Observational Study

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# Extubation in neurocritical care patients: the ENIO international prospective study

## Abstract

**Purpose:**Neurocritical care patients receive prolonged invasive mechanical ventilation (IMV), but there is poor specific information in this high-risk population about the liberation strategies of invasive mechanical ventilation.

**Methods:**ENIO is an international, prospective observational study, in 73 intensive care units (ICUs) in 18 countries from 2018 to 2020. Neurocritical care patients with a Glasgow Coma Score (GCS) ≤ 12, receiving IMV ≥ 24 h, undergoing extubation attempt or tracheostomy were included. The primary endpoint was extubation failure by day 5. An extubation success prediction score was created, with 2/3 of patients randomly allocated to the training cohort and 1/3 to the validation cohort. Secondary endpoints were the duration of IMV and in-ICU mortality.

**Results:**1512 patients were included. Among the 1193 (78.9%) patients who underwent an extubation attempt, 231 (19.4%) failures were recorded. The score for successful extubation prediction retained 20 variables as independent predictors. The area under the curve (AUC) in the training cohort was 0.79 95% confidence interval (CI95) [0.71-0.87] and 0.71 CI95 [0.61-0.81] in the validation cohort. Patients with extubation failure displayed a longer IMV duration (14 [7-21] vs 6 [3-11] days) and a higher in-ICU mortality rate (8.7% vs 2.4%). Three hundred and nineteen (21.1%) patients underwent tracheostomy without extubation attempt. Patients with direct tracheostomy displayed a longer duration of IMV and higher in-ICU mortality than patients with an extubation attempt (success and failure).

**Conclusions:**In neurocritical care patients, extubation failure is high and is associated with unfavourable outcomes. A score could predict extubation success in multiple settings. However, it will be mandatory to validate our findings in another prospective independent cohort.

**Keywords:**Brain injury; Extubation; Intra-cranial haemorrhage; Tracheostomy; Traumatic brain injury.

Crit Care Med. 2022 Dec 1;50(12):e814-e816. doi: 10.1097/CCM.0000000000005697. Epub 2022 Nov 17.

# The authors reply

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No abstract available

Editorial

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# Genomic medicine in hepatology: Towards personalized medicine in obesity and chronic liver disease

**Free article**

No abstract available

Stroke. 2022 Nov;53(11):e479-e480. doi: 10.1161/STROKEAHA.122.039102. Epub 2022 Aug 24.

# Bilateral Earlobe Crease (Frank's Sign) and Multifocal Vascular Disease

No abstract available

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# What do we know about nutrient-based strategies targeting molecular mechanisms associated with obesity-related fatty liver disease?

Obesity is a risk factor for developing nonalcoholic fatty liver disease (NAFLD), and the associated molecular mechanisms could be targeted with nutrient-based strategies. Therefore, it is necessary to review the current mechanisms to propose further treatments. Obesity facilitates the onset of insulin resistance, lipidic abnormalities, hepatic fat accumulation, lipid peroxidation, mitochondrial dysfunction, excessive reactive oxygen species (ROS) production, and inflammation, all related to further steatosis progression and fibrosis. Microbiota alterations can also influence liver disease by the translocation of pathogenic bacteria, energy extraction from short chain fatty acids (SCFAs), intestinal suppression of the expression of fasting-induced adipose factor (FIAF), reduction of bile acids, and altered choline metabolism. There are also genetic polymorphisms in metabolic proteins that predispose to a higher risk of liver diseases, such as those found in the patatin-like phospholipase domain-containing 3 (PNPLA3), transmembrane 6 superfamily member 2 (TM6SF2), membrane-bound O-acyltransferase domain-containing 7 (MBOAT7) or also known as lysophosphatidylinositol acyltransferase 1 (LPIAT1), transmembrane channel-like 4 genes (TMC4), fat mass and obesity-associated protein (FTO), the b Klotho (KLB) and carboxylesterase (CES1). No clear dietary guidelines target all mechanisms related to NAFLD development and progression. However, energy and carbohydrate intake restriction, regular physical exercise, supplementation of antioxidants, and restoration of gut microbiota seem to have beneficial effects on the new proposed features of NAFLD.

**Keywords:**Diet; Insulin resistance; Metabolic syndrome; Nutrients; Nutrigenomics.

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# A randomized clinical trial of lipid metabolism modulation with fenofibrate for acute coronavirus disease 2019

## Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cytotoxicity may involve inhibition of peroxisome proliferator-activated receptor alpha. Fenofibrate activates peroxisome proliferator-activated receptor alpha and inhibits SARS-CoV-2 replication in vitro. Whether fenofibrate can be used to treat coronavirus disease 2019 (COVID-19) infection in humans remains unknown. Here, we randomly assigned inpatients and outpatients with COVID-19 within 14 d of symptom onset to 145 mg of oral fenofibrate nanocrystal formulation versus placebo for 10 d, in a double-blinded fashion. The primary endpoint was a severity score whereby participants were ranked across hierarchical tiers incorporating time to death, mechanical ventilation duration, oxygenation, hospitalization and symptom severity and duration. In total, 701 participants were randomized to fenofibrate (n = 351) or placebo (n = 350). The mean age of participants was 49 ± 16 years, 330 (47%) were female, mean body mass index was 28 ± 6 kg/m2 and 102 (15%) had diabetes. Death occurred in 41 participants. Compared with placebo, fenofibrate had no effect on the primary endpoint. The median (interquartile range) rank in the placebo arm was 347 (172, 453) versus 345 (175, 453) in the fenofibrate arm (P = 0.819). There was no difference in secondary and exploratory endpoints, including all-cause death, across arms. There were 61 (17%) adverse events in the placebo arm compared with 46 (13%) in the fenofibrate arm, with slightly higher incidence of gastrointestinal side effects in the fenofibrate group. Overall, among patients with COVID-19, fenofibrate has no significant effect on various clinically relevant outcomes ( [NCT04517396](http://clinicaltrials.gov/show/NCT04517396) ).

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# Whole-Exome Sequencing identified Olfactory Receptor genes as a key contributor to extreme obesity with progression to nonalcoholic steatohepatitis in Mexican patients: Olfactory receptor genes in obese NASH patients

## Abstract

**Introduction and objectives:**Obesity is a global health problem that triggers fat liver accumulation. The prevalence of obesity and the risk of non-alcoholic steatohepatitis (NASH) among young obese Mexican is high. Furthermore, genetic predisposition is a key factor in weight gain and disrupts metabolism. Herein, we used Whole-Exome Sequencing to identify potential causal variants and the biological processes that lead to obesity with progression to NASH among Mexican patients.

**Materials and methods:**Whole-Exome Sequencing was performed in nine obese patients with NASH diagnosis with a BMI ≥30 kg/m<sup>2</sup> and one control (BMI=24.2 kg/m<sup>2</sup>) by using the Ion S5<sup>TM</sup> platform. Genetic variants were determined by Ion Reporter software. Enriched GO biological set genes were identified by the WebGestalt tool. Genetic variants within ≥2 obese NASH patients and having scores of SIFT 0.0-0.05 and Polyphen 0.85-1.0 were categorized as pathogenic.

**Results:**A total of 1359 variants with a probable pathogenic effect were determined in obese patients with NASH diagnosis. After several filtering steps, the most frequent pathogenic variants found were rs25640-HSD17B4, rs8105737-OR1I1, rs998544-OR5R1, and rs4916685, rs10037067, and rs2366926 in ADGRV1. Notably, the primary biological processes affected by these pathogenic variants were the sensory perception and detection of chemical stimulus pathways in which the olfactory receptor gene family was the most enriched.

**Conclusions:**Variants in the olfactory receptor genes were highly enriched in Mexican obese patients that progress to NASH and could be potential targets of association studies.

**Keywords:**Extreme obesity; HSD17B4; NASH; Whole-exome sequencing; olfactory receptors.

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# Association of - 717 A > G (rs2794521) CRP polymorphism with high cardiovascular risk by C-reactive protein in systemic lupus erythematosus patients

## Abstract

**Introduction:**Systemic lupus erythematosus (SLE) is an autoimmune disease where genetic factors have been related to SLE susceptibility and disease severity. CRP polymorphisms have been associated with high C-reactive protein (CRP) serum levels, cardiovascular disease (CVD), and high clinical disease activity in SLE patients; however, the evidence is still inconclusive.

**Objective:**This study was aimed to assess the association of the - 717 A > G, - 409 G > A, + 1444 C > T, and + 1846 C > T CRP polymorphisms with genetic susceptibility, clinical disease activity, and CVD risk in Mexican-mestizo SLE patients.

**Methods:**A comparative cross-sectional study was conducted on 369 unrelated women: 183 with SLE according to the 1997 SLE-ACR criteria and 186 healthy subjects (HS). The clinical disease activity was assessed by the Mex-SLEDAI score; CRP and lipid profile were quantified by turbidimetry and colorimetric-enzymatic assays, respectively. The CRP polymorphisms genotyping was carried out by allelic discrimination.

**Results:**SLE patients with - 717 AA genotype had higher CRP serum levels than SLE carriers of AG and GG genotypes (AA = 5 mg/L vs. AG = 3.2 mg/L vs. GG = 2.4 mg/L; p = 0.01), and the AA genotype was associated with high CVD risk by CRP in SLE patients (OR = 3; CI: 1.2-7.6; p < 0.01).

**Conclusions:**The - 717 A > G CRP polymorphism is a risk factor for high CRP levels and high CVD risk in Mexican-mestizo SLE patients. Key Points • Cardiovascular disease is one of the major causes of death in SLE patients due to the higher prevalence of traditional and non-traditional cardiovascular risk factors. • C-reactive protein is a liver-derived acute-phase protein suggested as one powerful independent risk predictor factor for cardiovascular disease. • Single nucleotide polymorphisms in CRP have been suggested as genetic susceptibility factors that could modify the SLE pathophysiology outcomes. • Mexican-mestizo SLE patients carrying the -717 A>G CRP AA genotype had 3-fold high cardiovascular disease risk than SLE patients with AG or GG genotypes.

**Keywords:**C-reactive protein; CRP polymorphism; Cardiovascular risk; Systemic lupus erythematosus.