

0022

**Metabolic complications of highly active antiretroviral therapy in adult HIV-infected patients with heart failure: A 7-year prospective cohort study**

Kevin Sheng-Kai Ma

*Center of Global Health, Perelman School of Medicine, University of Pennsylvania***Abstract**

Long-term metabolic complications of highly active antiretroviral therapy (HAART) have been reported in general human immunodeficiency virus (HIV)-infected patients. We sought to determine whether patients with pre-existing heart failure (HF) using HAART are at high risk of subsequent metabolic syndrome (MetS) and cardiovascular complications, compared with HIV-infected patients without pre-existing HF. This is a prospective cohort study of 5 years of follow-up, in which 172 HIV-infected patients were recruited for the comparison of Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D), a cardiovascular disease (CVD) risk score for HAART, and lab data, between HF patients and age- and gender-matched non-HF patients. HAART was effective for both HIV-infected patients with or without HF, with a similar plasma viral load (PVL) of HIV ( $r=0.001$ ,  $P=0.69$ ) and CD4 count for HF patients ( $r=-0.06$ ,  $P=0.48$ ). HAART did not increase the risk of CVDs for patients with HF, with comparable D:A:D (R) ( $r=0.002$ ,  $P=0.97$ ) and D:A:D (F) ( $r=0.04$ ,  $P=0.62$ ) scores. HF patients presented with higher risk of T2DM ( $r = 0.24$ ,  $P=0.01$ ), increased total cholesterol (CHO) ( $r=0.23$ ,  $P=0.006$ ), compared to baseline. Moreover, patients with HF presented with significantly higher risk of increased LDL ( $r=0.18$ ,  $P=0.04$ ) and increased uric acid ( $r=0.35$ ,  $P=0.004$ ) in HF patients. In conclusion, HAART was equally effective for HF and non-HF patients, and did not result in more subsequent CVDs or renal toxicities, when compared with patients without HF; however, increased risk of metabolic complications, including T2DM, and increased levels of CHO, LDL, and uric acid, during follow-ups, were present.

**Keywords:** Heart failure, metabolic syndrome, highly active antiretroviral therapy, human immunodeficiency virus

**Abbreviations:** Highly active antiretroviral therapy, HAART; human immunodeficiency virus, HIV; Data Collection on Adverse Effects of Anti-HIV Drugs, D:A:D; heart failure, HF; type 2 diabetes mellitus, T2DM.

**Funding and Conflicts of Interest**

The authors reported no conflict of interests.

doi:10.1016/j.metabol.2021.154985

0024

**Aldose Reductase inhibition by AT-001 Prevents Diabetic Cardiomyopathy Via Reducing Myocardial Fatty Acid Oxidation Rates**

Keshav Gopal<sup>a,b</sup>, Qutuba G. Karwi<sup>a</sup>, S. Amirhossein Tabatabaei-Dakhili<sup>a,b</sup>, Cory S. Wagg<sup>a</sup>, Riccardo Perfetti<sup>c</sup>, Ravichandran Ramasamy<sup>d</sup>, John R. Ussher<sup>a,b</sup>, Gary D. Lopaschuk<sup>a</sup>

<sup>a</sup>Cardiovascular Research Centre, University of Alberta, Edmonton, Canada

<sup>b</sup>Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Canada

<sup>c</sup>Applied Therapeutics, New York, NY

<sup>d</sup>Diabetes Research Program, New York University, New York, NY

**Abstract**

Cardiovascular diseases, including diabetic cardiomyopathy (DbCM), are major causes of death in people with type 2 diabetes (T2D).

Several studies have suggested that aldose reductase (AR), an enzyme activated under hyperglycemic conditions, can alter cardiac energy metabolism and deteriorate cardiac function. We investigated whether inhibition of AR, using a next-generation inhibitor AT-001, can mitigate DbCM by modulating cardiac energy metabolism. Human AR overexpressing transgenic (hAR-Tg) and control C57BL/6J mice were subjected to experimental T2D (high-fat diet [60% kcal from lard] for 10-wks with a single intraperitoneal streptozotocin injection of 75 mg/kg at 4-wks). AR inhibition by AT-001 treatment (40 mg/kg/daily) for 3-wks significantly improved cardiac energetics in hAR-Tg mice with T2D. AT-001 treated mice exhibited significantly decreased cardiac fatty acid oxidation rates compared to the vehicle-treated mice ( $608 \pm 66$  vs  $1200 \pm 176$  nmol.min<sup>-1</sup>.g dry wt<sup>-1</sup>, respectively), which was accompanied by a decrease in cardiac oxygen consumption in AT-001 treated mice ( $44 \pm 8$  vs  $61 \pm 11$   $\mu$ mol.min<sup>-1</sup>.g dry wt<sup>-1</sup>). Furthermore, treatment with AT-001 prevented cardiac structural and functional abnormalities present in DbCM, including diastolic dysfunction as reflected by an increase in the tissue Doppler E'/A' ratio ( $1.6 \pm 0.12$  vs  $1.38 \pm 0.1$ ) and decrease in E/E' ratio ( $26.6 \pm 1$  vs  $33 \pm 4.9$ ). AT-001 treatment also prevented cardiac hypertrophy as reflected by a decrease in LV mass ( $90.5 \pm 2.2$  vs  $125 \pm 14$  mg). We conclude that AT-001 prevents cardiac structural and functional abnormalities in DbCM, and normalizes cardiac energetics by shifting cardiac metabolism towards a non-diabetic metabolic state.

**Keywords:** Aldose Reductase, Aldose Reductase Inhibitors, Diabetic Cardiomyopathy, and Type 2 Diabetes

**Abbreviations:** DbCM: Diabetic Cardiomyopathy, T2D: Type 2 Diabetes, AR: Aldose Reductase, hAR-Tg: AR overexpressing transgenic

**Funding and Conflicts of Interest**

This work was supported in part by a grant from Applied Therapeutics. Riccardo Perfetti is a shareholder and an employee of Applied Therapeutics.

doi:10.1016/j.metabol.2021.154986

0025

**Cardio-metabolic factors associated to mortality in patients with COVID-19**

Camey Eduardo, Arauz Guillermo, Cárcamo Alejandra, Celis Grecia

*Instituto Guatemalteco de Seguridad Social*

**Abstract**

**Background.** In March 2020, Guatemala reported the first case of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Epidemiological and clinical characteristics of patients with COVID-19 have been reported, but cardio-metabolic risk factors for mortality have not been correctly described. **Objective.** To evaluate the independent cardio-metabolic risk factors associated with mortality at 28 days after hospital admission in patients with a diagnosis of COVID-19 admitted to the Critical Care Unit of the Guatemalan Institute of Social Security, Guatemala. **Population and methods.** Two hundred patients admitted to the Critical Care Unit of the Guatemalan Social Security Institute, between May 1, 2021, and June 30, 2021, were included. Different factors were analyzed in bivariate analysis, and only those variables in which an association was found were included in a multivariate analysis of binary logistic regression. **Results.** The variables included in the binary logistic regression analysis were age, arterial hypertension, glycosylated hemoglobin, erythrocyte sedimentation rate, glycemic variability, fibrinogen, D-

dimer, Interleukin-6 (IL-6), vasopressor use. It was documented that the model predicts between 28-38% of the variability of the data according to Cox and Snell's and Nagelkerke's R-squared. Subsequently, an analysis was performed using the area under the ROC curve (area=0.82; 95%CI= 0.76-0.88; p=<0.05). Conclusions. Despite the variables studied, further studies are required to determine other factors that influence patient prognosis.

#### Funding and Conflicts of Interest

None

doi:10.1016/j.metabol.2021.154987

#### 0026

### Trends in Hyperinsulinemia Among U.S. Adults without Diabetes: A Joinpoint Analysis

James R. Churilla, Tammie M. Johnson, Michael R. Richardson, Ralph G. Cosentino

University of North Florida

#### Abstract

Hyperinsulinemia is associated with various chronic diseases and cardiovascular disease risk factors. Investigating changes in hyperinsulinemia over time is important due to its association with pervasive clinical outcomes. **PURPOSE:** Estimate the prevalence and examine trends in hyperinsulinemia among euglycemic U.S. adults between 1999 and 2018. **METHODS:** Weighted data from adults  $\geq 20$  years of age from the 1999-2018 cycles of the National Health and Nutrition Examination Survey (NHANES) were analyzed. Exclusion criteria included pregnancy, history of diabetes or blood glucose  $\geq 126$  mg/dL, and taking diabetes medications (n=23,447). The 20-year trend for hyperinsulinemia (defined as the 75th percentile of log-transformed insulin) was nonlinear. The 2009-2010 cycle was identified as a joinpoint, creating two segments – 1999/2000 to 2009/2010 and 2009/2010 to 2017/2018. Each segment was examined for significant trends. **RESULTS:** Overall, an initial rise in hyperinsulinemia was followed by a drop and plateau. The age-adjusted prevalence of hyperinsulinemia increased by ~18% in the study population between 1999/2000 and 2017/2018 (21.5% to 25.3%, P for trend 0.0034). The age-adjusted prevalence of hyperinsulinemia increased by ~65% in the first joinpoint segment (21.5% to 35.4%, P for trend <0.0001). The prevalence of hyperinsulinemia decreased ~29% in the second joinpoint segment, but not significantly (35.4% to 25.3%, P for trend=0.10). **CONCLUSION:** Hyperinsulinemia rates in U.S. adults without diabetes significantly increased at the turn of the century, however, the more recent decline and steadying of rates may be due to improved medication regimens and lifestyle modifications. Both warrant further investigation in this population.

**Keywords:** Insulin; Lifestyle; NHANES

**Abbreviations:** mg/dL=milligrams per deciliter; NHANES=National Health and Nutrition Examination Survey; U.S.=United States

#### Funding and Conflicts of Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors  
No conflicts of interest to report

doi:10.1016/j.metabol.2021.154988

#### 0027

### Leveraging Automated Machine Learning to provide NAFLD screening diagnosis: Proposed machine learning models

Ali Haider Shah<sup>a,\*</sup>, Ali Haider Bangash<sup>a,b</sup>, Arshiya Fatima<sup>a</sup>, Saiqa Zehra<sup>a</sup>, Syed Mohammad Mehmood Abbas<sup>a</sup>, Syed Mohammad Qasim Shah<sup>a</sup>, Muhammad Ashraf<sup>c</sup>, Aliya Ali<sup>a</sup>, Adil Baloch<sup>a</sup>, Ayesha Khalid Khan<sup>a</sup>, Hashir Fahim Khawaja<sup>a</sup>, Noor Ayesha<sup>a</sup>, Saleha Yurf Asghar<sup>a</sup>, Tatheer Zahra<sup>d</sup>

<sup>a</sup>STMU Shifa College of Medicine, Islamabad, Pakistan

<sup>b</sup>Member, Working Group 3, COST Action Evidence-Based REsearch (EVBRES)

<sup>c</sup>Rawalpindi Medical College, Rawalpindi Medical University, Rawalpindi, Pakistan

<sup>d</sup>Associate Professor of Anatomy, STMU Shifa College of Medicine, Islamabad, Pakistan

\*Corresponding authors.

#### Abstract

**Background and Objective:** Non-alcoholic fatty liver disease (NAFLD) is reported to be the only hepatic ailment increasing in its prevalence concurrently with both; obesity & Type 2 Diabetes Mellitus. Abdominal ultrasonography is done for NAFLD screening diagnosis which has a high monetary cost associated with it. • In the wake of a massive strain on global health resources due to COVID-19 pandemic, NAFLD is bound to be neglected and shelved. Machine learning is explored, here, to propose screening-diagnostic tools for NAFLD that can be easily deployed without the requirement of substantial resources and can provide instantaneous screening-diagnosis predictive results.

**Methods:** The study takes in data from Huang BX et al. : 4053 subjects, 2436 men and 1617 women between 20 and 88 years of age, after excluding those patients that had a history of co-morbid conditions as well as those with a lack of hepatic ultrasonography data. The Graif's criteria was adopted to diagnose Fatty liver disease on ultrasonography. Mljar , the current state-of-the-art automated ML zero-code machine learning web platform, was adopted with a 'homogenous' approach for the development of the models vis-à-vis the preprocessing & tuning protocols as well as system specifications so as to keep the model development bias to a minimum. The discriminative ability of the models were the primary outcome variables. The 'Area under the receiver operating curve' (AUROC) analysis was adopted to measure that ability.

**Results:** All 8 of the algorithms, trained in accordance with the aforementioned Homogenous Development Framework, came out to have good discriminating ability to designate the dichotomous variable of interest. Random Forest came out to have the highest discriminating ability with a computation time of minutes 9 seconds. Out of the proposed models, K-Nearest Neighbor had the least AUC but a considerably less computation time of only 6 seconds.

**Conclusion:** Our proposed models are the very first effort, to the best of our knowledge, to leverage the current state-of-the-art for autoML to develop machine learning models that are trained to have a good discriminating ability to predict NAFLD using only anthropometric measures. The proposed models neither require costly analysis so that variables, such as ultrasonographic signals, may be fed into them for training nor do they require considerably high computation time & resources to be deployed. A study comparing the presented models' predicted diagnosis with an abdominal ultrasound diagnosis for NAFLD, the predictions subsequently assessed against hepatic biopsy, is proposed to be in order to explore the presented models' potential to replace abdominal ultrasound as a cost-effective screening diagnostic modality for NAFLD.

**Keywords:** Non-alcoholic fatty liver disease, Machine learning, prediction, abdominal ultrasonography, Diabetes mellitus