Long-term outcomes and predictors of patients with ST elevated versus non-ST elevated myocardial infarctions in non-obstructive coronary arteries: A retrospective study in Northern China

Lin Chen [1,2], **Yinghong Fan** [1,2], **Zhen Fang** [3], **Ning Liu** [Corresp. 3]

[1] Yangzhou University, Institute of Gastroenterology, Affiliated Hospital of Yangzhou University, Yangzhou, Jiangsu Province, China

[2] Yangzhou University, Pancreatic Center, Department of Gastroenterology, The Affiliated Hospital of Yangzhou University, Yangzhou, Jiangsu Province, China

[3] Department of Cardiology, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu Province, China

Corresponding Author: Ning Liu
Email address: 844465791@qq.com

Background. Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a heterogeneous disease entity with diverse etiologies and no uniform treatment protocols. Patients with MINOCA can be clinically classified into two groups based on whether they have an ST-segment elevation (STE) or non-ST segment elevation (NSTE), based on electrocardiogram (ECG) results, whose clinical prognosis is unclear. This study aimed to compare the outcomes and predictors of patients with STE and NSTE in the MINOCA population. Methods. We collected the data for 196 patients with MINOCA (115 with STE and 81 with NSTE) in China. Clinical characteristics, prognoses, and predictors of major adverse cardiovascular events (MACE) were analyzed during the follow-up of all patients. Results. The proportion of patients with STE was greater than that with NSTE in the MINOCA population. Patients with NSTE were older and had a higher incidence of hypertension. No differences were observed in the outcomes between the STE and NSTE groups during a median follow-up period of 49(37,46) months. No significant differences were observed in those with MACE (24.35% vs 22.22%, P = 0.73) and those without MACE. The multivariable predictors of MACE in the NSTE groups were Killip grades ≥ 2(HR 9.035, CI 95%:1.657-49.263, P=0.011), reduced use of β-blockers during hospitalization (HR 0.238, CI 95%:0.072-0.788, P=0.019), and higher levels of low-density lipoprotein cholesterol (LDL-C) (HR 2.267, CI 95%; 1.008-5.097, P=0.048); the reduced use of β-blockers during hospitalization was the only independent risk factor of MACE in the STE group. Conclusions. There were differences between the clinical characteristics of patients with STE and NSTE in the MINOCA population, even though outcomes during follow-up were similar. Independent risk factors for major adverse cardiac events were not identical

in the STE and NSTE groups, which could be attributable to the differences in disease pathogenesis.

1

Long-term outcomes and predictors of patients with ST elevated versus non-ST elevated myocardial infarctions in non-obstructive coronary arteries: A retrospective study in Northern China

Lin Chen, MD[1,2], Yinghong Fan[1,2], Zhen Fang, MD[3], Ning Liu, MD[3*]

1 Pancreatic Center, Department of Gastroenterology, The Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou 225001, Jiangsu Province, China

2 Institute of Gastroenterology, Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou 225001, Jiangsu Province, China

3 Department of Cardiology, Northern Jiangsu People's Hospital, Yangzhou 225001, Jiangsu Province, China

*Corresponding author: Ning Liu

E-mail: 844465791@qq.com

Telephone: +86-18051062118

25 Abstract

26 **Background.** Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a

27 heterogeneous disease entity with diverse etiologies and no uniform treatment protocols. Patients

28 with MINOCA can be clinically classified into two groups based on whether they have an ST-

29 segment elevation (STE) or non-ST segment elevation (NSTE), based on electrocardiogram

30 (ECG) results, whose clinical prognosis is unclear. This study aimed to compare the outcomes

31 and predictors of patients with STE and NSTE in the MINOCA population.

32 **Methods**. We collected the data for 196 patients with MINOCA (115 with STE and 81 with

33 NSTE) in China. Clinical characteristics, prognoses, and predictors of major adverse

34 cardiovascular events (MACE) were analyzed during the follow-up of all patients.

35 **Results**. The proportion of patients with STE was greater than that with NSTE in the MINOCA

36 population. Patients with NSTE were older and had a higher incidence of hypertension. No

37 differences were observed in the outcomes between the STE and NSTE groups during a median

38 follow-up period of 49(37,46) months. No significant differences were observed in those with

39 MACE (24.35% vs 22.22%, P = 0.73) and those without MACE. The multivariable predictors of

40 MACE in the NSTE groups were Killip grades $\geq$ 2(HR 9.035, CI 95%:1.657-49.263, P=0.011),

41 reduced use of β-blockers during hospitalization (HR 0.238, CI 95%:0.072-0.788, P=0.019), and

42 higher levels of low-density lipoprotein cholesterol (LDL-C) (HR 2.267, CI 95%; 1.008-5.097,

43 P=0.048); the reduced use of β-blockers during hospitalization was the only independent risk

44 factor of MACE in the STE group.

45 **Conclusions**. There were differences between the clinical characteristics of patients with STE

46 and NSTE in the MINOCA population, even though outcomes during follow-up were similar.

47 Independent risk factors for major adverse cardiac events were not identical in the STE and

48 NSTE groups, which could be attributable to the differences in disease pathogenesis.

49

50

51

52

53

54

55 Introduction

56　Myocardial infarction with nonobstructive coronary arteries (MINOCA) is a heterogeneous

57　group of diseases with different pathogeneses. It is characterized by acute myocardial infarction

58　with normal coronary arteries or mild coronary artery stenosis (stenosis < 50%), and occurs

59　commonly in young women [1]. The prevalence of MINOCA reportedly ranges between 1-15%

60　in patients with acute myocardial infarction (AMI), according to different studies [2], and its

61　overall prevalence was 6% in a recent meta-analysis[3]. MINOCA is a group of syndromes with

62　multiple causes. Individuals with MINOCA can be classified into multiple subgroups, such as

63　those with plaque rupture, coronary dissection, coronary artery spasm, and clinically

64　unrecognized myocarditis or Takotsubo cardiomyopathy; all of these have different underlying

65　pathophysiological mechanisms [4, 5]. Therefore, it is potentially challenging to effectively treat

66　MINOCA patients for whom multiple pathogenic mechanisms have various underlying causes.

67　The pathogenesis and prognosis of MINOCA patients need to be assessed further in future

68　studies.

69　Previous studies have reported that patients with MINOCA had lower rates of major adverse

70　cardiovascular events (MACE) and mortality during follow-up than patients with MI-CAD [3, 6,

71　7]. Although patients with MINOCA appear to have a slightly better long-term prognosis,

72　compared to MI-CAD(MI with obstructive coronary artery disease) patients, studies conducted

73　in recent years have shown that MINOCA is not always benign [8, 9]. Notably, a Swedish study

74　conducted over 4 years has shown that adverse cardiovascular events occurred in 23.9% of

75　MINOCA patients during follow-up; among these, the mortality rate could be as high as

76　13.4%[10]. Moreover, a Japanese study also showed that MINOCA patients had a higher

77　mortality rate within 30 days of follow-up, as compared to MI-CAD patients (4.48% VS

78　3.46%)[11].

79　However, the differences in clinical features and prognosis between patients with ST-segment

80　elevated myocardial infarction (STEMI) and non-ST segment elevated myocardial infarction

81　(NSTEMI) remain controversial. The occurrence of NSTEMI is more common than STEMI in

82　the MINOCA population[3, 12]. Previous studies have reported that STEMI patients had a

83　poorer short-term prognosis and a more favorable long-term prognosis[13, 14]. A large-scale

84　Swedish study of MINOCA patients reported that during the 2.6-year follow-up period, the

85　mortality rate for STEMI patients was 8%, while the mortality rate for NSTEMI patients was

86　lower at 5%[15], which was inconsistent with the results reported by Li et al.[16]. Nevertheless,

87   some studies suggest that there were no differences in prognosis between patients with STEMI

88   and NSTEMI[17].

89   Some studies have shown that the history of atrial fibrillation, Killip grade, age, and treatment

90   strategy were significant independent risk factors for prognosis in MINOCA patients [14, 17],

91   while the predictors of prognosis in STE and NSTE patients are still unclear. Although the

92   differences in prognosis between STEMI and NSTEMI patients in the AMI population have been

93   reported hitherto, the differences in prognosis and predictors of prognosis among MINOCA

94   patients with STE and NSTE remain unclear. This study aimed to compare the clinical features,

95   prognosis, and predictors of MACE during the follow-up period among MINOCA patients with

96   STE and NSTE in Northern China.

97

Materials & Methods

99   **Patients**

100   We conducted a retrospective study of patients who had been admitted to the First Hospital at

101   Jilin University due to AMI from January 2015 to July 2018 and had undergone coronary

102   angiography during hospitalization. Patients were included in the study if: (1) they met the

103   diagnostic criteria specified in the AMI guidelines [18]; (2) no occlusion of any infarct-related

104   coronary artery and <50% stenosis could be observed in all epicardial vessels; (3) the patient

105   received no other alternative diagnosis during clinical presentation (e.g., non-ischemic causes

106   such as sepsis, acute renal failure, pulmonary embolism, and myocarditis); and (4) age >18 years.

107   Patients were excluded if: (1) thrombolytic therapy had been performed prior to coronary

108   angiography; (2) they had a previous myocardial infarction or coronary revascularization; (3)

109   previously underwent cardiac surgery; (4) had malignant tumors.

110   This study has been conducted in accordance with the Declaration of Helsinki and was approved

111   by the Ethical Review Board of the hospital (the First Hospital of Jilin University, Changchun,

112   China). Verbal consent was obtained from the participants prior to conducting the study.

113

114   **Data collection**

115   Most of the data were obtained from the medical records at the First Hospital of Jilin University

116   that contained data on the baseline characteristics, biochemical markers, electrocardiogram

117   (ECG) images, coronary angiography, and medications provided during hospitalization. Basic

118   patient information (e.g., age, sex) and past medical history (e.g., smoking history, history of

119   hypertension, hyperlipidemia, diabetes, arrhythmias) were recorded in detail. The history of

120   arrhythmias including previous atrial arrhythmias or ventricular arrhythmias or heart block. We

121   collected information regarding biochemical markers, including blood cardiac troponin-T(cTnT),

122   creatine kinase-MB(CK-MB), brain natriuretic peptide (BNP), total cholesterol (TC), low-

123   density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C),

124   triglyceride (TG) and indicators of echocardiography, including LV (left ventricle) and LVEF

125   (left ventricular ejection fraction) in 24 hours after hospitalization. We classified the patients into

126   the STE and NSTE groups based on their ECG results. STE and NSTE were defined in

127   accordance with the Fourth Universal Definition of Myocardial Infarction [18].

128   After discharge, all patients were followed up by means of telephonic interviews, clinical visits,

129   and the use of medical records. The primary clinical endpoint of our study was the occurrence of

130   major adverse cardiovascular events (MACE), including rehospitalization for increased chest

131   pain that did not meet the criteria of AMI, based on ECG results and myocardial injury marker

132   levels, and occurrence of non-fatal MI, heart failure, stroke, heart valve replacement, and all-

133   cause deaths, which included cardiovascular and non-cardiovascular deaths. A diagnosis of MI

134   was made if patients exhibited the dynamic development of cardiac troponin in conjunction with

135   symptoms suggestive of myocardial ischemia. Cardiovascular death was defined as death

136   because of acute coronary syndrome(ACS), cardiac rupture, severe arrhythmias, or refractory

137   severe heart failure. A stroke was defined as an ischemic cerebral infarction caused by

138   thrombotic or embolic occlusions in any major intracranial artery. A diagnosis of heart failure

139   (HF) was established according to the current guidelines of the European Society of

140   Cardiology(ESC)[19].

141

142   **Statistical analysis**

143   Statistical analysis was performed using SPSS 25.0 software. Normally distributed continuous

144   variables were presented as mean ± standard deviation (SD) values. Non-normally distributed

145   continuous variables were presented in terms of the median and inter-quartile range (IQR).

146   Categorical variables were presented as counts and percentages. An independent sample t-test

147   and the Mann-Whitney U test were used to perform a comparison of continuous variables

148   between groups. Categorical variables were compared using the Chi-square and Fisher's exact

149 tests. We used logistic regression analysis to evaluate the independent risk factors of outcomes in

150 the STE and NSTE groups, while the adjusted OR for MACE was calculated via logistic

151 regression analysis. All the tests performed were two-sided tests and values were identified to be

152 statistically significant at a P-value < 0.05.

153

Results

155 **Baseline characteristics of patients**

156 In our study, the median follow-up period was 49 （37,46） months. A total of 9696 patients

157 were diagnosed with MI; among these, 196 patients (2.02%) satisfied the diagnostic criteria for

158 MINOCA. Based on the ECG results, 115 patients (58.7%) were included in the STE group,

159 while 81 patients (41.3%) were included in the NSTE group (Figure 1). A comparison of the

160 baseline characteristics between patients with STE and NST among the MINOCA population has

161 been shown in Table 1.

162 In comparison to NSTE patients, patients with STE were younger. Patients with NSTE had a

163 higher incidence of hypertension, whereas no significant differences were observed in the

164 incidence of other coronary risk factors (e.g., diabetes, hyperlipidemia, previous arrhythmia,

165 smoking history). The medications administered at discharge have been shown in Table 1. There

166 were no significant differences between the two groups except for the fact that the more frequent

167 use of aspirin and lower use of ACEI/ARB at admission in the STE group. Thus, the proportions

168 of patients using clopidogrel, β-blockers, and statins were similar in the two groups. The level of

169 serum glucose on admission in the NSTE group was higher than that in the STE group, while the

170 other laboratory parameters were not significantly different among the two groups.

171

172 **Follow-up**

173 During a median follow-up period of 49 months (interquartile range [IQR] 37-61), MACE

174 occurred in 46 (23.47%) out of a total of 51 patients. In the STE and NSTE groups, we observed

175 the occurrence of MACE in 28 (24.35%) and 18 (22.22%) patients, respectively. The data are

176 shown in Table 2. Thirty-one cases of MACE were observed in 28 patients (24.35%) in the

177 STEMI group, including in patients who had to undergo rehospitalization for chest pain (4

178 cases,3.48%), non-fatal MI (3 cases,2.61%), heart failure (14 cases,12.17%), stroke (5

179 cases,4.35%), and all-cause deaths (5 cases,4.35%). In the NSTEMI group, 20 cases MACE

180   (24.35%) were observed in 18 patients (22.22%); these included chest pain (4 patients, 4.49%,

181   non-fatal MI (2 patients, 2.47%), heart failure (8 patients, 9.88%), stroke (3 patients, 3.70%),

182   heart valve replacement (2 patients, 2.47%), and all-cause death (1 patient,1.23%).

183   There were no statistical differences in the prevalence of MACE between the NSTE and STE

184   groups (P=0.73). In this study, 5 patients died of cardiogenic diseases. During the follow-up

185   period, there was no significant difference in the incidence of chest pain, non-fatal MI, heart

186   failure, stroke, heart valve replacement, and all-cause death between the STE and NSTE groups

187   among the MINOCA population (P>0.05).

188

189   **Predictive factors**

190   Univariate analysis showed that older age, Killip grade ≥2, longer hospitalization duration, being

191   born male, lower use of β-blockers during hospitalization, and red blood cell counts were

192   significant risk factors for MACE in the STE group (Table 3).

193   We conducted a multivariate analysis adjusted for age, Killip grades, hospitalization duration,

194   sex, use of β-blockers during hospitalization, red blood cell counts, history of diabetes, and level

195   of low-density lipoprotein cholesterol (LDL-C). The results showed that Killip grades ≥ 2(HR

196   9.035, Cl 95%:1.657-49.263, P=0.011), lowered use of β-blockers during hospitalization（HR

197   0.238, Cl 95%:0.072-0.788, P=0.019) and higher LDL-C levels (HR 2.267, Cl 95%: 1.008-5.097,

198   P=0.048) were independent risk factors for MACE in patients with STE (Table 4).

199   Univariate analysis showed that older age and lowered use of β-blockers during hospitalization

200   were associated with a higher extent of occurrence of MACE in the NSTE group (Table 3).

201   The age and extent of use of β-blockers and aspirin during hospitalization were adjusted via

202   multivariate analysis. The results revealed that the lowered use of β-blockers during

203   hospitalization was the only independent risk factor for MACE in patients with NSTE (HR

204   0.303, Cl 95%: 0.093-0.991, P=0.048). Thus, the use of β-blockers could improve the prognosis

205   of MINOCA patients with NSTE.

206

207   **Discussion**

208   The objective of this study was to compare the prognosis and predictors of MACE among

209   MINOCA patients with STE and NSTE. Our major findings were as follows: (1) There were

210   differences in clinical features between the STE and NSTE groups among MINOCA patients; (2)

211 there was no statistical difference in the incidence of MACE between the STE and NSTE groups

212 during follow-up; (3) the independent risk predictors of MACE in MINOCA patients with STE

213 include a higher level of LDL-C, Killip grades≥2, and lowered use of β-blockers during

214 hospitalization, whereas the lowered use of β-blockers during hospitalization was the only

215 multivariable predictor of MACE in MINOCA patients with NSTE.

216 MINOCA has always been a confusing clinical entity that is characterized by myocardial

217 infarctions with normal or near-normal coronary arteries of angiography [20]. Due to the

218 difference in sample size and definition among various cohorts, the incidence of MINOCA in

219 patients with acute myocardial infarction (AMI) is 1-15%[12, 15, 21], which is consistent with

220 the findings of our study. Although the underlying causes of MINOCA are diverse, patients can

221 be classified into the STEMI and NSTEMI groups based on their electrocardiogram (ECG)

222 results. Among MINOCA patients, the proportion of patients with NSTEMI is higher than that of

223 those with STEMI[3, 12], which was in contrast to the findings of our study. This result may be

224 attributable to the fact that our study is a single-center study with a small sample size. Certain

225 previous studies have reported that there were significant differences in the clinical features of

226 MINOCA patients with STEMI and NSTEMI [13, 22]. Recently, a Chinese study on MINOCA

227 reported that patients with NSTE were older, mostly female, and had a higher incidence of atrial

228 fibrillation. Furthermore, patients with STE were more likely to have a history of smoking and a

229 higher diastolic blood pressure, whereas there were no significant differences in the incidence of

230 other risk factors for coronary problems (e.g., hypertension, diabetes) between the two groups

231 [12]. Our study found that patients with NSTEMI had a higher age and a higher proportion of the

232 patients had hypertensive disease, compared to STEMI patients, which was consistent with the

233 findings of the study by Johnston et al. [23]. Therefore, these differences may be associated with

234 the different pathogeneses of the two groups; this needs to be confirmed in multi-center and

235 prospective studies with a large sample size.

236 The prognostic differences between STEMI and NSTEMI patients in the MINOCA population

237 remain controversial. Previous studies have reported higher short-term mortality in STEMI

238 patients and higher long-term mortality in NSTEMI patients [13, 24], which was also observed

239 in the MINOCA population [15]. Johnston et al. reported that all-cause mortality was

240 significantly higher in MINOCA patients with STEMI than in NSTEMI patients and that their

241 long-term prognosis was poorer [23]. A recent study demonstrated that the mortality of patients

242   with MINOCA presenting with STEMI was relatively high at 4.5% at year 1 [25]. This might be

243   related to the occurrence of congestive heart failure because of highly extensive and severe

244   myocardial damage. However, no statistically significant differences in mortality were observed

245   between STEMI and NSTEMI patients in this study. Our findings were similar to those of Xu

246   [12] because we found that there was no statistical difference in the incidence of MACE

247   (rehospitalization for chest pain, non-fatal MI, heart failure, stroke, heart valve replacement and

248   all-cause death, etc.) in the follow-up period between the STEMI and NSTEMI groups, which

249   may be related to the similar drug therapies administered to patients from different sub-groups.

250   There are several inconsistencies regarding the predictors of MACE in STEMI and NSTEMI

251   patients in previous studies. One study reported that STEMI and NSTEMI patients differed

252   significantly with regard to predictors of early and late-term mortality [14, 24]. In addition, the

253   study conducted by Xu demonstrated that the predictors of MACE in MINOCA patients with

254   STE and NSTE were different; the independent predictors of MACE in the NSTEMI group were

255   age, lower level of TC, hypertension, and smoking history, and the strongest predictors in the

256   STEMI group were reduced LVEF levels and a history of diabetes mellitus[12]. A large meta-

257   analysis showed that a further reduction in LDL-C levels was effective in reducing the incidence

258   of prognostic cardiovascular disease and stroke[26], which was consistent with our findings,

259   which showed that a higher LDL-C level was an independent risk factor for MACE in the

260   STEMI group. The use of statins in patients with MINOCA for reducing the LDL-C levels and

261   stabilizing and controlling coronary plaque progression has had a beneficial prognostic impact

262   [27]. Johnston et al. found that among STEMI patients, the all-cause mortality was significantly

263   higher in females than in males[23], while this difference in mortality between the sexes was not

264   observed in our research. We suggest that this complexity is reflective of the heterogeneous

265   features of MINOCA in terms of STE and NSTE.

266   Currently, there is no uniform treatment for the MINOCA population. We found that β-blocker

267   medication was a protective factor for MACE during the follow-up period in the MINOCA

268   population with NSTEMI and STEMI, which is consistent with the findings of Ciliberti et

269   al.[28]. However, the findings of the study by Adbu showed that the treatment of MINOCA with

270   statins and ACEI/ARB had long-term beneficial effects on the outcome, whereas β-blocker and

271   DAPT treatment seemed to have no significant effect on the occurrence of MINOCA[29]. The

272   administration of characteristic therapies is necessary for patients in whom the occurrence of

273 MINOCA is attributable to different underlying mechanisms. All the above-mentioned studies

274 suggest that the use of secondary preventative medications for cardiovascular disease may

275 significantly improve the prognosis of the MINOCA population and should be advocated, but

276 this needs to be confirmed in multicenter studies with longer follow-up periods.

277

278 **Limitations**

279 There are several limitations to our study. One of the major limitations is that our study was a

280 single-center retrospective study with a small sample size and a short follow-up period, because

281 of which our findings might lead to biased findings. Second, cardiac magnetic resonance (CMR)

282 cloud not be performed for all patients due to medical insurance-related issues and the lack of

283 CMR may influence the accuracy of our findings in MINOCA patients. Finally, information

284 regarding medications to be administered in the follow-up period could not be obtained for all

285 patients. Hence, we could not further analyze whether the long-term use of secondary

286 preventative medications was beneficial for patients with MINOCA. A larger multi-center

287 randomized controlled study is necessary to clarify the results of this study.

288

289 ## Conclusions

290 In conclusion, the clinical characteristics of the STE and NSTE groups differed in patients with

291 MINOCA, whereas the outcomes during the 49-month follow-up were similar. The predictors for

292 MACE in patients between the STE group and NSTE group were not thoroughly identical.

293

294 ## Acknowledgements

295

296 **Competing Interests**

297 The authors declare there are no competing interests.

298 Human Ethics

299 We declare that this study has been approved by the Ethics Committee of the First Hospital of Jilin

300 University.

301

302

303

304

References

1. Tamis-Holland JE, Jneid H, Reynolds HR, et al. Contemporary Diagnosis and Management of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease: A Scientific Statement From the American Heart Association. Circulation 2019;139:e891-e908.

2. Abdu FA, Liu L, Mohammed AQ, et al. Myocardial infarction with non-obstructive coronary arteries (MINOCA) in Chinese patients: Clinical features, treatment and 1 year follow-up. Int J Cardiol 2019;287:27-31.

3. Pasupathy S, Air T, Dreyer RP, et al. Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries. Circulation 2015;131:861-870.

4. Niccoli G, Scalone G, Crea F. Acute myocardial infarction with no obstructive coronary atherosclerosis: mechanisms and management. Eur Heart J 2015;36:475-481.

5. Agewall S, Beltrame JF, Reynolds HR, et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J 2017;38:143-153.

6. Montenegro Sá F, Ruivo C, Santos LG, et al. Myocardial infarction with nonobstructive coronary arteries: a single-center retrospective study. Coron Artery Dis 2018;29:511-515.

7. Pizzi C, Xhyheri B, Costa GM, et al. Nonobstructive Versus Obstructive Coronary Artery Disease in Acute Coronary Syndrome: A Meta-Analysis. J Am Heart Assoc 2016;5:

8. Raparelli V, Elharram M, Shimony A, et al. Myocardial Infarction With No Obstructive Coronary Artery Disease: Angiographic and Clinical Insights in Patients With Premature Presentation. Can J Cardiol 2018;34:468-476.

9. Barr PR, Harrison W, Smyth D, et al. Myocardial Infarction Without Obstructive Coronary Artery Disease is Not a Benign Condition (ANZACS-QI 10). Heart Lung Circ 2018;27:165-174.

10. Lindahl B, Baron T, Erlinge D, et al. Medical Therapy for Secondary Prevention and Long-Term Outcome in Patients With Myocardial Infarction With Nonobstructive Coronary Artery Disease. Circulation 2017;135:1481-1489.

11. Ishii M, Kaikita K, Sakamoto K, et al. Characteristics and in-hospital mortality of patients with myocardial infarction in the absence of obstructive coronary artery disease in super-aging society. Int J Cardiol 2020;301:108-113.

12. Xu B, Abdu FA, Liu L, et al. Clinical Outcomes and Predictors of ST-Elevation Versus Non-ST-Elevation Myocardial Infarction with Non-Obstructive Coronary Arteries. Am J Med Sci 2020;

335   13. Borrayo-Sánchez G, Rosas-Peralta M, Ramírez-Arias E, et al. STEMI and NSTEMI: Real-
336   world Study in Mexico (RENASCA). Arch Med Res 2018;49:609-619.

337   14. Polonski L, Gasior M, Gierlotka M, et al. A comparison of ST elevation versus non-ST
338   elevation myocardial infarction outcomes in a large registry database: are non-ST myocardial
339   infarctions associated with worse long-term prognoses? Int J Cardiol 2011;152:70-77.

340   15. Nordenskjöld AM, Baron T, Eggers KM, et al. Predictors of adverse outcome in patients with
341   myocardial infarction with non-obstructive coronary artery (MINOCA) disease. Int J Cardiol
342   2018;261:18-23.

343   16. Li M, He Y, Cheang I, et al. Clinical characteristics and outcome in patients with ST-segment
344   and non-ST-segment elevation myocardial infarction without obstructive coronary artery: an
345   observation study from Chinese population. BMC Cardiovasc Disord 2022;22:21.

346   17. Montalescot G, Dallongeville J, Van Belle E, et al. STEMI and NSTEMI: are they so different?
347   1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA
348   registry). Eur Heart J 2007;28:1409-1417.

349   18. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction
350   (2018). J Am Coll Cardiol 2018;72:2231-2264.

351   19. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and
352   treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of
353   acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the
354   special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail
355   2016;18:891-975.

356   20. Scalone G, Niccoli G, Crea F. Editor's Choice- Pathophysiology, diagnosis and management
357   of MINOCA: an update. Eur Heart J Acute Cardiovasc Care 2019;8:54-62.

358   21. Kilic S, Aydın G, Çoner A, et al. Prevalence and clinical profile of patients with myocardial
359   infarction with non-obstructive coronary arteries in Turkey (MINOCA-TR): A national multi-
360   center, observational study. Anatol J Cardiol 2020;23:176-182.

361   22. Hanssen M, Cottin Y, Khalife K, et al. French Registry on Acute ST-elevation and non ST-
362   elevation Myocardial Infarction 2010. FAST-MI 2010. Heart 2012;98:699-705.

363   23. Johnston N, Jönelid B, Christersson C, et al. Effect of Gender on Patients With ST-Elevation
364   and Non-ST-Elevation Myocardial Infarction Without Obstructive Coronary Artery Disease. Am
365   J Cardiol 2015;115:1661-1666.

366   24. Park HW, Yoon CH, Kang SH, et al. Early- and late-term clinical outcome and their predictors

367   in patients with ST-segment elevation myocardial infarction and non-ST-segment elevation

368   myocardial infarction. Int J Cardiol 2013;169:254-261.

369   25. Gue YX, Corballis N, Ryding A, et al. MINOCA presenting with STEMI: incidence, aetiology

370   and outcome in a contemporaneous cohort. J Thromb Thrombolysis 2019;48:533-538.

371   26. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of

372   LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet

373   2010;376:1670-1681.

374   27. Choo EH, Chang K, Lee KY, et al. Prognosis and Predictors of Mortality in Patients Suffering

375   Myocardial Infarction With Non-Obstructive Coronary Arteries. J Am Heart Assoc

376   2019;8:e011990.

377   28. Ciliberti G, Verdoia M, Merlo M, et al. Pharmacological therapy for the prevention of

378   cardiovascular events in patients with myocardial infarction with non-obstructed coronary arteries

379   (MINOCA): Insights from a multicentre national registry. Int J Cardiol 2020;

380   29. Abdu FA, Mohammed AQ, Liu L, et al. Myocardial Infarction with Nonobstructive Coronary

381   Arteries (MINOCA): A Review of the Current Position. Cardiology 2020;145:543-552.

382

383

384   Figure legends

385   Fig. 1 Flow chart of patients included in this study.

386   Abbreviations: AMI, acute myocardial infarction, CAG, coronary angiography, STE, ST-

387   segment elevation, NSTE, non-ST segment elevation, MINOCA, non-obstructive coronary

388   arteries

389

Figure 1

Flow chart of cases collection in this study.

Flow chart of cases collection in this study.


```
┌─────────────────────────────────┐
│   AMI patients performed CAG    │
│     January 2015 to July 2018   │
│ N=9696 (STEMI:5931;NSTEMI:3765) │
└─────────────────────────────────┘

┌──────────────────────┐      ┌────────────────────────────────┐
│   MINOCA patients    │      │    Excluded MI-CAD patients    │
│    N=196(2.02%)      │      │  ( angiographic stenosis > 50%)│
│ (STEMI:115;NSTEMI:81)│      │            N=9500              │
└──────────────────────┘      │    (STEMI:5816;NSTEMI:3684)    │
                              └────────────────────────────────┘

┌──────────────────────────────────┐
│ 190 MINOCA patients with follow up│
│     (STEMI:110;NSTEMI:80          │
│         ;6 patients died)         │
└──────────────────────────────────┘
```
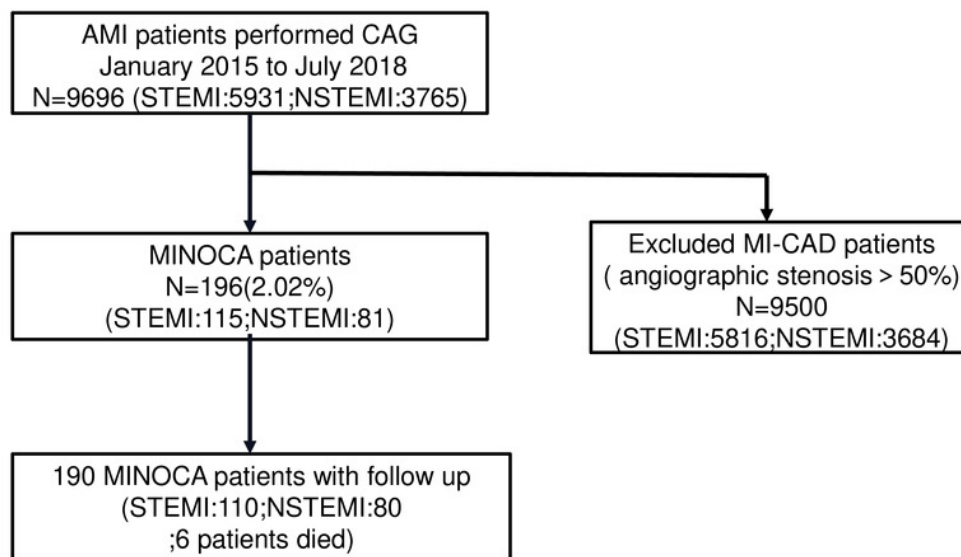
PeerJ

Table 1(on next page)

Table 1 Comparision of the baseline characteristics between STEMI and NSTEM among MINOCA population

1

2   Table 1 Comparision of the baseline characteristics between STEMI and NSTEM among MINOCA population

Variables	STEMI（n=115）	NSTEMI（n=81）	P
Demographics			
Age(years)	52.93±12.68	56.47±11.21	0.045
Male,n(%)	81（70.43）	60（74.07）	0.577
Coronary risk factors			
Diabetes, n (%)	11（9.57）	12（14.81）	0.261
Hypertension, n (%)	47（40.87）	48（59.26）	0.011
hyperlipidaemia, n (%)	33（28.70）	23（28.39）	0.927
previous arrhythmia, n (%)	9（7.83）	7（8.64）	0.837
Smoking history, n (%)	83（72.13）	52（64.20）	0.235
Killip grade, n (%)			
1 grade	103（89.57）	64（79.01）	0.040
≥2 grades	12（10.43）	17（20.99）	
hospitalization days(days）	6（4,8）	7（4,8）	0.305
Medications during hospitalization			
Aspirin, n (%)	112（97.39）	73（90.12）	0.018
Clopidogrel, n (%)	108（93.91）	73（90.12）	0.415
β-blocker, n (%)	51（44.35）	41（50.62）	0.468
Statins, n (%)	110（95.65）	77（95.06）	0.721
ACEI/ARB(%)	44(38.26)	45(55.56)	0.017
Laboratory indicators			
Myoglobin (ng/ml)	94（46.8,309.00）	101.5（53.08,178.75）	0.917
cTnT((ng/ml))	3.02（0.18,13.5）	1.34（0.22,5.87）	0.076
CK-MB	5.95（1.08,33,45）	3.80（1.00,12.81）	0.102
BNP	112（27.13,297.75）	61.90（20.40,186.00）	0.106
WBC count(×10^12/L)	8.24（6.24,10.38）	7.52（6.01,9.28）	0.158
NE(%)	5.24（3.94, 8.04）	4.99（3.71,6.55）	0,231
RBC count(×10^12/L)	4.61（4.27,4.97）	4.69（4.45,4.94）	0.457

PLT count(×10^12/L)	221.5（182.00,266.75)	210（172.25,255.75)	0.262
TC (mmol/L)	4.20（3.67,4.95)	4.51（3.75, 5.25)	0.115
LDL-C (mmol/L	2.44（1.99,1.45)	2.45（2.09,3.35)	0.109
HDL-C (mmol/L)	1.18（0.99,1.45)	1.2（1.05,1.48)	0.305
TG (mmol/L	1.45（1.06,2.37)	1.51（1.11,2.21)	0.718
Serum glucose(mmol/L)	5.19（4.66,5.95)	5.55（4.87,6.44)	0.047
Echocardiography			
LV(mm)	49（46, 52)	50（46.75,52)	0.333
LVEF(%)	57（54,60)	59（55, 60)	0.128

3 Abbreviation:cTnT,blood cardiac troponin-T,CK-MB,creatine kinase-MB,BNP,brain natriuretic

4 peptide,RBC,Red blood cell,WBC,White blood cell,NE,

5 neutrophilicgranulocyte,PLT,Platelet,TC,total cholesterol,LDL-C,low-density lipoprotein

6 cholesterol,HDL-C,high-density lipoprotein cholesterol,TG,triglyceride, LV, left

7 ventricle,LVEF,left ventricular ejection fraction .

8
9
10
11
12
13

Table 2(on next page)

Table 2 Comparision of the rate of MACE in MINOCA during follow-up period.

1

2   Table 2 Comparision of the rate of MACE in MINOCA during follow-up period.

	STEMI（n=115）	NSTEMI（n=81）	*P*
MACE,n(%)	28（24.35）	18（22.22）	0.73
Chest pain rehospitalization, n (%)	4（3.48）	4（4.94）	0.72
nonfatal MI, n (%)	3（2.61）	2（2.47）	1
Heart failure, n (%)	14（12.17）	8（9.88）	0.654
Stroke, n (%)	5（4.35）	3（3.70）	1
Heart valve replacement, n (%)	-	2（2.47）	0.17
All-cause deaths, n (%)	5（4.35）	1（1.23）	0.404

3
4
5
6
7

Table 3(on next page)

Table 3 Univariate analysis of MACE among STEMI and NSTEMI population

1
2 Table 3 Univariate analysis of MACE among STEMI and NSTEMI population

Factors	MACE$_{STE}$(n=28)	P$_{STE}$	MACE$_{NSTE}$(n=18)	P$_{NSTE}$
Age(years)	57.39±13.74	0.003	60.44±9.94	0.049
Male,n(%)	15 (53.57)	0.025	15 (83.33)	0.376
Diabetes, n (%)	5 (17.86)	0.086	5 (27.78)	0.126
Hypertension, n (%)	14 (50.00)	0.259	13 (72.22)	0.204
hyperlipidaemia, n (%)	6 (21.43)	0.266	3 (16.67)	0.245
previous arrhythmia, n (%)	2 (7.14)	1.000	3 (16.67)	0.339
Smoking history, n (%)	19 (67.85)	0.558	11 (61.11)	0.757
Killip grade, n (%)				0.145
1 grade	20 (71.43)	0.001	12 (66.67)	
≥2 grades	8 (28.57)		6 (33.33)	
Laboratory indicators				
Myoglobin (ng/ml)	97.25 (50.20,248.25)	0.539	105.00 (53.63,173.25)	0.934
cTnT(ng/ml)	2.65 (0.07,14.57)	0.661	0.54 (0.19,8.99)	0.578
CK-MB(ng/ml)	4.17 (1.00,25.55)	0.481	3.79 (1.00,15.12)	0.986
BNP	120.00 (32.60,848.00)	0.305	85.45 (31.55,249.45)	0.150
WBC count(×10^12/L)	8.20 (5.97,11.65)	0.931	7.52 (5.59,8.79)	0.461
RBC count(×10^12/L)	4.43 (4.15,4.66)	0.016	4.68 (4.43,4.93)	0.773
PLT count(×10^12/L)	219.00 (186.00,255.00)	0.401	198.50 (154.75,250.50)	0.450
TC (mmol/L)	4.11 (3.35,4.94)	0.276	4.68 (3.52,5.37)	0.775
LDL-C (mmol/L)	2.32 (1.77,2.80)	0.085	2.63 (1.98,3.20)	0.579
HDL-C (mmol/L)	1.21 (1.02,1.60)	0.372	1.31 (1.17,1.59)	0.113
TG (mmol/L	1.33 (0.90,1.73)	0.170	1.36 (0.95,2.00)	0.229
Serum glucose(mmol/L)	5.46 (4.73,6.72)	0.262	5.62 (4.84,6.74)	0.775
Echocardiography				
LV (mm)	49.00 (46.00,52.00)	0.989	50.50 (47.75,55.00)	0.191
LVEF (%)	58.00 (51.00,60.00)	0.949	58.00 (50.75,60.50)	0.330

hospitalization days(days)	7.00 (5.00,8.00)	0.037	6.50 (3.75,9.00)	0.991
Medications during hospitalization				
Aspirin, n (%)	28 (100.00)	1.000	14 (77.78)	0.086
Clopidogrel, n (%)	26 (92.86)	0.634	17 (94.45)	0.677
β-blocker, n (%)	8 (28.57)	0.048	5 (27.78)	0.028
Statins, n (%)	28 (100.00)	0.571	17 (94.45)	1.000
ACEI/ARB(%)	25 (89.28)	0.754	16(88.89)	0.534

3 Abbreviation: cTnT, blood cardiac troponin-T, CK-MB, creatine kinase-MB, BNP, brain

4 natriuretic peptide, RBC, Red blood cell, WBC, White blood cell, PLT, Platelet, TC, total

5 cholesterol, LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein

6 cholesterol, TG, triglyceride, LV, left ventricle, LVEF, left ventricular ejection fraction.

7

8

9

Table 4(on next page)

Table 4 Multivariable predictors of MACE in STEMI patients.

1

2

3   Table 4 Multivariable predictors of MACE in STEMI patients.

Factors	OR	95%Cl	P
Killip grade	9.035	（1.657,49.263）	0.011
β-blocker	0.238	（0.072,0.788）	0.019
LDL-C	2.267	（1.008,5.097）	0.048

4   Abbreviation:LDL-C,low-density lipoprotein cholesterol.

5

6