantitative real-time PCR and sequencing of RNA were used to profile non-coding RNA expression.

To find variations in non-coding RNA and their possible objectives, bioinformatics techniques and statistical investigation were employed. Results: In compare cardiovascular disease patients to healthy controls, there were 26 non-coding RNA that were expressed significantly. Many physiological processes, such as inflammation, replication of cells, and death, were affected by these non-coding RNA. The results of our research concluded that non-coding RNA have a high level of specificity and sensitivity for differentiating both healthy controls and patients with CVD. Conclusion: In addition to identifying possible therapeutic and prognostic indicators, this research gives new knowledge into the role of non-coding RNA in Cardiovascular disease. More investigation will be needed for authenticate results and examine the possible medical advantages of non-coding RNA treatment in cardiovascular disease.

Keywords: Cardiovascular disease, Non coding RNA, Micro RNA, long non coding RNA.

Introduction

The leading cause of death worldwide is still due to cardiovascular diseases (CVDs), which also carry significant, financial and health costs (Lu Dongchao, 2019).



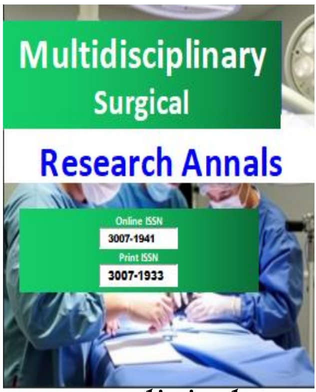
Congenital heart disease, arrhythmia, heart failure, and atherosclerosis are the primary components of cardiovascular disease, with atherosclerosis being the most t prevalent (yu, et al., 2023). There aren't therapy choices available for cardiovascular disease. Therefore, it is imperative to identify and validate new treatment targets to combat CVDs. Protein-targeting medications are used in the majority of conventional treatments for heart failure patients. Since RNA molecules are involved in many biological processes, including development and progression of disease. These have become more attractive treatment possibilities for a wide range of illnesses. Despite making up a small portion of all RNA molecules, protein-coding RNAs have now been studied many times (Lu Dongchao, 2019).

Myocyte and non-myocyte development continuation and function, it is the final results of many factors including condition in the same thing is expressed. (Kumarswamy & Thum, 2013) . Although human genome is transcriptionally very active and produces a wide variety of noncoding RNAs (ncRNAs) with regulatory roles and it does not encode any proteins. A significant function for non-coding RNAs (ncRNAs) in humans is suggested by the finding of a sharply rising fraction of ncRNAs, which contrasts with the slight rise in the in the strength of genes that code for protein .In the time of the evolution from basic creatures to living soul these RNA have single strand structure. (Wolfgang, et al., 2017).

The RNA molecules that do not encode a protein like microRNA, little interfering RNA, with long non coding RNA are Innovative modulators of myocardial hazard part and cellular activities that may enhance prognosis and diagnosis. Essentially, non-coding RNAs have greatly develop our healing range. (Wolfgang, et al., 2017). Non coding RNA which is also responsible to the breakdown and modification in transcription processing editing and translation when they are bind with DNA and RNA in a specific manner (Roy, Trautwein, leudde, & Roderburg, 2018) . Non-coding RNA has also important in human to detect the various disease such as cardiovascular disease cancer, genetic disorder, and inflammatory disease. (Roy, Trautwein, leudde, & Roderburg, 2018).

It is moreover, in prokaryotes 80-90% of the genome is made up of protein coding genes, with just a small amount of non-coding RNA (which varies even across strains that are closely related). In contrast, in eukaryotes protein coding genes are significantly it's a tiny portion. The quantity of this proteome fall other the trait, examination and buildup of these organisms from decreased non-chordates to humans become more difficult because the rise of intron and intragenic arrangements. (Bhatti, et al., 2021) . The classes of non-coding RNA, like RNA polymerase I, RNA polymerase II, and RNA polymerase III are competent of transcription. Non coding RNAs are frequently separated into two types short and long. The 200 nt to 100 kb long non coding RNAs (lncRNAs) undergo full processing from their templates. Although they resemble mRNA, lncRNAs have minimal conservation and are not utilized as templates for protein synthesis. (kim & Reitmair , 2013).

Another aspect of RNA that is transcribed from DNA but does not encode proteins is known as non-coding RNA (ncRNA). On the report of evidence non coding RNA have the ability to control gene expression through a variety of pathways, including influencing messenger RNA (mRNA) transcription or translation or DNA/RNA methylation. They are essential in coordinating the pathophysiological of human illness. According to a study, the name coding RNA plays a fundamental role in depression such as neuroplasticity, neurogenesis, its



clinical symptoms, suicidal behavior and is an anti-depressant treatment. (shi, wang , song, kong, & Zhang , 2021) . It's becoming evident that the coding region of the genome only accounts for a small percentage of the total genetic information as next-generation sequencing tools improve. Large scale genome-wide sequencing has shown that non-coding RNAs (ncRNA) are produced in specific tissues and play a crucial role as regulators in fundamental biological processes. (Latowska, et al., 2020).

Research Objective

The major goal of this study is to identify the crucial role of non-coding RNA to regulate the gene expression, cellular differentiation and development. Environmental factor can affect the expression of non-coding RNA. Non coding RNA help in cancer development, prognosis, and it is also responsible to the breakdown and modification in transcription and translation process.

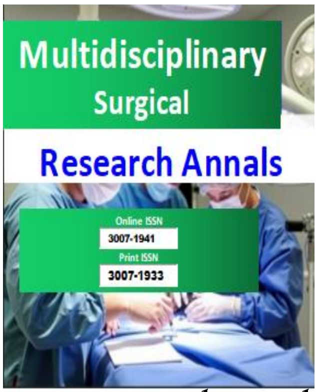
Study Gap

Previous studies have just discussed the non-coding RNA which effects on the heart failure, genes regulation and cancer diagnosis. This study focus on atherosclerosis which is caused by accumulation of lipids and inflammatory cells in blood vessel wall and causing the death of people.

Literature

In humans, cardiovascular disorders are the leading cause of death, which claimed over 17 million lives in 2020. Congenital heart disease, arrhythmia, heart failure, and atherosclerosis are the primary components of cardiovascular disease, with atherosclerosis being the most prevalent (yu, et al., 2023) .Most traditional therapies for cardiovascular patients include the use of drugs that target proteins (Lu Dongchao, 2019) . Hypertension, diabetes, and hyperlipidemia are additional CV risk factors completely or partially influenced by life style or environmental changes. In the diagnosis and treatment of a wide range of illnesses, including CVD's and the control of CV risk factors, RNA-based therapies have become a rapidly expanding specialty. It has been established that various RNA types are essential for controlling the expression of genes that determine health outcomes in a variety of CVDs (Ardiana, et al., 2023).

The hallmark of atherosclerosis is fibro-fat lesions on the arterial walls, which have a very high risk of morbidity and death. Cerebrovascular and cardiovascular conditions including myocardial infarction, coronary heart disease, and cerebral infarction are thought to have atherosclerosis as a major pathophysiological foundation (Liu, et al., 2023). Chronic inflammation is the cause of atherosclerosis, which has been the subject of much research in recent years. Other factors include inflammatory responses, aging, cell death, and the transition from endothelium to mesenchymal tissue. Endothelial cell aging and chronic inflammation are caused by the accumulation of telomere, genomic, and mitochondrial DNA damage in vascular endothelial cells at the molecular level (Liu, et al., 2023). Chronic inflammation is another name for sluggish, persistent inflammation that lasts for several months to years. Chronic inflammation's degree and consequences often depend on the injury's source and the body's capacity to heal and recover from the harm (Pahwa, Goyal, & Jialal, 2003). Cardiovascular disease, diabetes, cancer, autoimmune disorders, chronic hepatic and renal diseases, strokes heart attacks and other conditions are among the many illnesses linked to chronic inflammation (Pahwa, Goyal, & Jialal, 2003). In clinical practices, a systematic evolution of the RIR to identify individuals at increased cardiovascular risk is not used, despite the fact that inflammation has long been recognized as a significant contributor

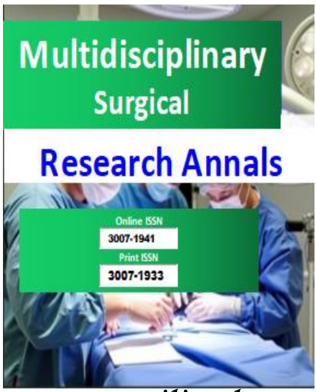


to atherosclerosis. High sensitivity C reactive protein is the biomarker that been used in circulating inflammatory indices to measure RIR and determine the advantages of anti-inflammatory treatment in the cardiovascular domain (fusco , et al., 2023).

Early on in atherosclerosis, inflammation is brought on by an accumulation of low-density lipoproteins (LDL), which are then phagocytosed by macrophages creating foam cells that set off the inflammatory reaction (yu, et al., 2023) .The RNA molecules that does not encode a protein like microRNA, little interfering RNA, with long non coding RNA (Wolfgang, et al., 2017) . MicroRNA are non-coding RNA with a length of about 20 nucleotides. Pre-miRNA is created when miRNA is first transcribed, travels from the nucleus to the cytoplasm, goes through a series of processing steps and eventually matures. By loosely partnering with mRNAs that have corresponding miRNA responsive elements (MREs), mature miRNA's contribute to the development of RNA silencing complexes (RISCs) and provide RISC targeting (yu, et al., 2023) . It has been demonstrated that non coding RNA regulate inflammatory response, cell activation and proliferation, and lipid metabolism, all of which are key factors in the pathophysiology of atherosclerosis (Liu, et al., 2023).

Conventional main arteries have atherosclerosis, which normally starts in early adolescence. During life, atherosclerosis is asymptomatic and not detectable by conventional diagnostic techniques. Heart attacks or sudden cardiac death (death within an hour of the beginning of the symptom) are the initial signs of atherosclerotic cardiovascular disease (Kakadiya, 2009) . Until an artery is significantly narrowed or completely blocked, atherosclerosis typically doesn't show any symptoms. The Angina may cause your chest to feel constricted or squeezing. Additionally, it could be felt in your back, neck, jaw, shoulders, or arms. Activity tends to exacerbate this ache, which then subsides with rest. Pain can also be brought on by emotional stress. Inability to breathe arrhythmias, or irregular heartbeats. Suddenly feeling weak, numb, and lightheaded. (Kakadiya, 2009).

Fasting LDL and cardiovascular events are decreased by statins, which inhibit hydroxymethylglutarate CoA (HMG-CoA) reductase, the rate-limiting step in cholesterol formation. Combining those effects with ezetimibe, a medication that prevents the absorption of cholesterol, intensifies them. (Spence, 2006) Many herbal remedies have been



utilized to treat disorders linked to atherosclerosis since ancient times, and the primary method of traditional Chinese medicine utilized in clinics is decoction. According to current research, a number of active monomers used in traditional Chinese medicine, including alkaloid flavonoids and saponins have beneficial effects on atherosclerosis. One active component of Berberis aristata DC, berberine for instance, can activate the PPAR in macrophages, which lowers the expression of inflammatory markers such as monocyte chemo attractant protein-1 (MCP-1) (Liu, et al., 2023).

There are two types of non-coding RNA tiny transcripts (less than 200 nucleotides), which includes microRNA and other endogenous RNA species, and long noncoding RNAs, which have a length between 200 and thousands of nucleotides. This description is based on an operational length threshold. It is clear that while changed non coding RNA expression or function might hinder biological processes that contribute to the development of (cardiovascular) illness, it also holds great promise for use in diagnostic and prognostic tools. (Viereck & Thum, 2017).

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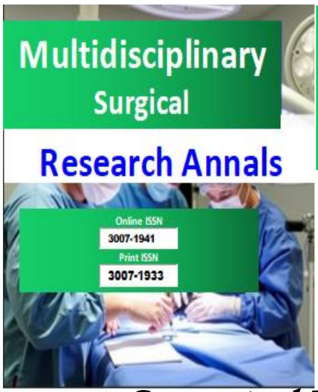
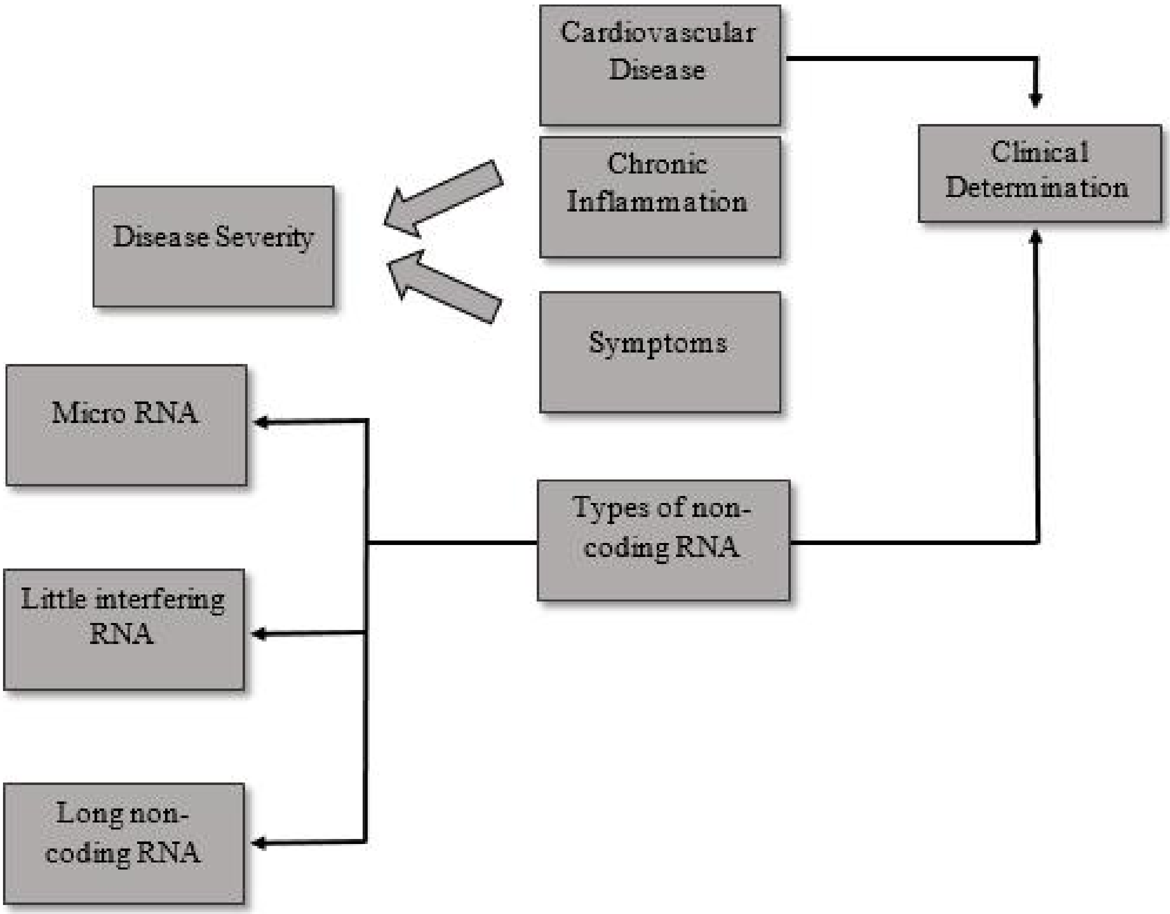


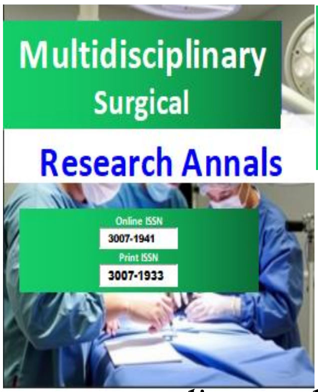
Conceptual Framework

To explain the topic Study of cardiovascular disease by non-coding RNAs and its determination diagrammatic in one view. There are two independent variable undertaken my study are diseases severity and types of Non-coding RNA which are microRNA, Long non coding RNA with Small interfering RNA.



Hypothesis

H1: Non coding RNA has vital effect in development and diagnosis of



cardiovascular disease.

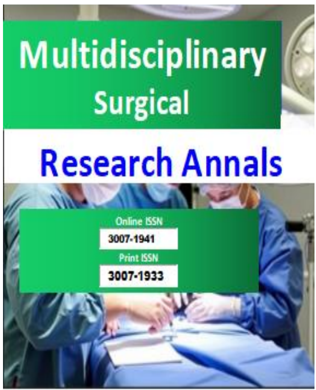
H2: Non coding RNA has vital effect on cardiovascular disease which has the help of biomarker.

H3: Micro RNA has vital effect to regulate the genes expression in cardiovascular disease.

H4: long non coding RNA has vital effect on the treatment of cardiovascular disease.

Research Methodology

The following data collection methods and processes are used in this study. This semi structured study was conducted to examine the Study of cardiovascular disease by non-coding RNAs and its determination. This study was based on the secondary data source to investigate the interaction between non-coding RNA in cardiovascular disease. The focus of the examination on cardiovascular disease by non-coding RNA in which the patients with diagnosed cardiovascular disease for example arterial disease with cardiac failure, both male and female are affected on the different ages and change the appearance of non-coding RNA. Patients with cardiovascular diseases were the population that was studied. A sample is the population chosen for a proper study based on



certain criteria in order to assess data and research finding. To finding the data needed for this research around, a survey of about 384 respondents will be conducted. A standard spreadsheet performance evaluation is what morgen suggests using to guarantee accurate data evaluation. According to Morgan table (Krejcie & Morgan, 1970) respondents are chosen sources of data.

A systematic questionnaire was used for the collection of secondary data, with the help of medical lab technologists and doctors (physicians). The secondary data consist of the clinical history, physical examination and laboratory tests results. Non coding RNA was used as a therapeutics for the investigation of cardiovascular diseases in the laboratory. Different RNA translation patterns such as Reverse transcription polymerase chain reaction, microarray analysis, and non-coding RNA analysis were utilized for the diagnosis of cardiovascular diseases. Examination of protein levels, particularly cardiac markers (i.e. creatine phosphokinase, troponin) was used for the diagnosis of CVDs disease. SPSS software was used to examine medical information, asses the accuracy of data and find interaction between cardiovascular disease and non-coding RNA expression, descriptive Statistics tools were used for the analyses of data.

Results

A critical field of biomedical research is the utilization of fresh biomarkers in therapeutic settings. More specifically, RNSs that don't code protein are regarded as possible indications because they are satisfy requirements, they are empirically changed in congestive heart failure. Overall 384 respondents were selected for study out of which 26 patients were determined as a cardiac-patient by using diagnostic methods non-coding RNA (miR-1 expression, miR-21 expression, Long non-coding RNA-19 expression). As in table 1, most of the patients 19(73.1%) of 26 were determined as the cardiac-patient in the age of 61-80 while some patients were also diagnosed in the age of 41-60> these were 7(26.9%) of 26.

Table 1: Age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	41-60	7	26.9	26.9	26.9

61-80	19	73.1	73.1	100.0
Total	26	100.0	100.0	

As in table 2, most of the patients 10(38.5% which is 38.5<50 where approximation of 50%>value) of 26 were determined as the cardiac-patient in the hypertension while 16(61.5%) of 26 patients were also diagnosed in the hypertension.

Table 2: Hypertension

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	16	61.5	61.5	61.5
	No	10	38.5	38.5	100.0
	Total	26	100.0	100.0	

As in table 3, most of the patients 9(34.6%) of 26 were determined as the cardiac-patient in the hyperlipidemia while some patients were also diagnosed in the hyperlipidemia these were 17(65.4%) of 26. The values also diagnose that the overall 100% is needed to be assured where 100 %.< 65.4 where 34.6>100.

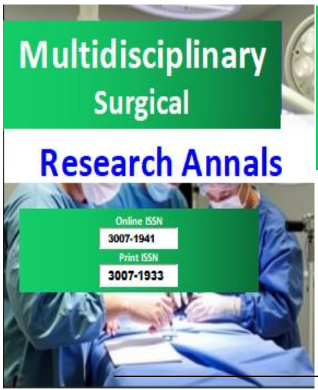
Table 3: Hyperlipidemia

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	17	65.4	65.4	65.4
	No	9	34.6	34.6	100.0
	Total	26	100.0	100.0	

As in table 4, most of the patients 2(7.7%) of 26 were determined as the cardiac-patient in the miR-1 Expression while some patients were also diagnosed in the miR-1 Expression these were 1(3.8%), 3(11.5%), 6(23.1%), 9(34.6%), 5(19.2%) of 26.

Table 4: MiR-1 Expression

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.0-0.5	2	7.7	7.7	7.7
	0.6-1.0	1	3.8	3.8	11.5
	1.1-	3	11.5	11.5	23.1

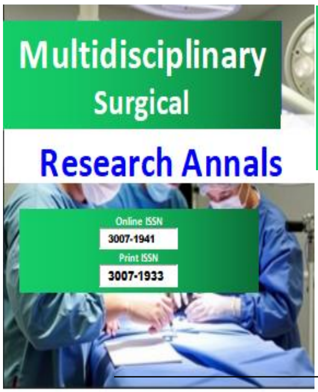


	1.5				
	1.6-2.0	6	23.1	23.1	46.2
	2.1-2.5	9	34.6	34.6	80.8
	2.6-3.0	5	19.2	19.2	100.0
	Total	26	100.0	100.0	

As in table 5, most of the patients 3(11.5%) of 26 were determined as the cardiac-patient in the miR-21 Expression while some patients were also diagnosed in the miR-21 Expression these were 1(3.8%), 7(26.9%), 6(23.1%), 9(34.6%) of 26 respectively.

Table 5: MiR-21 Expression

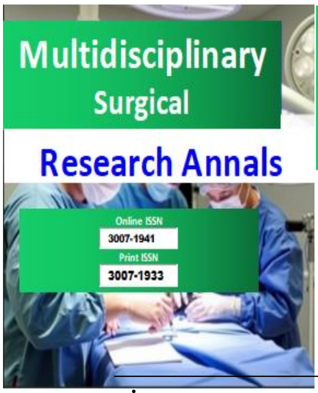
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.0-0.5	3	11.5	11.5	11.5
	0.6-1.0	1	3.8	3.8	15.4



1.1-1.5	7	26.9	26.9	42.3
1.6-2.0	6	23.1	23.1	65.4
2.1-2.5	9	34.6	34.6	100.0
Total	26	100.0	100.0	

Table 6: Descriptive Statistics

	N	Range	Minimum	Maximum	Mean		Std. Deviation	Variance
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic
Age	26	1.00	2.00	3.00	2.7308	.08871	.45234	.205
Hyperlipidemia	26	1.00	1.00	2.00	1.3462	.09515	.48516	.235
Hypertens	26	1.00	1.00	2.00	1.38	.097	.4961	.246



ion					46	30	4	
miR1	26	5.00	1.00	6.00	4.3077	.28158	1.43581	2.062
miR21	26	4.00	1.00	5.00	3.6538	.25984	1.32491	1.755
LncRNA	26	3.00	1.00	4.00	2.6538	.17490	.89184	.795

Descriptive Statistics

A group of strategies used to condense and clarify an information set's major qualities, for example its spread, variation, and numerical average are known as descriptive statistics. To make information easier to identify, descriptive statistics are employed to manage and collect it. Characteristic statistics then explain ranges using data. The graphical representation of charts, diagrams, and documents are examples of visual illustrations of knowledge used in statistical calculations that can help provide data interpretation and analysis. The histograms pie graphs, bar graphs, dispersion plots, and box graphs are examples of common diagrammatic strategies. Standard error is a acceptance and rejection of overall data which is below 1 which shows that there is significant impact of Non coding RNA.

Conclusion

The investigation of cardiac failure using non-coding RNA has changed our knowledge of the molecular processes that cause these conditions. Major mediators of the beginning and growth of cardiovascular illness have been presented to be RNAs that do not code protein particularly, little interfering RNA, long non coding RNA and micro RNAs. The ability of these RNAs that don't code protein to alter gene expression, impact signaling processes, and affect cellular functions makes them desirable candidates for medical treatment. Heart failure, atherosclerosis, and cardiac hypertrophy are several cardiovascular diseases that involve different non-coding RNAs. RNAs that do not protein have the capacity to act as a biomarker for the detection and treatment of heart disorders. Angiogenesis, apoptosis, and inflammation are some of the main signaling processes associated with heart illness that non-coding RNAs can regulate.

Limitation

It is difficult to generalize outcomes of several research to more people due to their small number of participants and little a variety.

Methodological changes in RNA collection, replication, and methods for identification can have an effect on non-coding RNA expression examinations. As several cell types compose heart disease tissues, it could be difficult to determine sequences of non-coding RNA expression specific to particular cells. The regulatory problems for non-coding RNA-based treatments consist of making that they are secure, successful, and unique.

References

Ardiana, M., fadila , A. N., Zuhra , Z., kusuma , N. M., Oceandy, D., & Rurus, M. S. (2023). Non-coding RNA therapeutics in cardiovascular diseases and risk factors. Systematic review, 1.

Bhatti, G. k., Khullar, N., sidhu , I. s., navik, U. s., Reddy, A., Reddy , P., & bhatti, J. s. (2021). Emerging role of non-coding RNA in health and disease. Metabolic Brain Disease , 1120.

fusco , s. A., Aldo , p. m., scicchitano , p., zuin , m., D'Emilia , e., & colivicchi , f. (2023). Lipoprotein,inflammation and Atherosclerosis. 3.

Kakadiya, J. (2009). CAUSES, SYMPTOMS, PATHOPHYSIOLOGY AND DIAGNOSIS OF ATHEROSCLEROSIS- A REVIEW.

Harmacologyonline , 422-423.

kim, T., & Reitmair , A. (2013). Non-Coding RNAs: Functional Aspects and Diagnostic Utility in Oncology. Review article , 2-3.

Krejcie, R. V., & Morgan, D. W. (1970). we recommended to the authorities that the use of the proper tools and method for the diagnosis of the patients . Education and psychological Measurement .

Kumarswamy, R., & Thum, T. (2013). Non-coding RNAs in Cardiac Remodeling and Heart Failure. Heart Failure Compendium, 3.

Roy, S., Trautwein, C., leudde, T., & Roderburg, C. (2018). A General Overview on Non-coding RNA based diagnostic and therapeutic approches for liver diseases. Frontiers in Pharmacology, 9(2018), 1.

Viereck, J., & Thum, T. (2017). Circulating Noncoding RNAs as Biomarkers of Cardiovascular Disease and Injury. Circulation Research, 120, 382.

Latowska, J., Grabowska, A., Zarębska, Ż., Kuczyński, K., Kuczyńska, B., & rolle , K. (2020). Non-Coding RNAs in Brain Tumors, the Contribution of lncRNAs, circRNAs, and snoRNAs to Cancer Development—Their Diagnostic and Therapeutic Potential.

International Journal of Molecular Scieneces , 1.

Liu, G., Tan, L., Zhao, X., Wang, M., Zhang , Z., Zhang, J., . . . qin, W. (2023). Anti-atherosclerosis mechanisms associated with regulation of non-coding RNAs by active monomers of traditional Chinese medicine . Frotiers in Pharmacology , 1.

Lu Dongchao, T. T. (2019). Non-coding RNAs in cardiovascular diseases,diagnostic and therapeutic perspectives. Cardiology(2019), 1.

Pahwa, R., Goyal, A., & Jialal, I. (2003). Chronic Inflammation. Europe pmc, 1.

shi, Y., wang , Q., song, R., kong, Y., & Zhang , Z. (2021). Non-coding RNAs in depression: Promising diagnostic and therapeutic biomarkers. eBioMedicine Home, 71, 1.

Spence, J. D. (2006). Recent advances in pathogenesis, assessment, and treatment of atherosclerosis. F1000Research , 3.

Wolfgang, P., Dimmeler, S., Heymans, S., Zeller, T., Haas, J., Karakas, M., . . . Landmesser, U. (2017). Non-coding RNAs in cardiovascular diseases,diagnostic and therapeutic perspectives. European Heart Journal, 1,2.

yu, Z., yin, J., Tang , Z., HU, T., Wang, Z., chen, Y., . . . Zhang, W. (2023). Non-coding RNAs are key players and promising of therapeutic targets in atherosclerosis . Frontiers in Cell and Developmental Biology , 1.