Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15979
DOI URL: http://dx.doi.org/10.21474/IJAR01/15979

RESEARCH ARTICLE

STUDY OF LIPID PROFILE OF PATIENT WITH ACUTE MYOCARDIAL INFARCTION

Dr. Nihar Patidar[1,2], Dr. Kshitij Kumar[1], Dr. B.B. Gupta[2] and Dr. R.K. Jha[2]

1. Department of General Medicine.
2. Sri Aurobindo Medical College & Postgraduate Institute-Indore (M.P.)-India.

Manuscript Info

Manuscript History
Received: 31 October 2022
Final Accepted: 30 November 2022
Published: December 2022

Abstract

Background- There is discussion over the biomarker potential of using different lipid fractions to predict the risk of acute myocardial infarction (AMI). In order to compare the lipid profiles of 67 AMI patients, we looked at serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides (TG).

Material And Method- A prospective, cross-sectional study was conducted in the SAIMS emergency/opd. Within 24hours of onset of chest pain. All patients admitted with AMI were included after providing informed consent.

Results- Among 200 AMI Patients included 100 STEMI (ST- elevated myocardial infarction) patients, 100 NSTEMI (non-ST-elevated myocardial infarction) patients. The median age of STEMI patient was 57.7years while that of NSTEMI patients 60.3 years. BMI of STEMI 24.6 kg/m^2 and NSTEMI 24.9 $kg/m^{2.}$ History of diabetes was present in 22% STEMI patient while that of NSTEMI patients 39%. History of hypertension is present in 52 % STEMI patient and 68% of NSTEMI patients. 49 % STEMI patients were currently smoking while only 36% among NSTEMI patients.

Conclusion- The lipid paradox exists for STEMI patients' LDL-C and TC levels and hospitalisation, 30-day, and 1-year mortality. NSTEMI patients have a lipid pseudo-paradox. HDL-C, myocardial infarction type, and hospital death are interrelated. These results need more study.

Introduction:-

The most frequent type of ischemic heart disease (IHD) is acute myocardial infarction (AMI), which accounts for the majority of mortality in the United States (US). Every year, approximately 1.5 million Americans suffer from acute MI, with one-third of them dying [1-2].Modifiable risk factors can be reduced to minimise the severity of IHD and its related mortality. Among the modifiable risk factors for IHD—hypertension (HTN), diabetes (DM), cigarette smoking, dyslipidemia (hyperlipidemia and hypercholesterolemia), and severe obesity—dyslipidemia (hyperlipidemia and hypercholesterolemia) has garnered the most attention recently [3]. Epidemiological studies have shown that dyslipidemia is connected with an increased risk of IHD. Hypercholesterolemia, specifically greater plasma cholesterol levels in low-density lipoproteins (LDL- C), has been linked to coronary artery disease (CAD) [4-5]. AMI risk was elevated in patients with low plasma levels of high-density lipoprotein (HDL-C) cholesterol [6]. These two variables have been found as linear risk factors for coronary artery disease and stroke [8-9]. In a study of

Corresponding Author:- Dr. Nihar Patidar
Address:- PG Student Department of General Medicine.

young AMI patients (within 24 hours), 60.83% were dyslipidemic, with TG being the most common isolated disordered lipid component (45%), and low HDL being the least common (10.83%) [10].The goal of this study is to evaluate changes in serum lipid profiles in AMI patients, which will influence their choice of cholesterol-lowering medicine.

Materials and Methods:-

A prospective, cross-sectional study was conducted in the SAIMS emergency/opd. Within 24 hours of onset of chest pain. All patients admitted with AMI were included after providing informed consent. AMI was identified utilising pertinent history, electrocardiograms (ECGs), and cardiac biomarkers. Patients who were already on lipid-lowering medications, presented after 24 hours of MI, and had previously been diagnosed with hyperthyroidism were among those who were excluded. To avoid bias in the results, participants with certain comorbidities were excluded. Their lipid profile (in mg/dl) was routinely evaluated, along with all other forms of biochemical testing, as part of a hospital protocol. There were no additional interventions in this experiment, and there was no increased strain on the patient or hospital resources. Age, gender, smoking history, co-morbidities such as diabetes and hypertension, previous history of major cardiovascular events (MACE including MI and stroke), and body weight and height were all documented for all participants. BMIs more than 30 kg/m2 were categorised as obese. The lipid profile was collected within the first 24 hours of the event and again 48 hours later. Five patients died within 48 hours of being admitted, and two were moved to a different hospital. All seven patients were replaced with new patients. For statistical analysis, online available free stat calculator was utilised. Continuous data such as age and lipid profile were analysed and reported as mean and standard deviation (SD), whereas categorical variables such as gender, cardiovascular history, smoking history, and lipid abnormality type were presented as percentages and frequencies. To compare frequencies, confounding factors such as age, gender, cardiovascular history, and smoking history were controlled for using stratified chi-square. To compare the means of blood biochemical levels at two time intervals, the paired sample T-test was performed. P-values less than 0.05 were deemed significant.

Results:-

Table 1. Characteristics of ST elevation (STEMI) and non-ST elevation myocardial infarction (NSTEMI) patients in the study. The median age of STEMI patient was 57.7years while that of NSTEMI patients 60.3 years the age of NSTEMI group was higher than STEMI.there is preponderance of male gender in both the groups.BMI of STEMI 24.6 kg/m^2 and NSTEMI 24.9 $kg/m^{2.}$ History of diabetes was present in 22% STEMI patient while that of NSTEMI patients 39%. History of hypertwnsion is present in 52 % STEMI patient and 68% of NSTEMI patients. 49 % STEMI patients were currently smoking while only 36% among NSTEMI patients. 15 % STEMI patient and 32% of NSTEMI patients were either having history of AMI/CABG.

Table 1:- Characteristics of ST elevation (STEMI) and non-ST elevation myocardial infarction (NSTEMI) patients in the study.

	STEMI (n = 100)	**NSTEMI (n = 100)**	**p**
Age in years, median (IQR)	57.7 (50.7–66.0)	60.3 (52.5–69.4)	<0.001
Sex, n (%)			
Male	85 (85.0)	78 (78)	<0.001
Female	15 (15.0)	22 (22)	
History of diabetes, n (%)			
Yes	22 (28)	39 (39)	<0.001
No	72 (72)	61(61)	
History of hypertension, n (%)			
Yes	52 (52)	68 (68)	<0.001
No	48 (48)	32 (32)	
Smoking, n (%)			
Never	37 (37)	44 (44)	
Former	14 (14)	20 (20)	<0.001
Current	49(49)	36 (36)	
History of AMI/CABG n (%)			
Yes	15 (15)	32 (32)	<0.001
No	85 (85)	68 (68)	

BMI in kg/m^2, median (IQR)	24.6 (22.3–27.3)	24.9 (22.6–27.9)	<0.001
Anterior infarct on admission, n (%)			
Yes	**49 (49)**	Not applicable	
No	**51(51)**		
LDL-C in mmol/l within 72 h from MI onset median (IQR)	3.4 (2.6–4.1)	3.2 (2.4–4.0)	<0.001
TC in mmol/lwithin 72 h from MI onset median (IQR)	5.1 (4.3–6.0)	5.0 (4.1–5.9)	<0.001
HDL-C in mmol/l within 72 h from MI onset, median (IQR)	1.0 (0.9–1.2)	1.0 (0.9–1.2)	0.261
TG in mmol/l within 72 h from MI onset, median (IQR)	**1.4 (1.0–2.0)**	**1.6 (1.1–2.3)**	**<0.001**
Random glucose in mmol/L within 72 h from MI onset, median (IQR)	9.1 (7.2–13.2)	8.2 (6.3–12.5)	<0.001
Serum creatinine in 10µmol on admission, median (IQR)	9.0 (7.7–10.9)	8.6 (7.3–10.8)	<0.001
Haemoglobin in g/dL on admission, median (IQR)	14.6 (13.4–15.7)	14.0 (12.6–15.2)	<0.001
Elevated first troponin within 72 h from MI onset, n (%)			
Yes	**49 (49)**	56 (56)	<0.001
No	**51(51)**	44 (44)	
LVEF < 50% during hospitalization, n (%)			
Yes	61 (61)	40 (40)	<0.001
No	39 (39)	60 (60)	
Days from MI onset to discharge, median (IQR), median (IQR)	4 (3–5)	4 (3–6)	<0.001

Table 2 examining the correlations between low density lipoprotein cholesterol levels and the primary and secondary outcomes in ST elevation myocardial infarction (STEMI) and Non-ST elevation myocardial infarction (NSTEMI).

Table 2:- The Correlations Between Low Density Lipoprotein Cholesterol Levels And The Primary And Secondary Outcomes In ST Elevation Myocardial Infarction (STEMI) And Non-ST Elevation Myocardial Infarction (NSTEMI).

	All STEMI + NSTEMI patients						**All STEMI + NSTEMI patients discharged alive**			
	Death during hospitalization		**Death within 30 days from MI onset**		**Death within 1 year from MI onset**		**Rehospitalization for HF within 1 year from MI discharge**		**Rehospitalization for MI within 1 year from MI discharge**	
	HR (95% CI)	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
LDL-C in mmol/l	0.77 (0.74–0.80)	<0.001	0.65 (0.62–0.68)	<0.001	0.68 (0.66–0.70)	<0.001	0.97 (0.90–1.04)	0.411	0.95 (0.89–1.03)	0.220
HDL-C in mmol/l	1.17 (0.89–1.53)	0.264	1.13 (0.87–1.47)	0.356	1.24 (1.03–1.50)	0.020	1.09 (0.80–1.48)	0.576	1.09 (0.75–1.58)	0.638

Table 3:- Interaction Between Type Of Myocardial Infarction And Lipids.

	Death during hospitalization	**Death within 30 days from MI onset**	**Death within 1 year from MI onset**	**Rehospitalization for Heart Failure within 1 year from MI discharge**	**Rehospitalization for MI within 1 year from MI discharge**
LDL-C	0.400	0.317	**0.001**	0.056	0.495

TG	0.910	0.612	0.948	0.158	**0.042**
TC	0.081	**0.026**	**<0.001**	**0.018**	0.448
HDL-C	**0.034**	0.057	**0.040**	0.333	0.694

The following were our primary study findings: 1. The lipid paradox for LDL-C exists for STEMI patients undergoing PCI for the primary outcomes of death during hospitalisation, at 30 days, and at 1 year, but not for NSTEMI patients, indicating that a pseudo-paradox exists for NSTEMI patients; 2. The lipid paradox for TG levels did not exist in our study after adjustment, indicating that a pseudo-paradox exists for NSTEMI patients; 3. HDL-C levels trended towards a paradox for STEMI patients Several studies have been conducted to look into the lipid paradox in patients with acute coronary syndromes. These studies were conducted in STEMI and NSTEMI populations as a whole, but did not specifically compare these two groups[11-15]. Cho et al. investigated 30-day and 1-year outcomes in a population of AMI patients following PCI, but did not differentiate between STEMI and NSTEMI groups. They discovered that patients with higher LDL-C levels, with the exception of patients with LDL-C > 160 mg/dL (>4.1 mmol/L), had better outcomes. They did, however, report age, systolic blood pressure, acute myocardial infarction, LVEF, renal function, Killip class, N-terminal-pro-B-type natriuretic level, and use of renin-angiotensin receptor blockers (RAB) as independent predictors of 12-month mortality, and concluded that their observation was an apparent paradox due to confounding factors. In our study, we found that the lipid paradox persisted in the STEMI population but not in the NSTEMI. The lipid paradox was observed in STEMI patients even for LDL-C during the index hospitalisation for myocardial infarction, which would not have been long enough for RABs to exert their myocardial remodelling effects. As a result, we believe that, while RAB use may be beneficial in the long run, it cannot explain our short-term observation.

Cheng et al. investigated triglyceride levels in ACS patients and discovered that serum triglyceride levels had an inverse relationship with in-hospital death and late outcomes[16]. They believe that higher TG levels may help to stabilise infarct size, lowering the risk of arrhythmias. Another proposed explanation is that TG actually reflects nutritional status, and that a lower TG indicates that the body's nutritional state is poorer, which may stall the patient's recovery from STEMI. In our study cohort, we did not find the same results, nor were there any significant differences in TG levels between STEMI and NSTEMI groups. One possible explanation is that our study controlled for more variables than Cheng et alstudy, .'s and that there may be an apparent paradox for TG in that study due to residual confounding. STEMI patients have a higher pro-inflammatory state than NSTEMI patients[17,18]. Our findings support the role of inflammation as an underlying factor in the lipid paradox, as we found it in STEMI patients but not in NSTEMI patients. Furthermore, the clinical characteristics of STEMI and NSTEMI patients may have contributed to this. In our population, STEMI patients were more likely to be smokers, which contributes to a pro-inflammatory state[19]. The subjects in our STEMI population were more likely to be on oral hyperlipidemia medications, and statins have been shown to have a pleiotropic anti-inflammatory effect[20]. Statins reduce the levels of TC, LDL-C, and TG[21]. A study found that statins improved outcome in patients with low LDL-C levels. Oduncu et al. demonstrated that patients with statin-induced low LDL-C on admission have better outcomes in STEMI and have a lower mortality rate, whereas patients with spontaneously low LDL-C without statin treatment have a higher mortality rate [22]. They also believe that statins have anticoagulant, antiplatelet, and anti-inflammatory properties. Those with spontaneously low LDL-C were associated with increased inflammation, as evidenced by higher inflammatory markers (leukocyte count, neutrophil/lymphocyte ratio, and C-reactive protein levels) in their study[22]. Building on this, patients with lower HDL-C levels had better outcomes for STEMI patients (HDL-C lipid paradox). On the contrary, lower HDL-C levels were associated with poorer outcomes in NSTEMI patients, though this was only statistically significant for death during hospitalisation at HDL-C levels ranging from 1.0 to 1.5 mmol/L. Previous research in AMI populations has shown that lower HDL-C levels are associated with increased mortality in both STEMI[23] and NSTEMI[24] patients. This finding could be explained by the presence of dysfunctional HDL-C, which has been found in patients with coronary artery disease, obesity, diabetes, and smokers [25]. It is becoming increasingly clear that the function and subclass of HDL-C must be considered in addition to plasma concentrations, because plasma concentrations alone cannot account for epidemiological observations and lack of treatment efficacy when increasing HDL-C levels[26-28]. Dysfunctional HDL-C has a lower pro-oxidative and higher pro-inflammatory effect. Different levels of inflammation are present in NSTEMI and STEMI patients, and this difference in the inflammatory process can modify HDL-C functionality [28], potentially leading to the findings in our study. Also, compared to NSTEMI, STEMI patients were less likely to have a history of AMI/CABG/PCI (a surrogate for CAD), a lower BMI, and diabetes mellitus, despite having a higher proportion of smokers. This difference in baseline characteristics may also explain why STEMI patients have lower levels of dysfunctional HDL-C and thus have a better outcome.

Further research on HDL-C function and subfractions, as well as levels in this population, would be beneficial in understanding this observation in the future. Unfortunately, we did not have information on inflammatory markers such as C-reactive protein and total white cell count in our population, nor did we have statin compliance data, so we were unable to specifically examine inflammation as a factor, but this can be the focus of future studies. Other studies have been conducted to investigate the lipid paradox in non-MI cardiac patients. The authors described the potential pathophysiological mechanisms of low LDL-C in conditions of increased inflammation, such as heart failure. They explain that increased intestinal edoema causes an increase in the translocation of bacterial lipoprotein saccharides (LPS) from the intestines into the blood, which causes inflammatory markers like tumour necrosis factor-alpha to be produced. Lipoproteins form micelles around the bacterial LPS in order to inactivate the bacterial components, resulting in lower LDL-C levels [29,30]. While our study did not look into the biological mechanisms of the lipid paradox in post-MI PCI patients, gut bacteria have been linked to myocardial infarction, which could be a mechanism of action [31]. Other potential explanations for the lipid paradox in heart failure patients include statin pre-medication and poorer nutritional status [30], both of which can be a factor but were not included in our study.

Non-cardiac conditions have also been linked to the lipid paradox. Amezaga Urruela et al. reported lower lipid levels in active rheumatoid arthritis patients, hypothesising that this was due to an inflammatory process [32]. A similar inflammatory cytokine release is observed in acute pancreatitis, which also exhibits the lipid paradox [33]. The inflammatory hypothesis is thought to play a significant role in the pathophysiology of AMI [34]. This inflammatory hypothesis was recently reinforced in the landmark Canakinumab Anti-inflammatory Thrombosis Outcome Study (CANTOS) trial, which investigated the use of the orphan drug canakinumab to reduce the risk of developing cardiovascular events using anti-inflammatory therapy with interleukin-1 inhibition4[35].

Conclusion:-

The lipid paradox appears to exist for STEMI patients' LDL-C and TC levels and outcomes of death during hospitalisation, death at 30 days, and death at 1 year. There appears to be a lipid pseudo-paradox in NSTEMI patients. The interaction between HDL-C, the type of myocardial infarction, and the outcome of death during hospitalisation is significant. These findings merit further investigation.

Reference:-

1. Myocardial infarction. (2018). Accessed: March 7, 2019: https://emedicine.medscape.com/article/155919-overview.
2. Leading causes of death. (2017). Accessed: March 7, 2019: https://www.cdc.gov/nchs/fastats/leading- causes-of-death.htm.
3. De Backer G, Ambrosioni E, Borch-Johnsen K: European guidelines on cardiovascular disease prevention in clinical practice: Third joint task force of European and other societies on cardiovascular disease prevention in clinical practice. Eur Heart J. 2003, 24:1601-1610. 10.1016/S0195-668X (03)00347-6.
4. Rasheed SJ, Ahmed S, Samad A: Effect of statins on triglycerides in the management of hypercholesterolemia in patients with coronary heart disease. Pak J Cardiol. 2002, 13:65-72.
5. Cannon CP, Braunwald E, McCabe CH: Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004, 350:1495-1504. 10.1056/NEJMoa040583
6. Khan HA, Alhomida AS, Sobki SH: Lipid profile of patients with acute myocardial infarction and its correlation with systemic inflammation. Biomark insights. 2013, 8:1-7. 10.4137/BMI.S11015
7. Zaid M, Hasnain S: Plasma lipid abnormalities in Pakistani population: trends, associated factors, and clinical implications. Braz J Med Biol Res. 2018, 51:e7239. 10.1590/1414-431X20187239
8. Lee JS, Chang PY, Zhang Y, Kizer JR, Best LG, Howard BV: Triglyceride and HDL-C dyslipidemia and risks of coronary heart disease and ischemic stroke by glycemic dysregulation status: the strong heart study. Diabetes Care. 2017, 40:529-537. 10.2337/dc16-1958
9. Lazo-Porras M, Bernabe-Ortiz A, Málaga G, et al.: Low HDL cholesterol as a cardiovascular risk factor in rural, urban, and rural-urban migrants: PERU MIGRANT cohort study. Atherosclerosis. 2016, 246:36-43. 10.1016/j.atherosclerosis.2015.12.039.
10. Ali SN, Bashir M, Sherwani M: Pattern of dyslipidemia in young patients with acute ST elevation myocardial infarction. J Sheikh Zayed Med Coll. 2016, 7:998-1001.\
11. Reddy, V. S. et al. Relationship between serum low-density lipoprotein cholesterol and in-hospital mortality following acute myocardial infarction (the lipid paradox). Am J Cardiol 115, 557–562, https://doi.org/10.1016/j.amjcard.2014.12.006 (2015).

12. Cho, K. H. et al. Low-density lipoprotein cholesterol level in patients with acute myocardial infarction having percutaneous coronary intervention (the cholesterol paradox). Am J Cardiol 106, 1061–1068, https://doi.org/10.1016/j.amjcard.2010.06.009 (2010).
13. Cheng, K. H. et al. Lipid paradox in acute myocardial infarction-the association with 30-day in-hospital mortality. Crit Care Med 43, 1255–1264, https://doi.org/10.1097/ccm.0000000000000946 (2015).
14. Pokharel, Y. et al. Association of low-density lipoprotein pattern with mortality after myocardial infarction: Insights from the TRIUMPH study. J Clin Lipidol 11, 1458–1470.e1454, https://doi.org/10.1016/j.jacl.2017.09.002 (2017).
15. Wang, T. Y. et al. Hypercholesterolemia Paradox in Relation to Mortality in Acute Coronary Syndrome. Clinical Cardiology 32, E22–E28, Anavekar, N. S. & Solomon, S. D. Angiotensin II receptor blockade and ventricular remodelling. J Renin Angiotensin Aldosterone Syst 6, 43–48, https://doi.org/10.3317/jraas.2005.006 (2005)
16. Cheng, Y. T. et al. Lower serum triglyceride level is a risk factor for in-hospital and late major adverse events in patients with ST- segment elevation myocardial infarction treated with primary percutaneous coronary intervention- a cohort study. BMC Cardiovasc Disord 14, 143, https://doi.org/10.1186/1471-2261-14-143 (2014).
17. Habib, S. S., Kurdi, M. I., Al Aseri, Z. & Suriya, M. O. CRP levels are higher in patients with ST elevation than non-ST elevation acute coronary syndrome. Arq Bras Cardiol 96, 13–17 (2011).
18. Bakhru, A. & Erlinger, T. P. Smoking cessation and cardiovascular disease risk factors: results from the Third National Health and Nutrition Examination Survey. PLoS medicine 2, e160–e160, https://doi.org/10.1371/journal.pmed.0020160 (2005).
19. Antonopoulos, A. S., Margaritis, M., Lee, R., Channon, K. & Antoniades, C. Statins as anti-inflammatory agents in atherogenesis: molecular mechanisms and lessons from the recent clinical trials. Curr Pharm Des 18, 1519–1530, https://doi. org/10.2174/138161212799504803 (2012).
20. Meor Anuar Shuhaili, M. F. R. et al. Effects of Different Types of Statins on Lipid Profile: A Perspective on Asians. Int J Endocrinol Metab 15, e43319, https://doi.org/10.5812/ijem.43319 (2017).
21. Oduncu, V. et al. The prognostic value of very low admission LDL-cholesterol levels in ST-segment elevation myocardial infarction compared in statin-pretreated and statin-naive patients undergoing primary percutaneous coronary intervention. International journal of cardiology 167, 458–463, https://doi.org/10.1016/j.ijcard.2012.01.009 (2013).
22. Ji, M. S. et al. Impact of low level of high-density lipoprotein-cholesterol sampled in overnight fasting state on the clinical outcomes in patients with acute myocardial infarction (difference between ST-segment and non-ST-segment-elevation myocardial infarction). Journal of cardiology 65, 63–70, https://doi.org/10.1016/j.jjcc.2014.04.002 (2015).
23. Duffy, D., Holmes, D. N., Roe, M. T. & Peterson, E. D. The impact of high-density lipoprotein cholesterol levels on long-term outcomes after non-ST-elevation myocardial infarction. American heart journal 163, 705–713, https://doi.org/10.1016/j. ahj.2012.01.029 (2012).
24. Cybulska, B. & Klosiewicz-Latoszek, L. The HDL paradox: what does it mean and how to manage low serum HDL cholesterol level?
25. Kardiologia polska 72, 681–686, https://doi.org/10.5603/KP.a2014.0110 (2014).
26. Vergani, C. & Lucchi, T. Plasma HDL cholesterol and risk of myocardial infarction. The Lancet 380, 1990, https://doi.org/10.1016/ S0140-6736(12)62148-5 (2012).
27. Martin, S. S. et al. HDL cholesterol subclasses, myocardial infarction, and mortality in secondary prevention: the lipoprotein investigators collaborative. European heart journal 36, 22–30, https://doi.org/10.1093/eurheartj/ehu264 (2014).
28. Ramirez, A. & Hu, P. P. Low High-Density Lipoprotein and Risk of Myocardial Infarction. Clin Med Insights Cardiol 9, 113–117, https://doi.org/10.4137/cmc.s26624 (2015).
29. Von Haehling, S., Schefold, J. C., Springer, J. & Anker, S. D. The cholesterol paradox revisited: heart failure, systemic inflammation, and beyond. Heart Fail Clin 4, 141–151, https://doi.org/10.1016/j.hfc.2008.01.009 (2008).
30. Velavan, P., Huan Loh, P., Clark, A. & Cleland, J. G. The cholesterol paradox in heart failure. Congest Heart Fail 13, 336–341 (2007).
31. Rogler, G. & Rosano, G. The heart and the gut. European heart journal 35, 426–430, https://doi.org/10.1093/eurheartj/eht271 (2013).
32. Amezaga Urruela, M. & Suarez-Almazor, M. E. Lipid paradox in rheumatoid arthritis: changes with rheumatoid arthritis therapies.

33. Curr Rheumatol Rep 14, 428–437, https://doi.org/10.1007/s11926-012-0269-z (2012).
34. Hong, W. et al. Relationship between low-density lipoprotein cholesterol and severe acute pancreatitis ("the lipid paradox"). Ther Clin Risk Manag 14, 981–989, https://doi.org/10.2147/tcrm.s159387 (2018).
35. Blankenberg, S. & Yusuf, S. The Inflammatory Hypothesis. Circulation 114, 1557–1560, https://doi.org/10.1161/ circulationaha.106.652081 (2006).