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Original Research

The Correlation Between Hypogonadism and Coronary Heart Disease at RSUP Prof. Ngoerah

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Abstract

Hypogonadism is a clinical syndrome associated with aging, characterized by low levels of testosterone in a man's body. Hypogonadism can lead to various diseases, one of which is coronary heart disease. Coronary heart disease is a cardiovascular disease caused by the buildup of plaque in the coronary arteries. This research aims to examine the relationship between hypogonadism and coronary heart disease in men at RSUP Prof. Ngoerah. The research was conducted analytically with a case-control design. Hypogonadism was measured using the ADAM score questionnaire, which consists of 10 questions. The research sample comprised men who were coronary heart disease patients and men who were non-coronary heart disease patients aged 35–45 years in the Gedung Pelayanan Jantung Terpadu RSUP Prof. Ngoerah. The sample was determined using a consecutive sampling technique, with a total of 50 participants. The research results found that 28 participants (56%) tested positive for hypogonadism, and 22 participants (44%) tested negative for hypogonadism. A p-value of 0.004 indicated a significant relationship ($p \leqslant 0.05$) between hypogonadism and coronary heart disease. The calculated Odds Ratio (OR 95% CI) between hypogonadism and coronary heart disease was 5.6 (1.648 – 19.232). Among the research participants, 19 (76%) were positive for hypogonadism and coronary heart disease. Meanwhile, 16 participants (64%) were negative for both hypogonadism and coronary heart disease. The lower the testosterone levels in men, the higher the risk of developing coronary heart disease. Coronary heart disease patients with hypogonadism were 5.6 times more likely to have the condition compared to those without hypogonadism. There is a significant correlation between andropause and coronary heart disease in men at RSUP Prof. Ngoerah

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1. Introduction

Every individual will inevitably go through a natural process in the body called aging. Aging occurs naturally and can cause physiological and psychological changes. Aging can affect the work of various body organs, one of which is reproduction. As people get older, the levels of sexual hormones in humans will decrease. Specifically in men, the testosterone hormone will decrease. Men who have reached the age of 35 experience a decline in testosterone levels.[1] The condition where testosterone levels are below normal is known as hypogonadism.[2]

Hypogonadism is a clinical syndrome characterized by low levels of the hormone testosterone in a man's body. The decline in testosterone levels can be caused by dysfunction in the hypothalamic-pituitary-gonadal axis due to aging, leading to a failure to produce normal levels of testosterone. Hypogonadism can occur due to issues with the gonads or problems in the brain, particularly in the pituitary or hypothalamus glands.[3] The risk of developing hypogonadism continues to increase as a person ages. This is proven by the large number of cases of hypogonadism found in men aged 65-80 years. More than 20% of men aged 60 years and over, and more than 30% of men aged 70 years and over suffer from hypogonadism.[4] Various risk factors, such as environmental factors, hypertension, diabetes mellitus, obesity, stress, and metabolic syndrome, can contribute to the onset of hypogonadism in men.[5]

Hypogonadism presents with various symptoms. These include decreased libido, erectile dysfunction, sleep disturbances, depression, lack of energy, and reduced bone strength.[6] Hypogonadism can lead to various diseases, one of which is coronary heart disease. According to previous research, coronary heart disease can be caused by hypogonadism. Coronary heart disease in men can be exacerbated by low testosterone levels.[7] Coronary heart disease is a disorder of heart function caused by the narrowing of the coronary arteries due to cholesterol deposits on the artery walls. This condition can cause a lack of supply of nutrients and oxygen to heart cells. This disease is considered very dangerous because it can cause a sudden heart attack without any symptoms beforehand.[8]

As many as 1,5% of the Indonesian population suffers from coronary heart disease and around 50% of coronary heart disease patients have the potential to experience sudden cardiac arrest or sudden cardiac death. Based on data from Riskesdas in 2018, deaths due to coronary heart disease have increased from 0,5% to 1,5%.[9] Coronary heart disease has many risk factors, such as type 2 diabetes mellitus, hypertension, stress, hyperlipidemia, smoking, lack of exercise, and obesity.[10] In particular, this disease is also influenced by low testosterone levels in a man's body. The lower the testosterone level, the higher the risk of developing coronary heart disease.[11]

Based on research, that has been conducted, hypogonadism can cause a man to suffer from coronary heart disease. Men with low testosterone levels are more at risk of developing coronary heart disease than men who have normal testosterone levels. Testosterone levels in a person's body can determine how severe the person's coronary heart disease is. The lower the testosterone levels in a person's body, the more severe the coronary heart disease they suffer.[11] Based on research, conducted on 930 men, it was found that testosterone levels in men with coronary heart disease were lower than in men without coronary heart disease. Men with coronary heart disease who also suffer from hypogonadism have reached 24%. This figure is three times greater than estimated by researchers.[12]

Research on the correlation between hypogonadism and coronary heart disease has never been conducted in Bali before. Therefore, the author is interested in investigating whether there is a significant relationship between hypogonadism and coronary heart disease at RSUP Prof. Ngoerah in Denpasar, Bali.

2. Method

This research was conducted at Gedung Pelayanan Jantung Terpadu RSUP Prof. Ngoerah in April – July 2024 in a case-control design. The Ethics Committee of the Faculty of Medicine, Udayana University has given the study its ethical approval with letter number 0544/UN14.2.2.VII.14/LT/2024. The sample of this study consists of men aged 35-45, both coronary heart patients and non-coronary heart patients. The data were obtained using a questionnaire that included age, blood pressure, body mass index, marital status, cigarette profile, alcohol consumption, other medical conditions, hypogonadism, and ADAM score questionnaire.

A consecutive sampling technique was used to choose the samples based on inclusion and exclusion criteria. The inclusion criteria included men aged 35-45 years old, located in the polyclinic area of Gedung Pelayanan Jantung Terpadu (PJT) RSUP Prof. Ngoerah, married and living with wife,

and agreed to this research informed consent. Specifically, the inclusion criteria for cases and controls differed in the diagnosis, where the inclusion criteria for the cases were diagnosed with coronary heart disease and the controls were diagnosed with heart disease other than coronary heart disease at the time of being a respondent. Questionnaires that were not filled out and patients with congenital diseases such as primary hypogonadism and congenital heart defects were excluded. Based on those criteria, there were 50 samples selected.

Dependent variable in this study is coronary heart disease, determined based on the patient's medical record. The independent variable in this study is hypogonadism, measured using ADAM score questionnaire consisting of 10 'Yes' or 'No' questions. Hypogonadism is considered positive if the sample answers "Yes" to question number 1 or 7, or if "Yes" is marked for more than 3 questions in the ADAM score questionnaire. Control variables in this study include age, blood pressure, body mass index, marital status, cigarette profile, alcohol consumption, and other medical conditions.

Blood pressure is stratified into 4 levels: systolic pressure < 120 mmHg and diastolic pressure < 80 mmHg is considered normal, systolic pressure is 120-129 mmHg and diastolic pressure < 80 mmHg is considered elevated, systolic pressure is 130-139 mmHg or diastolic pressure is 80-89 mmHg is considered hypertension stage 1, and systolic pressure is ≥ 140 mmHg or diastolic pressure is ≥ 90 mmHg is considered hypertension stage 2. Body mass index is divided into 6 levels: BMI ranged < 18.5 kg/m^2 is considered underweight, BMI ranged from 18.5 – 24.9 kg/m^2 is considered normal, BMI ranged from 25-29.9 kg/m^2 is considered overweight, BMI ranged from 30 – 34.9 kg/m^2 is considered obese class 1, BMI ranged from 35 – 39.9 kg/m^2 is considered obese class 2, and BMI ranged > 40 kg/m^2 is considered obese class 3.

Data that has been collected were analyzed statistically using the 29.0 version of Statistical Package for the Social Sciences (SPSS). The statistical analysis in this research includes univariate and bivariate analysis. The univariate analysis was presented to provide the characteristics of each research variable. The bivariate analysis was presented to determine the correlation between the independent and dependent variables using the Pearson Chi-Square test and calculation of odds ratio (OR 95% CI).

3. Result

The characteristics of the samples (25 case samples and 25 control samples) include age, blood pressure, body mass index, cigarette profile, alcohol consumption, and other medical conditions. The results can be seen in Table 1.

Table 1. Characteristics of Samples

Variables	Case (n=25)		Control (n=25)	
	n	%	N	%
Age				
Subclinical Phase (25 – 35 years)	0	0	8	32
Transition Phase (35 – 45 years)	5	20	8	32
Clinical Phase (>45 years)	20	80	9	36
Blood Pressure				
Normal	5	20	10	40
Elevated	14	56	12	48
Hypertension Stage 1	4	16	1	4
Hypertension Stage 2	2	8	2	8
Body Mass Index				
Underweight	1	4	0	0
Normal	11	44	6	24
Overweight	8	32	16	64
Obese Class 1	3	12	3	12
Obese Class 2	1	4	0	0
Obese Class 3	1	4	0	0
Cigarette Profile				
Non-Smoker	22	88	18	72
Light Smoker	1	4	4	16
Moderate Smoker	1	4	1	4
Heavy Smoker	1	4	2	8

Alcohol Consumption				
Non-Drinker	23	92	21	84
Light Drinker	1	4	4	16
Moderate Drinker	1	4	0	0
Heavy Drinker	0	0	0	0
Other Medical Conditions				
Yes	9	36	6	24
Gout	1	11,1	1	16,6
Type- 2 Diabetes Mellitus	3	33,3	0	0
Hyperlipidemia	1	11,1	0	0
Hypertension	1	11,1	3	50
Myocardial Infarction	1	11,1	0	0
Bladder Cancer	0	0	1	16,6
Chronic Obstructive Pulmonary Disease (COPD)	1	11,1	0	0
Heart Valve Disease	0	0	1	16,6
Vertigo	1	11,1	0	0
No	16	64	19	76
Hypogonadism				
Positive	19	76	9	36
Negative	6	24	16	64

Based on Table 1, most of the case (80%) and control (36%) samples are categorized as more than 45 years old, indicating a clinical stage. The majority of case samples experienced an increase in blood pressure, with 56% in the elevated category, 16% in the hypertension stage 1 category, and 8% in the hypertension stage 2 category. However, compared to these results, fewer control samples experienced an increase in blood pressure, with 48% in the elevated category, 4% in hypertension stage 1, and 8% in hypertension stage 2. A total of 52% of case samples and 76% of control samples have a body mass index (BMI) more than or equal to 25 kg/m^2, placing them in the obesity category.

Based on the cigarette profile, most of the case (88%) and control (72%) samples are non-smokers. An investigation is also conducted on alcohol consumption with most of the cases (92%) and controls (84%) samples being non-drinkers. Most samples have no other medical condition. However, some of the case samples have other medical conditions such as gout, type-2 diabetes mellitus, hyperlipidemia, hypertension, myocardial infarction, COPD, and vertigo. Some of the control samples also have other medical conditions that can be detailed as gout, hypertension, bladder cancer, and heart valve disease.

Hypogonadism is identified as positive if the response to question number 1 or 7 on the ADAM score questionnaire is "Yes", or if "Yes" is marked for more than 3 questions in total. Based on table 1, most of the cases testing positive for hypogonadism (76%) and most of the controls testing negative for hypogonadism (64%).

Table 2. Results of Questionnaire Responses: ADAM Score Questionnaire for CAD Patients

No.	Questionnaires	Frequency			
		Yes	%	No	%
1.	Do you have a decrease in libido (sex drive)?	15	60	10	40
2.	Do you have a lack of energy?	13	52	12	48
3.	Do you have a decrease in strength and/or endurance?	19	76	6	24
4.	Have you lost height?	1	4	24	96
5.	Have you noticed a decreased 'enjoyment of life'?	3	12	22	88
6.	Are you sad and/or grumpy?	7	28	18	72
7.	Are your erections less strong?	14	56	11	44
8.	Have you noticed a recent deterioration in your ability to play sports?	15	60	10	40
9.	Are you falling asleep after dinner?	11	44	14	56

10.	Has there been a recent deterioration in your work performance?	17	68	8	32

Table 2 presents the detailed results of the ADAM score questionnaire for CAD patients. Most of the samples answered 'Yes' to question number one (60%) and question number seven (56%). The question that has the highest 'No' answers is question number four (96%). Most of the samples did not feel any difference in their height, while 4% of the samples felt a decrease in their height. About 60% of samples felt a decrease in strength and/or endurance and a recent deterioration in their ability to play sports.

Table 3. Results of Questionnaire Responses: ADAM Score Questionnaire for Non-CAD Patients

No.	Questionnaires	Frequency			
		Yes	%	No	%
1.	Do you have a decrease in libido (sex drive)?	4	16	21	84
2.	Do you have a lack of energy?	4	16	21	84
3.	Do you have a decrease in strength and/or endurance?	7	28	18	72
4.	Have you lost height?	1	4	24	96
5.	Have you noticed a decreased 'enjoyment of life'?	1	4	24	96
6.	Are you sad and/or grumpy?	5	20	20	80
7.	Are your erections less strong?	5	20	20	80
8.	Have you noticed a recent deterioration in your ability to play sports?	11	44	14	56
9.	Are you falling asleep after dinner?	6	24	19	76
10.	Has there been a recent deterioration in your work performance?	5	20	20	80

Table 3 presents the detailed results of the ADAM score questionnaire for non-CAD patients. Most of the samples answered 'No' to question number one (84%) and question number seven (80%). The question that has the highest 'No' answers is question number four and five (96%). Most of the samples did not feel any difference in their height and did not have a decreased in enjoyment of life, while 4% of the samples felt a decrease in their height and have a decreased in enjoyment of life. About 44% of samples felt a decrease in strength and/or endurance and a recent deterioration in their ability to play sports.

Table 4. Correlation Between Hypogonadism and Coronary Heart Disease at PJT RSUP Prof. Ngoerah

Hypogonadism	Cases (n=25)		Controls (n=25)		p*	OR	CI (95%)
	n	%	N	%			
Hypogonadism							
Positive	19	76	9	36	0.004	5.6	1.6-19.2
Negative	6	24	16	64			
Total	25	100	25	100			

According to Table 4, the number of samples who tested positive for hypogonadism and positive for coronary heart disease was 76%. This result is higher than the number of respondents who were negative for hypogonadism but positive for coronary heart disease, totaling 6 samples (24%). Among those who tested negative for coronary heart disease, 9 samples (36%) tested positive for hypogonadism. Additionally, 16 samples (64%) of the sample who were negative for coronary heart disease tested negative for hypogonadism. This result shows that more coronary heart disease patients have hypogonadism, compared to non-coronary heart disease patients.

The correlation between hypogonadism and coronary heart disease is presented in Table 4. Correlation between hypogonadism and coronary heart disease was acquired from the bivariate

analysis of the 2x2 table. This research used the Pearson Chi-Square to analyze the correlation. The results of the analysis revealed a significant correlation between hypogonadism and coronary heart disease ($p \leq 0.05$). According to these findings, it was found that men with hypogonadism have a higher likelihood of developing coronary heart disease.

The risk of coronary heart disease events due to hypogonadism is based on the calculation of the odds ratio (OR 95% CI) as shown in Table 4. The OR 95% CI calculation result for coronary heart disease with hypogonadism is 5.6 (1.648 – 19.232). This result is interpreted to mean that the number of coronary heart disease patients with hypogonadism is 5.6 times higher than the number of coronary heart disease patients without hypogonadism.

4. Discussion

According to the univariate analysis, most samples over the age of 35 years old are at a higher risk of developing coronary heart disease. This finding aligns with a study by Melyani et al., which states that cases of coronary heart disease start to appear at age 35 and continue to increase with aging.[13] The result about blood pressure is also consistent with previous studies that indicate people with high blood pressure are 2.667 times more likely to develop coronary heart disease compared to those without high blood pressure.[14] The result about body mass index aligns with established theories that obesity can increase the risk of coronary heart disease. People with obesity are 2.7 times more likely to experience coronary heart disease.[15]

The result about cigarette profile and alcohol consumption contradicts previous research. Regarding the cigarette profile, this result suggests that the higher a person's smoking habits, the greater their risk of developing coronary heart disease.[16] Regarding alcohol consumption, based on existing studies, light alcohol consumption slightly increases the risk of coronary heart disease, and heavier alcohol consumption further elevates this risk.[17] This could be due to coronary heart disease patients changing their lifestyle to quit smoking and stop consuming alcohol after receiving health education. Regarding other medical conditions, linking this result to prior studies, coronary heart disease can emerge and worsen due to various factors such as hyperlipidemia, hypertension, type-2 diabetes mellitus, conditions that increase systemic inflammation, genetic factors, unhealthy environmental factors, and poor lifestyle choices.[18]

The results of the ADAM score questionnaire in this research are consistent with research that was conducted by Selim in 2022, which found that none of the respondents (0%) in the sample experienced a decrease in height.[19] This may be due to height reduction in men starting after age 50, with a more significant decline evident after age 70.[20] The feeling of a decrease in strength and/or endurance and a recent deterioration in their ability to play sports research could be due to a nutritional deficiency that results in a decrease in leptin levels in the body. When leptin decreases, the reproductive function becomes less maintained, leading to hypothalamic-pituitary-testicular axis dysfunction.[21]

The finding of this research is consistent with a study by Tang et al. in 2024, which reported a p-value of 0.004 ($p \leq 0.05$), indicating a significant relationship between hypogonadism and coronary heart disease.[22] Other studies have also stated that hypogonadism can lead to coronary heart disease. The risk of developing coronary heart disease increases in men with low testosterone levels. Furthermore, the lower the testosterone level in men, the more severe the coronary heart disease they suffer from.[11] In addition, the odds ratio calculation is also in line with previous studies stating that the risk of coronary heart disease with hypogonadism is higher than coronary heart disease without hypogonadism, with a risk value greater than one.[23]

5. Conclusion

To sum up, there is a significant correlation between hypogonadism and coronary heart disease in men at Gedung PJT RSUP Prof. Ngoerah, with a p-value ≤ 0.05. The prevalence of hypogonadism in men at Gedung PJT RSUP Prof. Ngoerah is 56%. Based on the calculation of the odds ratio (OR), men with coronary heart disease and hypogonadism at Gedung PJT RSUP Prof. Ngoerah are 5.6 times more common than men with coronary heart disease but without hypogonadism.

Author's Contribution

All authors have contributed to the final manuscript.

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Conflict of Interest

The authors declare no conflict of interest.

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Ethical Clearance

The Ethics Committee of the Faculty of Medicine, Udayana University has given the study its ethical approval with letter number 0544/UN14.2.2.VII.14/LT/2024.

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