In vitro potency of clinically used antiplatelet drugs in patients with Metabolic dysfunction Associated Fatty Liver Disease

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To compare the in vitro potency of commonly used antiplatelet drugs in the blood of patients with various stages of fibrosis due to MAFLD, compared to that in blood of individuals without underlying liver disease.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON51140

Source
ToetsingOnline

Brief title
Potency of AntiPlatelet drugs in patients with MAFLD (PAD-MAFLD)

Condition

- Diabetic complications
- Hepatic and hepatobiliary disorders

Synonym
Metabolic dysfunction Associated Fatty Liver Disease, Non-Alcoholic Steatohepatitis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Blood Platelets, Cirrhosis, Metabolic dysfunction Associated Fatty Liver Disease, Thrombosis

Outcome measures

Primary outcome

Change in platelet function after in vitro administration of active metabolites of antiplatelet drugs (aspirin, clopidogrel, ticagrelor) to the blood of patients with various stages of fibrosis due to MAFLD, compared to healthy controls. To estimate platelet function, we will assess platelet adhesion by Flow Based Adhesion, platelet activation by Flow Cytometry, and platelet aggregation by Whole Blood Aggregation.

Secondary outcome

Baseline values, such as body weight, height, medical history, use of medications, smoking will be assessed. Parameters to define stage of (fibrosis due to) MAFLD consist of FibroScan Controlled Attenuation Parameter Scores (dB/m) and FibroScan Fibrosis Score (kPa). Other parameters involved in assessing the hemostatic status consist of markers for activation of platelets and coagulation (platelet factor 4, prothrombin fragment 1+2, thrombin-antithrombin complex), routine blood tests (platelet count, hemoglobin, von Willebrand factor, fibrinogen, prothrombin time, international normalized ratio, activated partial thromboplastin time).

Study description

Background summary

Metabolic dysfunction Associated Fatty Liver Disease (MAFLD) is the most common cause of liver disease worldwide, with an estimated prevalence of 9-36.9% in the general population(1). It is regarded to as the hepatic manifestation of metabolic syndrome, a syndrome characterised by increased blood pressure, high blood sugar, excess body fat around the waist and abnormal cholesterol or triglyceride levels. The term MAFLD comprises of a spectrum of pathologic entities, varying from the benign presence of hepatic steatosis (HS) to the chronic inflammatory disease Non-Alcoholic Steatohepatitis (NASH), ultimately leading to cirrhosis.
The role of MAFLD as an adjunctive risk factor for the development of cardiovascular diseases (CVD) has been debated for a long time. Recent evidence has however demonstrated an existing relationship between these two conditions, as well as the association between MAFLD and traditional CVD risk factors such as type 2 diabetes and obesity. A meta-analysis involving 34.043 adult individuals has shown that patients with MAFLD have an increased risk of both fatal and non-fatal cardiovascular events (OR 1.64, 95% CI 1.26-2.13) compared to patients without MAFLD. Moreover, a further increase in the risk of cardiovascular events (OR 2.58, 95% CI 1.78-3.75) was observed among patients with more *severe* MAFLD(2).
Therapeutic modalities to improve of prevent MAFLD and/or liver fibrosis in general are insufficient, and current interventional strategies are mainly focused on lowering cardiovascular risk. These interventions mainly involve lipid lowering agents, antidiabetic drugs and antihypertensives(3). The role for antiplatelet therapy in cardiovascular primary prevention remains controversial, with potential benefits limited by an increased bleeding risk(4). There is however increasing evidence that supports the use of antiplatelet therapy as primary prevention in high risk cases, such as in patients with type 2 diabetes and MAFLD, provided that the risk of bleeding is low(5-7).
Even though prophylactic antiplatelet therapy might thus be indicated in a high risk patient population with MAFLD, and is even associated with lower risk for progression to advanced fibrosis with time(8,9), its* efficacy in patients with MAFLD has yet to be determined. Chronic liver disease, including MAFLD, is associated with complex changes of the haemostatic system, such as decreased coagulation factors and fibrinolysis, but also thrombocytopaenia and altered platelet function(10,11). Data on the effect of this altered haemostasis on the potency of antiplatelet drugs is however lacking. Given that current guidelines do not take the altered haemostasis in patients with MAFLD into account, the objective of this study is therefore to evaluate the in vitro potency of clinically used antiplatelet drugs in these specific patients.

1. Ong JP, Younossi ZM. Epidemiology and Natural History of NAFLD and NASH. Clin Liver Dis. 2007;11(1):1-16.
2. Targher G, Byrne CD, Lonardo A, Zoppini G, Barbui C. Non-alcoholic fatty liver disease and risk of incident cardiovascular disease: A meta-analysis. J Hepatol. 2016;65(3):589-600.
3. Tana C, Ballestri S, Ricci F, Di Vincenzo A, Ticinesi A, Gallina S, et al. Cardiovascular risk in non-alcoholic fatty liver disease: Mechanisms and therapeutic implications. Int J Environ Res Public Health. 2019;16(17):1-19.
4. Zheng SL, Roddick AJ. Association of Aspirin Use for Primary Prevention with Cardiovascular Events and Bleeding Events: A Systematic Review and Meta-analysis. JAMA - J Am Med Assoc. 2019;321(3):277-87.
5. Aimo A, De Caterina R. Aspirin for primary prevention of cardiovascular disease: Advice for a decisional strategy based on risk stratification. Anatol J Cardiol. 2020 Jan;23(2):70-8.
6. Niederseer D, Wernly B, Aigner E, Stickel F, Datz C. NAFLD and Cardiovascular Diseases: Epidemiological, Mechanistic and Therapeutic Considerations. J Clin Med. 2021;10(3):467.
7. Liu M, Zhuang X, Chen X, Zhang S, Yang D, Zhong X, et al. Antiplatelet strategy in primary and secondary prevention of cardiovascular disease in patients with type 2 diabetes mellitus: A perspective from the guideline appraisal. J Diabetes Investig. 2021;12(1):99-108.
8. Schwarzkopf K, Bojunga J, Rüschenbaum S, Martinez Y, Mücke MM, Seeger F, et al. Use of Antiplatelet Agents Is Inversely Associated With Liver Fibrosis in Patients With Cardiovascular Disease. Hepatol Commun. 2018;2(12):1601-9.
9. Simon TG, Henson J, Osganian S, Masia R, Chan AT, Chung RT, et al. Daily Aspirin Use Associated With Reduced Risk For Fibrosis Progression In Patients With Nonalcoholic Fatty Liver Disease. Clin Gastroenterol Hepatol. 2019;17(13):2776-2784.e4.
10. Lisman T, Leebeek FWG, De Groot PG. Haemostatic abnormalities in patients with liver disease. J Hepatol. 2002;37(2):280-7.
11. Lisman T, Porte RJ. Platelet function in patients with cirrhosis. J Hepatol. 2012;56(4):993-4.

Study objective

To compare the in vitro potency of commonly used antiplatelet drugs in the blood of patients with various stages of fibrosis due to MAFLD, compared to that in blood of individuals without underlying liver disease.

Study design

This study is a prospective cross-sectional study. Patients with various stages of Metabolic dysfunction Associated Fatty Liver Disease will be recruited at the outpatient clinics or whilst admitted to University Medical Center Groningen. Additionally, healthy controls will be recruited.

Study burden and risks

There are no expected adverse events or serious adverse events associated with participation in this study. Minor bruising or discomfort at the site of venepuncture might occur. The amount of blood taken from participants is 27 mL, which will not harm the participants in any way.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Inclusion criteria study groups:
• >= 18 years of age
• Signed informed consent
• Some degree of liver steatosis and fibrosis (FibroScan F1-F4) with or without

diagnosis of diabetes mellitus

Inclusion criteria control group:
• >= 18 years of age
• Signed informed consent

Exclusion criteria

• Underlying liver disease with other aetiology than Metabolic dysfunction Associated Fatty Liver Disease
• Use of anti-platelet (salicylates, P2Y12 inhibitors, dipyridamole) or anti-hemostatic (heparins, vitamin K antagonists, direct oral anticoagulants) drugs
• Use of Non-Steroid Anti-Inflammatory Drugs 4 days prior to inclusion
• Documented history of hereditary thrombophilia or haemophilia
• Current malignancy
• Pregnancy
• Pre-existing immunosuppressive status (HIV positivity, previous solid organ transplant)
• Transfusion of blood products 7 days prior to inclusion
• Not willing to be notified of FibroScan results

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2022
Enrollment:	160

Type:	Actual

Ethics review

Approved WMO Date:	08-11-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL77056.042.21