

Association of Depression with adverse outcomes in Patients with Myocardial Infarction with Non-obstructive Coronary Arteries (MINOCA)

UMAIR ASGHAR¹, MUHAMMAD HUSSAIN², KASHIF ZAFAR³, SYED MAHMOOD-UL-HASSAN⁴

¹Department of Cardiology, Punjab Institute of Cardiology, Lahore

²Senior Registrar, Cardiology Department, Punjab Institute of Cardiology, Lahore

³Assistant Professor of Cardiology, Cardiology Department, Punjab Institute of Cardiology, Lahore

⁴Assistant Professor of Medicine, Services Hospital, Lahore

Correspondence to Dr. Umair Asghar, Email: umairasghar51@yahoo.com, Cell: 0300-9676452

ABSTRACT

Background: Depression has a significant relationship with cardiovascular diseases. But evidence is scarce regarding its impact on adverse outcome in patients of non-obstructive coronary artery disease.

Aim: To assess the association of depression with adverse outcome in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA).

Methods: This cohort study was conducted in the Department of Cardiology, Punjab Institute of Cardiology, Lahore for 12 months i.e. July 2017 to June 2018. 260 patients; 130 in exposed group and 130 in unexposed group fulfilling selection criteria were enrolled for the study with or without depression. Patients were then evaluated for adverse outcome. SPSS v. 25 was used to analyse the data.

Results: The mean age of exposed group was 42.85 ± 9.33 years and the mean age of unexposed group was 52.52 ± 8.18 years. There were 49(37.7%) males and 81(62.3%) females in exposed group with the male-to-female ratio was 1: 1.7, while in unexposed group there were 55(42.3%) males and 75(57.7%) females with the male-to-female ratio was 1: 1.4. ST-segment elevation was observed in 31(23.8%) exposed patients while in 27(20.8%) unexposed patients. In exposed group, cardiovascular events were noted in 44(33.8%) patients, while in 27(20.8%) patients in unexposed group (OR=1.362, 95% CI; 1.071, 1.731, P=0.018). In exposed group, cardiovascular related mortality were noted in 38(29.2%) patients, while in 17(13.1%) patients in unexposed group (OR=1.54, 95% CI; 1.22, 1.943, P = 0.001). In exposed group, all-cause mortality were noted in 19 (14.6%) patients, while in 9 (6.9%) patients in unexposed group (OR=1.418, 95% CI; 1.063, 1.892, p=0.045).

Conclusions: Our study results showed that depression in patients having MINOCA is significantly related to adverse cardiovascular sequel and leads to more severe sequel.

Keywords: Depression, adverse outcome, mortality, myocardial infarction, non-obstructive coronary arteries, MINOCA

INTRODUCTION

Cardiologists know when to go beyond blocked arteries that indicate obstructive coronary artery disease (CAD) when treating symptoms like chest pain. They understand that non-obstructive coronary artery disease can affect your heart's arteries. When coronary arteries constrict improperly, malfunction after bifurcating into tiny capillaries, or are compressed by the overlying heart muscle, you have this less common form of CAD¹. At coronary angiography, a growing number of stable patients diagnosed to have myocardial ischemia but no obstructive coronary artery disease, now known as MINOCA, are found².

Since there is likely overlap between MINOCA and myocardial infarction with no obstructive coronary arteries, which is becoming more widely recognised, our main focus is on MINOCA, or nonmyocardial infarction syndromes. In the setting of no obstructive coronary artery disease at coronary angiography, these stable patients frequently report sensations of chest discomfort assumed to be angina and/or negative stress testing^{3, 4}.

MINOCA is a diverse disease entity that affects 5-10% of all myocardial infarction patients, mostly women. MINOCA can be difficult to distinguish from other non-ischaemic illnesses that elicit comparable symptoms and myocardial damage in the clinic. The diagnosis, examination, and therapy of patients with MINOCA are still a bit hazy⁵.

In individuals with MINOCA, anxiety was found to be strongly and independently linked to an elevated risk of all-cause death and major adverse cardiovascular events⁶. Anxiety and depression have been linked to an increased risk of unfavourable outcomes in cases of CVDs and MINOCA, according to a number of studies^{7, 8}. Furthermore, anxiety and depression frequently occur together⁹. Therefore the present study is designed to assess the impact of depression on the cardiovascular related consequences after cardiovascular event in adult population. This would help us to

determine the magnitudes of local setting and in future, we would implement the findings and implement the need and importance of psychiatrist or a psychologist to reduce the depression or its severity in such patients. This would help to improve the prognosis of patients after cardiovascular event.

The objective of the study was to assess the association of depression with adverse outcomes in patients of myocardial infarction with non-obstructive coronary arteries (MINOCA)

MATERIALS & METHODS

This cohort study was conducted in the Department of Cardiology, Punjab Institute of Cardiology, Lahore from 1st July 2017 to 30th June 2018 after approval from IRB. Sample size of 260 patients; 130 in both groups had been estimated by keeping 95% level of confidence, 5% significance level and percentage of cardiovascular events i.e. 23.1% in depressed patients while 37.3% in non-depressed patients. Non probability; consecutive sampling technique was used.

Sample selection method: Patients aged between 35-65 years, both gender with diagnosed with MINOCA were included. Exposed patients were those who had depression (Hamilton Depression Scale score of ≥ 7) and unexposed were those who had Hamilton Depression Scale score of < 7 were taken into consideration. While patients with cognitive dysfunction or dementia, h/o psychiatric disorders, recurrent myocardial infarction, severe chronic obstructive pulmonary disease, renal dysfunction, atrial fibrillation, cancer, pulmonary embolism, and myocarditis

Data collection procedure: 260 patients presenting in Punjab Institute of Cardiology, fulfilled the above stated selection criteria, were recruited. Written consent was obtained from attendants. Demographics of patients were obtained. Patients were segregated in two groups i.e., exposed with depression and unexposed without depression. Patients were admitted in followed-up in cardiology wards for 3-5 days. Patients were then discharged and were followed-up in OPD for 2 years. During follow-up, patients were evaluated for cardiovascular events and

Received on 13-08-2021

Accepted on 23-01-2022

cardiovascular events including re-current myocardial infarction, stroke, and mortality. All the information was recorded in a proforma.

Data analysis: SPSS version 21.0 was used for entry of data and analysis. Association of depression with adverse outcome was calculated by calculating relative risk with 95% confidence interval. $RR > 1$ was taken as significant.

RESULTS

In this study, we included 260 patients; 130 in exposed group and 130 in unexposed group. The mean age of exposed group was 42.85 ± 9.33 years and the mean age of unexposed group was 52.52 ± 8.18 years. There were 49(37.7%) males and 81(62.3%) females in exposed group with the male-to-female ratio as 1: 1.7, while in unexposed group there were 55(42.3%) males and 75(57.7%) females with the male-to-female ratio as 1: 1.4. History of smoking was positive in 44(33.8%) exposed group while in 51(39.2%) patients of unexposed group. History of hypertension was positive in 68(52.3%) exposed group while in 54(41.5%) patients of unexposed group. History of diabetes was positive in 68(52.3%) exposed group while in 64(49.2%) patients of unexposed group. Hyperlipidemia was positive in 97(74.6%) exposed group while in 86(66.2%) patients of unexposed group. ST-segment elevation was observed in 31(23.8%) exposed patients while in 27(20.8%) unexposed patients. Antiplatelet therapy was given to 123 (94.6%) exposed while to 125(96.2%) unexposed patients. B-blockers were given to 109(83.8%) exposed while to 114 (87.7%) unexposed patients. RAAS inhibitor therapy was given to 94(72.3%) exposed while to 95(73.1%) unexposed patients. Statin therapy was given to 123(94.6%) exposed while to 124(95.4%) unexposed patients (Table 1).

Table 2: Comparison of platelets count between cases and controls

Outcome	Exposed	Unexposed	RR (95% CI)
Cardiovascular event	44 (33.8%)	27 (20.8%)	1.362 (1.071, 1.731)
Cardiovascular related Mortality	38 (29.2%)	17 (13.1%)	1.54 (1.22, 1.943)
All-cause mortality	19 (14.6%)	9 (6.9%)	1.418 (1.063, 1.892)

DISCUSSION

Cardiovascular disease is a major global health concern, with growing evidence of variations in epidemiology, pathophysiology, clinical therapy, and prognosis between men and women¹¹. According to research, women have a twice-as-high risk of dying from cardiovascular disease, and angina, heart failure, and stroke are becoming more common in women^{12,13}.

According to new findings from big clinical trials, MINOCA is a clinical entity that should not be overlooked. MINOCA is identified in around half of the females who have coronary angiography. The prevalence of MINOCA is also increasing in both genders, which is most likely related to the gradual expansion of clinical reasons for angiography in patients having angina¹⁴.

Nearly, 20–25 percent of females develop depression at some time in their lives, and depressive symptoms have been identified as a new, non-customary risk factors for CVD in this group of people¹⁵. Behavioral to biological risk factors, such as sympathetic nervous system hyperactivity and impairment in hypothalamic-pituitary-adrenal function, may be at the root of the relationship between depression and cardiovascular disease^{16,17}. Nevertheless, the neuroendocrine-driven backdrop might only explain a portion of the above-mentioned abnormalities in chronic systemic inflammation, impaired hemostasis, and cardiac autonomic control modulation¹⁷.

In our study, we observed that cardiovascular events occurred in 44(33.8%) exposed patients, while in 27(20.8%) patients in unexposed group ($OR=1.362$, 95% CI; 1.071, 1.731, $P = 0.018$), cardiovascular related mortality were noted in 38(29.2%) exposed patients, while in 17(13.1%) patients in unexposed group ($OR=1.54$, 95% CI; 1.22, 1.943, $P=0.001$) and all-cause mortality were noted in 19 (14.6%) exposed patients, while in 9 (6.9%)

Out of 130 patients in exposed group, cardiovascular events were noted in 44 (33.8%) patients. Out of 130 patients in unexposed group, cardiovascular events were noted in 27 (20.8%) patients. A significant difference was observed in both groups ($OR=1.362$, 95% CI; 1.071, 1.731, P -value = 0.018). Out of 130 patients in exposed group, cardiovascular related mortality were noted in 38 (29.2%) patients. Out of 130 patients in unexposed group, cardiovascular related mortality were noted in 17(13.1%) patients. There was statistically significant difference in both groups ($OR=1.54$, 95% CI; 1.22, 1.943, P -value = 0.001). Out of 130 patients in exposed group, all-cause mortality were noted in 19(14.6%) patients. Out of 130 patients in unexposed group, all-cause mortality were noted in 9 (6.9%) patients. There was statistically insignificant difference in both groups ($OR=1.418$, 95% CI; 1.063, 1.892, p -value = 0.045) (Table 2).

Table 1: Baseline characteristics of patients in both groups

	Exposed	Unexposed
n	130	130
Age (years)	42.85 ± 9.33	52.52 ± 8.18
Gender		
Male	49 (37.7%)	55 (42.3%)
Female	81 (62.3%)	75 (57.7%)
H/o smoking	44 (33.8%)	51 (39.2%)
Hypertension	68 (52.3%)	54 (41.5%)
Diabetes	68 (52.3%)	64 (49.2%)
Hyperlipidemia	97 (74.6%)	86 (66.2%)
ST-segment elevation	31 (23.8%)	27 (20.8%)
Medications at discharge		
Antiplatelet	123 (94.6%)	125 (96.2%)
β Blockers	109 (83.8%)	114 (87.7%)
RAAS inhibitor	94 (72.3%)	95 (73.1%)
Statins	123 (94.6%)	124 (95.4%)

patients in unexposed group ($OR=1.418$, 95% CI; 1.063, 1.892, $p=0.045$).

According to a cohort of 85,465 patients in China, the predictable 49 percent of individuals with anxiety had depressive condition along with CVD¹⁸. Depression status, on the other hand, was not designated at baseline feature and was not corrected in the multi-variate cox regression model in He et al study¹⁹ Gu et al., conducted a study in depressed and non-depressed patients with cardiovascular event, and found that cardiovascular events i.e. 23.1% in depressed patients while 37.3% in non-depressed patients ($p < 0.001$)¹⁰.

In the last few years, many studies, both prospective and epidemiological, tried to clarify the relationship existing between depressive disorder and coronary artery disease.^{20, 21} Compared to sporadically manifest depression, depressive disorder are associated with a higher incidence of myocardial infarction, especially in long-lasting anxious-depressive syndromes. A diagnosis of depressive disorder at any time after angiographically confirmed diagnosis of coronary artery disease is associated with a two-fold risk of death.²⁰ Moreover, a high percentage of people with myocardial infarction frequently develop a depressive disorder during the first months after the acute event, while the most significant rate is observed among younger women as compared to men²¹.

CONCLUSION

Our study results showed that depression in patients with myocardial infarction with non-obstructive coronary arteries is significantly associated with adverse cardiovascular outcomes and leads to more severe sequel.

Conflict of interest: Nil

REFERENCES

1. Stanford. Non-obstructive Coronary Artery Disease 2021 [cited 2021]. Available from: <https://stanfordhealthcare.org/medical-conditions/blood-heart-circulation/non-obstructive-coronary-artery-disease.html>.
2. Herscovici R, Sedlak T, Wei J, Pepine CJ, Handberg E, Merz CNB. Ischemia and No Obstructive Coronary Artery Disease (INOCA): What Is the Risk? *Journal of the American Heart Association*. 2018;7(17):e008868.
3. Bairey Merz CN, Pepine CJ, Walsh MN, Fleg JL. Ischemia and No Obstructive Coronary Artery Disease (INOCA): Developing Evidence-Based Therapies and Research Agenda for the Next Decade. *Circulation*. 2017;135(11):1075-92.
4. Pepine CJ, Ferdinand KC, Shaw LJ, Light-McGroary KA, Shah RU, Gulati M, et al. Emergence of Nonobstructive Coronary Artery Disease: A Woman's Problem and Need for Change in Definition on Angiography. *Journal of the American College of Cardiology*. 2015;66(17):1918-33.
5. Bertil L, Tomasz B, Mario A, Francesco P. Myocardial infarction with non-obstructive coronary artery disease. *EuroIntervention*. 2021;17(11):e875-e87.
6. Liu M, Deng C, Yuan P, Ma J, Yu P, Chen J, et al. Anxiety, depression, and medication adherence in Chinese patients with myocardial infarction in the absence of obstructive coronary artery disease. *Clin Cardiol*. 2020;43(12):1350-1.
7. Wulsin LR, Singal BM. Do depressive symptoms increase the risk for the onset of coronary disease? A systematic quantitative review. *Psychosomatic medicine*. 2003;65(2):201-10.
8. Gu XH, He CJ, Shen L, Han B. Association Between Depression and Outcomes in Chinese Patients With Myocardial Infarction and Nonobstructive Coronary Arteries. *J Am Heart Assoc*. 2019;8(5):e011180.
9. Devane CL, Chiao E, Franklin M, Kruep EJ. Anxiety disorders in the 21st century: status, challenges, opportunities, and comorbidity with depression. *The American journal of managed care*. 2005;11(12 Suppl):S344-53.
10. Gu XH, He CJ, Shen L, Han B. Association between depression and outcomes in chinese patients with myocardial infarction and nonobstructive coronary arteries. *Journal of the American Heart Association*. 2019;8(5):e011180.
11. Edition F. Diagnostic and statistical manual of mental disorders. Am Psychiatric Assoc. 2013;21.
12. Organization WH. Depression and other common mental disorders: global health estimates: World Health Organization; 2017 [cited 2021]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf?sequence=1>.
13. Bucciarelli V, Caterino AL, Bianco F, Caputi CG, Salerni S, Sciomer S, et al. Depression and cardiovascular disease: The deep blue sea of women's heart. *Trends in Cardiovascular Medicine*. 2020;30(3):170-6.
14. Makarović Z, Makarović S, Bilić-Čurčić I, Mihaljević I, Mlinarević D. Nonobstructive coronary artery disease - clinical relevance, diagnosis, management and proposal of new pathophysiological classification. *Acta Clin Croat*. 2018;57(3):528-41.
15. Goldstein BI, Carnethon MR, Matthews KA, McIntyre RS, Miller GE, Raghuvver G, et al. Major depressive disorder and bipolar disorder predispose youth to accelerated atherosclerosis and early cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2015;132(10):965-86.
16. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation*. 2014;129(12):1350-69.
17. Garcia M, Mulvagh SL, Bairey Merz CN, Buring JE, Manson JE. Cardiovascular disease in women: clinical perspectives. *Circulation research*. 2016;118(8):1273-93.
18. Wu Z, Fang Y. Comorbidity of depressive and anxiety disorders: challenges in diagnosis and assessment. *Shanghai archives of psychiatry*. 2014;26(4):227-31.
19. He CJ, Zhu CY, Han B, Hu HZ, Wang SJ, Zhai CL, et al. Association between anxiety and clinical outcomes in Chinese patients with myocardial infarction in the absence of obstructive coronary artery disease. *Clin Cardiol*. 2020;43(7):659-65.
20. May HT, Horne BD, Knight S, Knowlton KU, Bair TL, Lappé DL, et al. The association of depression at any time to the risk of death following coronary artery disease diagnosis. *European Heart Journal-Quality of Care and Clinical Outcomes*. 2017;3(4):296-302.
21. Smolderen KG, Strait KM, Dreyer RP, D'Onofrio G, Zhou S, Lichtman JH, et al. Depressive symptoms in younger women and men with acute myocardial infarction: insights from the VIRGO study. *Journal of the American Heart Association*. 2015;4(4):e001424.