

## REFERENCES

- [1] Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2224-60.
- [2] Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:766-81.
- [3] Poobalan A, Aucott L. Obesity Among Young Adults in Developing Countries: A Systematic Overview. Current Obesity Reports 2016;5:2-13.
- [4] Dietz WH. Obesity and excessive weight gain in young adults: New targets for prevention. JAMA 2017;318:241-42.
- [5] Aekplakorn W, Mo-Suwan L. Prevalence of obesity in Thailand. Obes Rev 2009;10:589-92.
- [6] Fan JG, Kim SU, Wong VW. New trends on obesity and NAFLD in Asia. J Hepatol 2017;67:862-73.
- [7] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64:73-84.
- [8] Mrad RA, Merjaneh N, Mubarak G, Lopez R, Zein NN, Alkhouri N. The increasing burden of nonalcoholic fatty liver disease among young adults in the United States: A growing epidemic. Hepatology 2016;64:1386-7.

- [9] Doycheva I, Watt KD, Alkhouri N. Nonalcoholic fatty liver disease in adolescents and young adults: The next frontier in the epidemic. *Hepatology* 2017;65:2100-09[10] Heilbronn L, Smith SR, Ravussin E. Failure of fat cell proliferation, mitochondrial function and fat oxidation results in ectopic fat storage, insulin resistance and type II diabetes mellitus. *Int J Obes Relat Metab Disord* 2004;28 Suppl 4:S12-21.
- [11] Centis E, Marzocchi R, Di Domizio S, Ciaravella MF, Marchesini G. The effect of lifestyle changes in non-alcoholic fatty liver disease. *Dig Dis* 2010;28:267-73.
- [12] Zelber-Sagi S, Godos J, Salomone F. Lifestyle changes for the treatment of nonalcoholic fatty liver disease: a review of observational studies and intervention trials. *Therap Adv Gastroenterol* 2016;9:392-407.
- [13] Zelber-Sagi S, Lotan R, Shlomai A, Webb M, Harrari G, Buch A, et al. Predictors for incidence and remission of NAFLD in the general population during a seven-year prospective follow-up. *J Hepatol* 2012;56:1145-51.
- [14] Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, Torres-Gonzalez A, Gra-Oramas B, Gonzalez-Fabian L, et al. Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis. *Gastroenterology* 2015;149:367-78.e5.
- [15] Bambha K, Belt P, Abraham M, Wilson LA, Pabst M, Ferrell L, et al. Ethnicity and nonalcoholic fatty liver disease. *Hepatology* 2012;55:769-80.
- [16] Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Contreras M, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology* 2011;140:124-31.
- [17] Ballestri S, Nascimbeni F, Baldelli E, Marrazzo A, Romagnoli D, Lonardo A. NAFLD as a Sexual Dimorphic Disease: Role of Gender and Reproductive Status in the Development and Progression of Nonalcoholic

Fatty Liver Disease and Inherent Cardiovascular Risk. *Adv Ther*  
2017;34:1291-326.

- [18] Lazo M, Hernaez R, Eberhardt MS, Bonekamp S, Kamel I, Guallar E, et al. Prevalence of nonalcoholic fatty liver disease in the United States: the Third National Health and Nutrition Examination Survey, 1988-1994. *Am J Epidemiol* 2013;178:38-45.
- [19] Schwimmer JB, Celedon MA, Lavine JE, Salem R, Campbell N, Schork NJ, et al. Heritability of nonalcoholic fatty liver disease. *Gastroenterology* 2009;136:1585-92.
- [20] Glass CK, Olefsky JM. Inflammation and lipid signaling in the etiology of insulin resistance. *Cell Metab* 2012;15:635-45.
- [21] Kitade H, Chen G, Ni Y, Ota T. Nonalcoholic Fatty Liver Disease and Insulin Resistance: New Insights and Potential New Treatments. *Nutrients* 2017;9.
- [22] Magkos F, Mohammed BS, Mittendorfer B. Effect of obesity on the plasma lipoprotein subclass profile in normoglycemic and normolipidemic men and women. *Int J Obes (Lond)* 2008;32:1655-64.
- [23] LeRoith D. Dyslipidemia and glucose dysregulation in overweight and obese patients. *Clin Cornerstone* 2007;8:38-52.
- [24] Wang L, Folsom AR, Zheng ZJ, Pankow JS, Eckfeldt JH. Plasma fatty acid composition and incidence of diabetes in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr* 2003;78:91-8.
- [25] Johnson NA, Walton DW, Sachinwalla T, Thompson CH, Smith K, Ruell PA, et al. Noninvasive assessment of hepatic lipid composition: Advancing understanding and management of fatty liver disorders. *Hepatology* 2008;47:1513-23.

- [26] Nielsen S, Guo Z, Johnson CM, Hensrud DD, Jensen MD. Splanchnic lipolysis in human obesity. *J Clin Invest* 2004;113:1582-8.
- [27] Fabbrini E, Sullivan S, Klein S. Obesity and Nonalcoholic Fatty Liver Disease: Biochemical, Metabolic and Clinical Implications. *Hepatology* (Baltimore, Md) 2010;51:679-89.
- [28] Loomis AK, Kabadi S, Preiss D, Hyde C, Bonato V, St. Louis M, et al. Body Mass Index and Risk of Nonalcoholic Fatty Liver Disease: Two Electronic Health Record Prospective Studies. *The Journal of Clinical Endocrinology and Metabolism* 2016;101:945-52.
- [29] Rao W, Su Y, Yang G, Ma Y, Liu R, Zhang S, et al. Cross-Sectional Associations between Body Mass Index and Hyperlipidemia among Adults in Northeastern China. *Int J Environ Res Public Health* 2016;13:516.
- [30] Karanjia RN, Crossey MME, Cox IJ, Fye HKS, Njie R, Goldin RD, et al. Hepatic steatosis and fibrosis: Non-invasive assessment. *World J Gastroenterol* 2016;22:9880-97.
- [31] Ratziu V, Charlotte F, Heurtier A, Gombert S, Giral P, Bruckert E, et al. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. *Gastroenterology* 2005;128:1898-906.
- [32] Pola A, Sadanathan SA, Yaligar J, Nagarajan V, Han W, Kuchel PW, et al. Skeletal muscle lipid metabolism studied by advanced magnetic resonance spectroscopy. *Prog Nucl Magn Reson Spectrosc* 2012;65:66-76.
- [33] Hamilton G, Yokoo T, Bydder M, Cruite I, Schroeder ME, Sirlin CB, et al. In vivo characterization of the liver fat (<sup>1</sup>H MR spectrum. *NMR Biomed* 2011;24:784-90.
- [34] Lee SS, Park SH. Radiologic evaluation of nonalcoholic fatty liver disease. *World Journal of Gastroenterology : WJG* 2014;20:7392-402.

- [35] Bohte AE, van Werven JR, Bipat S, Stoker J. The diagnostic accuracy of US, CT, MRI and 1H-MRS for the evaluation of hepatic steatosis compared with liver biopsy: a meta-analysis. *Eur Radiol* 2011;21:87-97.
- [36] Georgoff P, Thomasson D, Louie A, Fleischman E, Dutcher L, Mani H, et al. Hydrogen-1 MR spectroscopy for measurement and diagnosis of hepatic steatosis. *AJR Am J Roentgenol* 2012;199:2-7.
- [37] Nicholson JK, Foxall PJ, Spraul M, Farrant RD, Lindon JC. 750 MHz 1H and 1H-13C NMR spectroscopy of human blood plasma. *Anal Chem* 1995;67:793-811.
- [38] Nicholson JK, O'Flynn MP, Sadler PJ, Macleod AF, Juul SM, Sonksen PH. Proton-nuclear-magnetic-resonance studies of serum, plasma and urine from fasting normal and diabetic subjects. *Biochem J* 1984;217:365-75.
- [39] Hanson AJ, Bayer-Carter JL, Green PS, Montine TJ, Wilkinson CW, Baker LD, et al. Effect of apolipoprotein E genotype and diet on apolipoprotein E lipidation and amyloid peptides: randomized clinical trial. *JAMA Neurol* 2013;70:972-80.
- [40] Elmsjo A, Rosqvist F, Engskog MK, Haglof J, Kullberg J, Iggman D, et al. NMR-based metabolic profiling in healthy individuals overfed different types of fat: links to changes in liver fat accumulation and lean tissue mass. *Nutr Diabetes* 2015;5:e182.
- [41] Gao H, Lu Q, Liu X, Cong H, Zhao L, Wang H, et al. Application of 1H NMR-based metabonomics in the study of metabolic profiling of human hepatocellular carcinoma and liver cirrhosis. *Cancer Sci* 2009;100:782-5.
- [42] Szczepaniak LS, Nurenberg P, Leonard D, Browning JD, Reingold JS, Grundy S, et al. Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. *Am J Physiol Endocrinol Metab* 2005;288:E462-8.

- [43] Naressi A, Couturier C, Devos JM, Janssen M, Mangeat C, Beer Rd, et al. Java-based graphical user interface for the MRUI quantitation package. Magnetic Resonance Materials in Physics, Biology and Medicine 2001;12:141-52.
- [44] Stefan D, Cesare FD, Andrasescu A, Popa E, Lazariev A, Vescovo E, et al. Quantitation of magnetic resonance spectroscopy signals: the jMRUI software package. Measurement Science and Technology 2009;20:104035.
- [45] Vanhamme L, van den Boogaart A, Van Huffel S. Improved method for accurate and efficient quantification of MRS data with use of prior knowledge. J Magn Reson 1997;129:35-43.
- [46] Longo R, Pollesello P, Ricci C, Masutti F, Kvam BJ, Bercich L, et al. Proton MR spectroscopy in quantitative in vivo determination of fat content in human liver steatosis. J Magn Reson Imaging 1995;5:281-5.
- [47] Martin SS, Blaha MJ, Elshazly MB, Toth PP, Kwiterovich PO, Blumenthal RS, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. JAMA 2013;310:2061-8.
- [48] Sathiyakumar V, Park J, Golozar A, Lazo M, Quispe R, Guallar E, et al. Fasting Versus Nonfasting and Low-Density Lipoprotein Cholesterol Accuracy. Circulation 2018;137:10-19.
- [49] Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.
- [50] Introduction: Standards of Medical Care in Diabetes—2018. Diabetes Care 2018;41:S1.
- [51] McKnight TR, Yoshihara HA, Sitole LJ, Martin JN, Steffens F, Meyer D. A combined chemometric and quantitative NMR analysis of HIV/AIDS serum

discloses metabolic alterations associated with disease status. Mol Biosyst 2014;10:2889-97.

- [52] Fages A, Duarte-Salles T, Stepien M, Ferrari P, Fedirko V, Pontoizeau C, et al. Metabolomic profiles of hepatocellular carcinoma in a European prospective cohort. BMC Med 2015;13:242.
- [53] Cali AM, De Oliveira AM, Kim H, Chen S, Reyes-Mugica M, Escalera S, et al. Glucose dysregulation and hepatic steatosis in obese adolescents: is there a link? Hepatology 2009;49:1896-903.
- [54] Corbin KD, Zeisel SH. Choline Metabolism Provides Novel Insights into Non-alcoholic Fatty Liver Disease and its Progression. Curr Opin Gastroenterol 2012;28:159-65.
- [55] Numminen K, Tervahartiala P, Halavaara J, Isoniemi H, Hockerstedt K. Non-invasive diagnosis of liver cirrhosis: magnetic resonance imaging presents special features. Scand J Gastroenterol 2005;40:76-82.
- [56] Hagstrom H, Stal P, Hultcrantz R, Hemmingsson T, Andreasson A. Overweight in late adolescence predicts development of severe liver disease later in life: A 39years follow-up study. J Hepatol 2016;65:363-8.
- [57] Kopelman P. Health risks associated with overweight and obesity. Obes Rev 2007;8 Suppl 1:13-7.
- [58] Schult A, Mehlig K, Bjorkelund C, Wallerstedt S, Kaczynski J. Waist-to-hip ratio but not body mass index predicts liver cirrhosis in women. Scand J Gastroenterol 2018;53:212-17.
- [59] Zheng RD, Chen ZR, Chen JN, Lu YH, Chen J. Role of Body Mass Index, Waist-to-Height and Waist-to-Hip Ratio in Prediction of Nonalcoholic Fatty Liver Disease. Gastroenterol Res Pract 2012;2012:362147.
- [60] VanWagner LB, Khan SS, Ning H, Siddique J, Lewis CE, Carr JJ, et al. Body mass index trajectories in young adulthood predict non-alcoholic fatty

liver disease in middle age: The CARDIA cohort study. Liver Int  
2018;38:706-14.

- [61] Bae JC, Cho YK, Lee WY, Seo HI, Rhee EJ, Park SE, et al. Impact of nonalcoholic fatty liver disease on insulin resistance in relation to HbA1c levels in nondiabetic subjects. Am J Gastroenterol 2010;105:2389-95.
- [62] Amor AJ, Pinyol M, Sola E, Catalan M, Cofan M, Herreras Z, et al. Relationship between noninvasive scores of nonalcoholic fatty liver disease and nuclear magnetic resonance lipoprotein abnormalities: A focus on atherogenic dyslipidemia. J Clin Lipidol 2017;11:551-61.e7.
- [63] Vance DE. Role of phosphatidylcholine biosynthesis in the regulation of lipoprotein homeostasis. Curr Opin Lipidol 2008;19:229-34.
- [64] Yao ZM, Vance DE. The active synthesis of phosphatidylcholine is required for very low density lipoprotein secretion from rat hepatocytes. J Biol Chem 1988;263:2998-3004.
- [65] Amathieu R, Nahon P, Triba M, Bouchemal N, Trinchet JC, Beaugrand M, et al. Metabolomic approach by <sup>1</sup>H NMR spectroscopy of serum for the assessment of chronic liver failure in patients with cirrhosis. J Proteome Res 2011;10:3239-45.
- [66] Newgard CB, An J, Bain JR, Muehlbauer MJ, Stevens RD, Lien LF, et al. A branched-chain amino acid-related metabolic signature that differentiates obese and lean humans and contributes to insulin resistance. Cell Metab 2009;9:311-26.