Calculations and Ratios on a Blood Chemistry

Dr. Bryan Walsh

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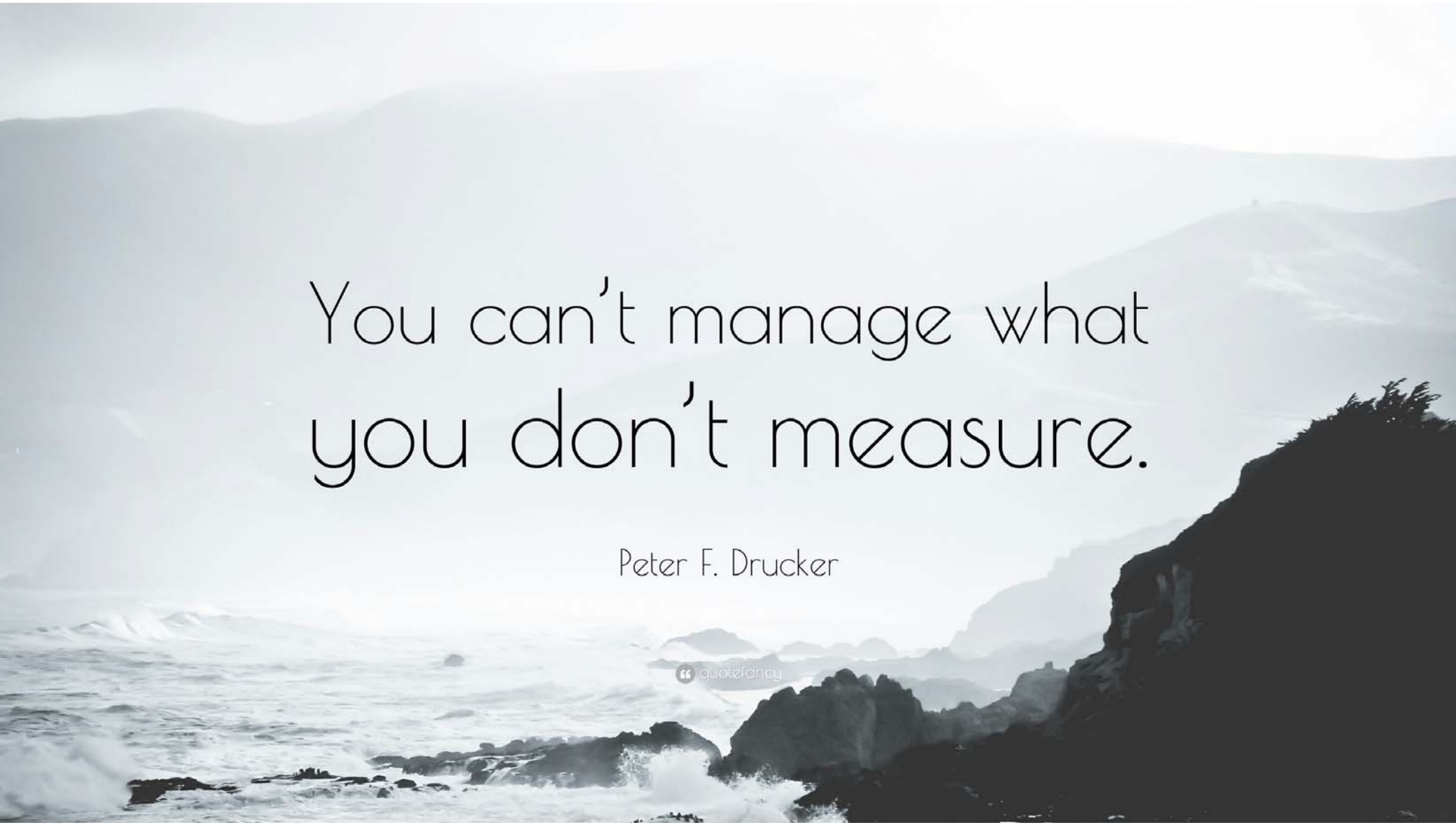
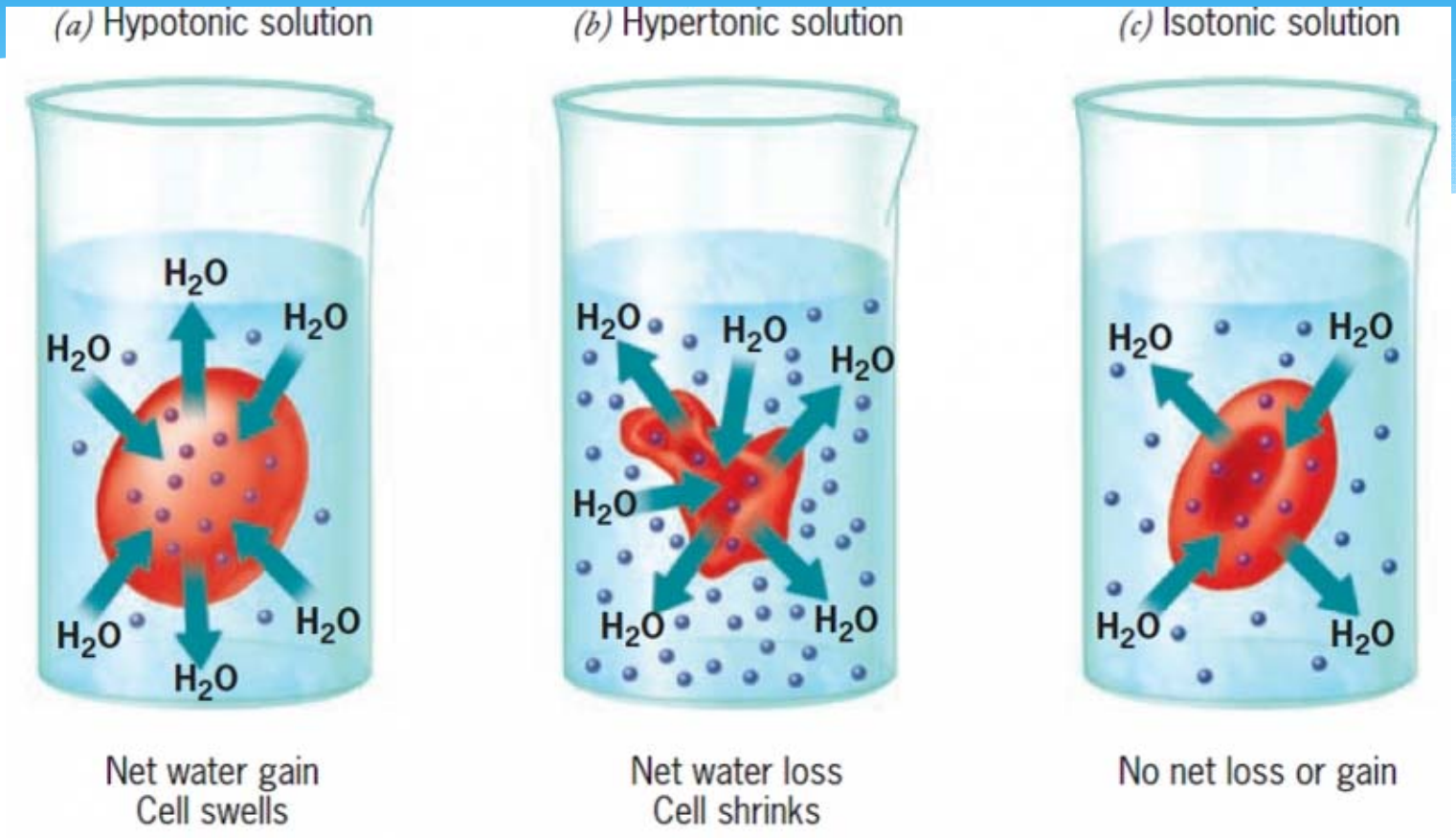

You can't manage what
you don't measure.
Peter F. Drucker
quotefancy

Overview

* Osmolarity
* Viscosity
* Fatty Liver
* Fibrosis
* N/L Ratio
* RBC Lifespan

Osmolarity


(a) Hypotonic solution
(b) Hypertonic solution
(c) Isotonic solution
H_2O
Net water gain
Cell swells
Net water loss
Cell shrinks
No net loss or gain

Osmolarity

* Suggested that serum osmolarity (extracellular fluid) reflects intracellular osmolarity

Osmolarity

Increased Osmolarity	Decreased Osmolarity
Hyperglycemia Hypernatremia (dehydration)	Hyponatremia (hypothyroidism, adrenal insufficiency)

Physiologic basis for understanding quantitative dehydration assessment[1–4]

Samuel N Cheuvront, Robert W Kenefick, Nisha Charkoudian, and Michael N Sawka

ABSTRACT

Dehydration (body water deficit) is a physiologic state that can have profound implications for human health and performance. Unfortunately, dehydration can be difficult to assess, and there is no single, universal gold standard for decision making. In this article, we review the physiologic basis for understanding quantitative dehydration assessment. We highlight how phenomenologic interpretations of dehydration depend critically on the type (dehydration compared with volume depletion) and magnitude (moderate compared with severe) of dehydration, which in turn influence the osmotic (plasma osmolality) and blood volume–dependent compensatory thresholds for antidiuretic and thirst responses. In particular, we review new findings regarding the biological variation in osmotic responses to dehydration and discuss how this variation can help provide a quantitative and clinically relevant link between the physiology and phenomenology of dehydration. Practical measures with empirical thresholds are provided as a starting point for improving the practice of dehydration assessment. *Am J Clin Nutr* 2013;97:455–62.

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INTRODUCTION

Dehydration (body water deficit) is a common physiologic state that can have profound implications for human health (1–7) and performance (8). Although mild dehydration can be easily corrected and is principally associated with impaired physical performance (8), it may be linked with common public health disorders if left chronically untreated (9, 10). A greater severity of dehydration can result in significant medical costs, morbidity, and mortality across the life span (11, 12). Although the physiology of osmotic and vascular volume responses to dehydration in humans have been well described (13, 14), the phenomenology of dehydration assessment has not. For example, there is no single, universal gold standard method of dehydration assessment for clinical decision making (7, 15, 16), which contributes greatly to the difficulty that clinicians encounter when trying to accurately assess dehydration in practice (17–25). This discordance between the physiology and phenomenology of dehydration is a recognized source of clinical confusion (17) for which clarity is needed to improve the practice of dehydration assessment.

In this review, we highlight how phenomenologic interpretations of dehydration depend critically on the type (dehydration compared with volume depletion) and magnitude (moderate compared with severe) of dehydration, which, in turn, influence the plasma osmolality (Posm)[5]– and blood volume (BV)–dependent compensatory thresholds for antidiuretic and thirst responses. We also discuss the recent application of biological variation analysis to osmotic responses during dehydration for its novel potential as an adjunct (17) to clinical decision making. Posm is the primary focus of this review because it is the key regulated variable in fluid balance (13, 14, 26–28), and it is commonly used to screen for dehydration and complement more quantitative differential diagnoses of dysnatremias and other diseases (3, 5, 28–30). The osmolality of other body fluids commonly used to assess dehydration (ie, urine and saliva) are also mentioned as is the practical assessment of volume depletion. Descriptions of other potential methods of dehydration and volume-depletion assessment have been provided by other authors (7, 16, 19, 31, 32). Complementary reviews (33) are similarly suggested for detailed information related to sodium (natriuresis and appetite) and nonosmotic contributors (eg, baroreceptors) to osmotic homeostasis.

FUNDAMENTALS OF OSMOTIC RESPONSES TO DEHYDRATION IN HUMANS

In its simplest form, the net body water balance is generally the zero sum of food (water and solute) and fluid intake minus insensible and obligatory renal water losses (7). Fluid intakes,

[1] From the US Army Research Institute of Environmental Medicine, Natick, MA.

[2] The opinions or assertions contained herein are the private views of the authors and should not be construed as official or reflecting the views of the Army the Department of Defense.

[3] Supported by the United States Army Medical Research and Materiel Command.

[4] Address correspondence to SN Cheuvront, Thermal and Mountain Medicine Division, US Army Research Institute of Environmental Medicine, Kansas Street, Building 42, Natick, MA 01760-5007. E-mail: samuel.n.cheuvront@us.army.mil.

[5] Abbreviations used: AVP, arginine vasopressin; Bm, body mass; BV, blood volume; Posm, plasma osmolality; PV, plasma volume; Sosm, saliva osmolality; TBW, total body water; Uosm, urine osmolality.

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Osmolality Calculation

Osmolarity	**2 x Na + .9 x glucose + .93 x .5 x urea + 8** **1.897 x Na + glucose + urea x .5 + 13.5** **1.9 x (Na + K) + glucose + urea x .5 + 5**	**288-292 mOsm/kg**
Example	1.9 x (Na + K) + glucose + urea x .5 + 5 1.9 x (141 + 4.1) + 5.8 + 5.36 x .5 + 5 = 289.17	
	Glucose (mg/dl)/18 = mmol/L • 104/18 = 5.7777 BUN x .357 = mmol/L • 15 x .357 = 5.355	

(MVMM) supplementation had no significant effect on the risk of all-cause mortality, mortality due to cancer, or mortality due to cardiovascular disease.

Despite our overall finding, Hemilä asserts that some vitamins and minerals may be beneficial for specific subpopulations. We concur with his suggestion that variables such as age, sex, and lifestyle factors might modify the effects of some vitamins, such that differential effects may emerge in different subpopulations. However, as pointed out by Hemilä, we were unable to perform subanalyses to examine the modifying effect of these different variables given that only trial-level data were available.

If individual-level data were accessible we could have performed any number of subanalyses. A limitation of this approach is that each subanalysis involves an additional statistical comparison and thus a greater risk of a type I error. Furthermore, subgroup analysis based on post hoc examination of data can lead to erroneous conclusions (2). The findings discussed by Hemilä, relating to vitamin E mortality risk across different age groups, still require replication for this reason. To avoid these issues, we used a limited number of prespecified analyses to determine the overall effects of MVMM supplementation in the general population, rather than in specific subpopulations.

Our results were strengthened by the large number of trials included in our analyses, generating a large pooled sample size. Although there are several advantages to undertaking an individual-level data meta-analysis, such an analysis is not always feasible. For example, we excluded 7 relevant trials from our analysis simply because trial-level data were unobtainable. Given the difficulty in obtaining raw data from chief investigators (especially when many of the trials included in our analysis were more than a decade old), undertaking a patient-level meta-analysis would have further diminished the number of trials included in our analysis.

Hemilä states that our meta-analysis is "important in discouraging ordinary middle-aged people from taking MVMMs." We are not sure how this conclusion was derived from our work given that our meta-analysis did not specifically focus on middle-aged adults. Moreover, whereas we found no effect of MVMMs on mortality across adults of all ages, this does not rule out other possible benefits to health or well-being.

Before our investigation, information on the association of MVMM use and mortality had frequently been obtained from observational studies (3). Our meta-analysis showed that, across randomized controlled trials, MVMM supplementation had no effect on mortality (1). Although we acknowledge that vitamins may have different effects in different subpopulations, it was first necessary to investigate the overall effects of MVMM supplementation in the general population. Identifying a harmful effect of MVMM use across all adults would have shown greater implications than identifying a harmful effect in one of many narrow subgroups. As discussed in our meta-analysis, we call for further research into the effects of MVMM use on all aspects of human health (1). This includes examination of MVMM use in specific subpopulations.

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Helen Macpherson
Andrew Pipingas
Matthew P Pase
Centre for Human Psychopharmacology
Swinburne University of Technology
Advanced Technology Building
427–451 Burwood Road
Hawthorn, Victoria 3122
Australia
E-mail: matthewpase@gmail.com

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Limitations to the use of plasma osmolality as a hydration biomarker

Dear Sir:

In some laboratories, plasma osmolality (P_{osm}) is used as the gold standard for detecting dehydration (1), without consideration of its limitations; however, published data dispute this technique (2, 3), which prompts us to write in response to the recent article by Cheuvront et al (4) with regard to quantitative dehydration assessment. This article correctly states that P_{osm} is the key regulated variable in fluid balance, which means that P_{osm} is constantly regulated toward a central set point as the kidneys modify urine concentration and water excretion in response to diet and daily activities. We believe that this controlled regulation limits the efficacy of P_{osm} as an index of hydration change in many experimental designs. This article (4) also states that the "criticisms for adopting P_{osm} as a gold standard for dehydration assessment are minimal" (p 460). We disagree and write to describe several limitations to the use of P_{osm} as a gold standard for dehydration.

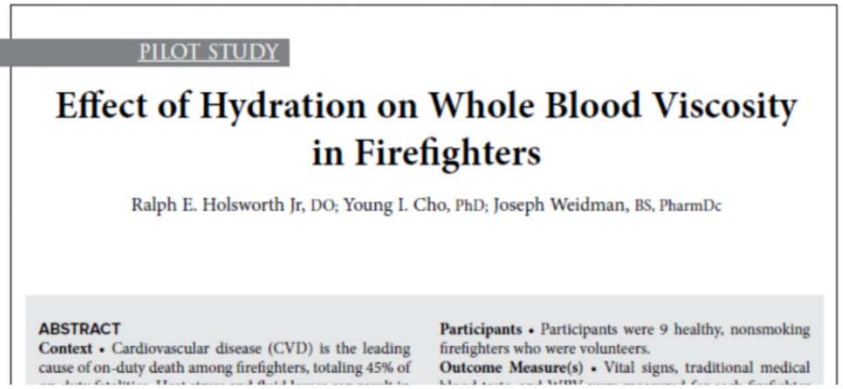
First, individuals who lose a large amount of body water (reported as % body mass loss relative to a beginning euhydrated state) may exhibit a decreased P_{osm} contrary to anticipated hemoconcentration. For example, a summary of 2 studies (5) reported that the P_{osm} of 6 individuals (out of 39) decreased after they lost 3–8% of body mass. In a different study, men and women who consumed a 500-mL bolus of fluid acutely exhibited an increased P_{osm}, contrary to anticipated hemodilution (1); that is, after 90 min of rest, 4 of 30 P_{osm} measurements increased. These values show that P_{osm} may not reflect widely accepted physiologic principles, and that variance of P_{osm} measurements may be large.

Second, evidence suggests that P_{osm} changes are time- and protocol-specific. Unpublished observations (CX Muñoz, EC Johnson, JK DeMartini, et al, 2012) show that dehydration equivalent to 2% of body mass resulted in P_{osm} changes that were twice as large during mild cycling exercise (2.3 h; ΔP_{osm} of 9 mOsm/kg) compared with a passive exposure (5.0 h; ΔP_{osm} of 4 mOsm/kg); participants consumed no water during either trial in

Dehydration

* Increased osmolarity
* Increased RBC, hemoglobin, hematocrit
* Increased albumin (4.9 or above)
* Urine specific gravity
  * If high, likely not drinking enough water
  * If low, likely losing water

Viscosity



PILOT STUDY

Effect of Hydration on Whole Blood Viscosity in Firefighters

Ralph E. Holsworth Jr, DO; Young I. Cho, PhD; Joseph Weidman, BS, PharmDc

ABSTRACT

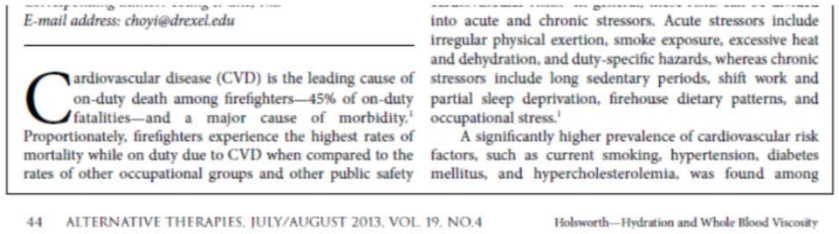
Context • Cardiovascular disease (CVD) is the leading cause of on-duty death among firefighters, totaling 45% of

Participants • Participants were 9 healthy, nonsmoking firefighters who were volunteers.

Outcome Measure(s) • Vital signs, traditional medical

Dehydration during the mock fire drill resulted in elevated WBV at both low- and high-shear rates. HCT and Hb increased due to dehydration and hemoconcentration. Hb and HCT returned to baseline values after exercise and rehydration, and while WBV improved, baseline values were not restored. After exercise but before rehydration, WBV changes were significantly larger than HCT and Hb changes, suggesting the profound influence of hydration states on WBV.

WBV measurements were better determinants of hydration states than HCT or Hb and should be performed to monitor the cardiovascular health of at-risk firefighters.



E-mail address: choyi@drexel.edu

Cardiovascular disease (CVD) is the leading cause of on-duty death among firefighters—45% of on-duty fatalities—and a major cause of morbidity.[1] Proportionately, firefighters experience the highest rates of mortality while on duty due to CVD when compared to the rates of other occupational groups and other public safety

into acute and chronic stressors. Acute stressors include irregular physical exertion, smoke exposure, excessive heat and dehydration, and duty-specific hazards, whereas chronic stressors include long sedentary periods, shift work and partial sleep deprivation, firehouse dietary patterns, and occupational stress.[1]

A significantly higher prevalence of cardiovascular risk factors, such as current smoking, hypertension, diabetes mellitus, and hypercholesterolemia, was found among

Increased whole blood viscosity is associated with silent cerebral infarction.

A cross-sectional study was conducted to evaluate the association between hemorheological parameters and SCI in 1487 subjects (868 men and 619 women) undergoing medical check-up.

The participants with SCI had higher whole blood viscosity (WBV) levels at low shear rate than those without SCI. Moreover, the subjects with a high WBV had a higher prevalence of SCI.

Whole blood viscosity at low shear rate is a novel indicator for SCI regardless of classical cardiovascular risk factors. Early measurement of whole blood viscosity may be helpful to assess the risk of stroke.

Li, Rui-yan, Zhi-gang Cao, Ying Li, and Rui-tao Wang. 2015. "Increased Whole Blood Viscosity Is Associated with Silent Cerebral Infarction." *Clinical Hemorheology and Microcirculation* 59 (4): 301–7. doi:10.3233/CH-131760.

Article Type: 3 Original Article - Australia, Japan, SE Asia

Elevated whole blood viscosity is associated with insulin resistance and nonalcoholic fatty liver disease-a population study

Short title: Elevated whole blood viscosity is associated with NAFLD

Authors: Hong-yan Zhao*, Jing Li*, Min Xu, Tian-ge Wang, Wan-wan Sun, Ying Chen, Yu-fang Bi, Wei-qing Wang+, Guang Ning

Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health, the National Clinical

Over 8,000 Chinese subjects were used. 30% had NAFLD. Positively association between WBV and NAFLD.

Corresponding author and person to whom reprint requests should be addressed :
Wei-qing Wang, MD, PhD
wqingw@hotmail.com
Address : 197 Rui-jin Er Road, Shanghai, China
Telephone : 0086-21-64370045-665391
Fax number : 0086-21-64373514

Keywords: whole blood viscosity, insulin resistance, nonalcoholic fatty liver disease

Disclosure statement: The authors have nothing to declare.

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Endocrine
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ORIGINAL ARTICLE

Association between whole blood viscosity and arterial stiffness in patients with type 2 diabetes mellitus

Ying Li · Xiu-xia Tian · Tiemin Liu · Rui-tao Wang

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The findings showed that baPWV increased as WBV (3 s(-1)) elevated in DM. Moreover, WBV (3 s(-1)) is independently associated with baPWV even after adjusting other cardiovascular risk factors. Early detection of abnormal WBV levels at low shear rate should warrant for early search of undetected arterial stiffness in patients with DM.

metabolic parameters were compared across WBV ($3\ s^{-1}$) quartiles. The mean values of baPWV gradually increased with WBV ($3\ s^{-1}$) quartiles. In addition, there was a positive correlation between baPWV and WBV $3\ s^{-1}$ in patients with DM after adjusting confounding factors ($r = 0.285$, $p = 0.039$). Stepwise multiple linear regression analysis further revealed that WBV ($3\ s^{-1}$) is a

Y. Li · X. Tian · R. Wang (✉)
Department of Geriatrics, The Second Affiliated Hospital, Harbin Medical University, NO. 246 Xuefu ST, Nangang District, Harbin 150086, Heilongjiang, China
e-mail: ruitaowang@126.com

Y. Li
International Physical Examination and Healthy Center, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, China

T. Liu
Division of Hypothalamic Research, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX 75390, USA

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Introduction

Type 2 diabetes mellitus (DM) is associated with an increased risk of stroke and coronary heart disease (CHD) and non-vascular mortality [1, 2]. The occurrence of insulin resistance accompanied with hyperviscosity worsens the state of atherosclerosis in patients with DM. Furthermore, both DM and hyperviscosity have the tendency to develop thrombosis [3]. Recent studies demonstrated that hyperviscosity in DM is strongly influenced by the excellence of glycemic control [4–6].

Arterial stiffness due to decreased arterial compliance is one of the major signs of vascular aging [7]. Elevated arterial stiffness, an indicator of subclinical atherosclerosis, is associated with myocardial infarction, heart failure, stroke, renal disease, and all-cause mortality [8]. Brachial-ankle pulse wave velocity (baPWV) measurement, a simple, non-invasive, and automated measurement method, reflects the stiffness of muscular arteries and is widely used

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HEPATOLOGY

Increased whole blood viscosity associated with arterial stiffness in patients with non-alcoholic fatty liver disease

Kai-jiang Yu,* Mei-jie Zhang,† Ying Li†,‡ and Rui-tao Wang†

Departments of *Intensive Care Unit and †Geriatrics, and ‡International Physical Examination and Healthy Center, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, China

Key words
arterial stiffness, brachial-ankle pulse wave velocity, non-alcoholic fatty liver disease, whole blood viscosity.

Abstract

Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is an independent risk factor for increased cardiovascular disease. The brachial-ankle pulse wave velocity

The present study showed that baPWV elevated as WBV (3/s) increased in NAFLD. Moreover, WBV(3/s) is independently associated with baPWV even after adjusting other cardiovascular risk factors. Early detection of abnormal WBV levels at low shear rate should warrant for early search of undetected arterial stiffness in patients with NAFLD.

chronic liver condition in the Western countries, affecting 20–40% of the general population. Recent studies showed that NAFLD is an independent risk factor for increased cardiovascular disease. Evidence also indicated a graded association between NAFLD severity and increased vascular risk.[1] However, there are no suitable noninvasive biomarkers of NAFLD severity to allow better risk stratification based on cardiovascular outcomes.

Elevated arterial stiffness, an index of subclinical atherosclerosis, is linked with myocardial infarction, heart failure, stroke, dementia, renal disease, and elevated total mortality.[2] Pulse wave velocity (PWV) reflects the stiffness of central and peripheral muscular arteries, and is widely used as an index of arterial stiffness and vascular damage. Brachial-ankle PWV (baPWV) measurement, a simple, noninvasive, and automated measurement method, is closely correlated with aortic PWV.[3] Previous studies found that increased baPWV is associated with metabolic syndrome, cardiovascular diseases, stroke, and renal disease, as well as elevated total mortality.[4–7]

are associated with changes in hemorheological parameters.[8–10] Moreover, increased viscosity is observed in metabolic syndrome, hypertension, diabetes, ischemic heart disease, stroke, and cognition.[11–14] A recent study confirmed that whole blood viscosity (WBV) is a predictor of cardiovascular events.

We speculated that WBV may be one of the major pathological mediators of cardiovascular disease in NAFLD. Therefore, the purpose of the study was to investigate if rheological parameters are independently associated with baPWV in patients with NAFLD.

Methods

Participants. The study included 2032 persons (1035 men and 997 women) who received general health examination in our hospital from January 2009 to December 2010. We obtained informed consent from all subjects. The study protocol was

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Table 1 Clinical and biochemical characteristics of male subjects with non-alcoholic fatty liver disease

	Quartiles of WBV (3/s)				
n	Q1 259	Q2 259	Q3 259	Q4 258	*P* value
Age (years)	48.5 (5.5)	48.2 (6.2)	47.3 (5.9)	49.9 (6.7)	< 0.001
BMI (kg/m^2)	24.5 (3.3)	24.4 (3.2)	24.9 (3.4)	24.8 (2.6)	0.124
Smoker (%)	116 (44.8%)	104 (40.2%)	135 (52.1%)	122 (47.3%)	0.050
SBP (mmHg)	126.1 (9.9)	124.8 (9.8)	124.6 (9.9)	128.8 (11.3)	< 0.001
DBP (mmHg)	74.4 (7.9)	73.1 (7.9)	73.8 (8.1)	75.7 (9.3)	< 0.001
Heart rate (bpm)	68.8 (9.8)	68.4 (9.1)	68.4 (9.6)	67.1 (8.6)	0.197
FPG (mmol/L)	4.83 (4.54–5.20)	4.75 (4.50–5.15)	4.79 (4.48–5.13)	4.91 (4.64–5.25)	0.019
TC (mmol/L)	4.88 (0.82)	4.81 (0.82)	4.87 (0.80)	4.96 (0.90)	0.223
TG (mmol/L)	2.89 (2.36–3.33)	2.94 (2.53–3.44)	2.89 (2.42–3.33)	3.19 (2.86–3.54)	< 0.001
HDL (mmol/L)	1.64 (1.37–1.85)	1.66 (1.43–1.87)	1.60 (1.33–1.80)	1.65 (1.49–1.84)	0.155
LDL (mmol/L)	2.98 (0.72)	2.96 (0.68)	3.00 (0.64)	3.17 (0.78)	0.002
AST (U/L)	22.0 (19.0–29.0)	24.0 (19.0–29.0)	23.0 (18.0–29.0)	21.0 (17.0–28.0)	0.001
ALT (U/L)	24.0 (18.0–42.0)	27.0 (19.0–49.0)	27.0 (18.0–43.0)	24.0 (16.0–38.0)	0.004
GGT (U/L)	37.0 (19.0–70.0)	36.0 (22.0–60.0)	41.0 (20.0–69.0)	37.0 (20.0–76.0)	0.648
Hemoglobin (g/dL)	125.9 (10.8)	125.0 (10.3)	124.1 (10.2)	125.2 (10.7)	0.292
Hematocrit (%)	42.5 (5.0)	43.1 (4.0)	42.8 (4.9)	43.8 (3.6)	0.010
Fibrinogen (mg/dL)	329.1 (69.4)	333.2 (65.9)	334.9 (72.8)	351.0 (55.1)	0.001
WBV200s^{-1} (mPa.s)	4.46 (0.39)	4.39 (0.30)	4.57 (0.37)	4.48 (0.40)	< 0.001
PV (mPa.s)	1.60 (0.08)	1.59 (0.08)	1.60 (0.09)	1.58 (0.10)	0.008

Data are expressed as means (SD) or median (interquartile range) or percentage.
P value was calculated by one-way ANOVA test or Kruskal–Wallis *H* or chi-square test.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GGT, gamma-glutamyl transpeptidase; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; PV, plasma viscosity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WBV, whole blood viscosity.

as elevated total mortality.[4–7]

informed consent from all subjects. The study protocol was

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Table 2 Clinical and biochemical characteristics of female subjects with non-alcoholic fatty liver disease

	Quartiles of WBV (3/s)				
n	Q1 251	Q2 248	Q3 251	Q4 247	*P* value
Age (years)	47.5 (4.2)	48.9 (4.6)	48.2 (4.1)	50.8 (4.7)	< 0.001
BMI (kg/m^2)	24.1 (3.1)	24.1 (2.9)	24.3 (3.4)	24.6 (3.0)	0.346
Smoker (%)	5 (2.0%)	4 (1.6%)	6 (2.4%)	8 (3.2%)	0.659
SBP (mmHg)	123.8 (11.0)	122.2 (10.9)	124.9 (11.4)	127.7 (11.2)	< 0.001
DBP (mmHg)	78.3 (9.7)	76.3 (9.2)	78.9 (9.3)	79.3 (9.4)	0.002
Heart rate (bpm)	65.7 (7.4)	66.2 (10.1)	65.9 (9.0)	66.8 (9.5)	0.571
FPG (mmol/L)	5.11 (4.72–5.64)	5.00 (4.72–5.33)	5.01 (4.77–5.47)	5.29 (4.90–5.72)	< 0.001
TC (mmol/L)	5.06 (1.00)	4.94 (0.85)	5.08 (0.87)	5.27 (1.12)	0.002
TG (mmol/L)	2.10 (1.60–2.97)	2.01 (1.66–2.81)	2.22 (1.83–2.80)	2.31 (1.82–2.89)	0.110
HDL (mmol/L)	1.38 (1.20–1.56)	1.39 (1.20–1.54)	1.36 (1.17–1.55)	1.30 (1.10–1.55)	0.047
LDL (mmol/L)	3.00 (0.88)	2.79 (0.83)	2.93 (0.77)	2.98 (0.87)	0.033
AST (U/L)	21.0 (18.0–24.0)	21.0 (18.0–24.8)	19.0 (16.0–23.0)	20.0 (17.0–23.0)	0.002
ALT (U/L)	16.0 (14.0–20.0)	17.0 (13.3–20.0)	17.0 (14.0–19.0)	17.0 (12.0–21.0)	0.936
GGT (U/L)	16.0 (12.0–27.0)	17.0 (10.3–23.0)	16.0 (11.0–23.0)	20.0 (11.0–26.0)	0.201
Hemoglobin (g/dL)	132.6 (10.5)	133.2 (11.0)	132.3 (10.2)	133.3 (10.6)	0.684
Hematocrit (%)	42.8 (4.8)	43.3 (3.9)	42.6 (4.9)	43.6 (3.9)	0.045
Fibrinogen (mg/dL)	323.0 (66.2)	329.9 (73.5)	332.2 (72.9)	321.6 (71.0)	0.264
WBV200s^{-1} (mPa.s)	3.92 (0.40)	3.99 (0.36)	4.20 (0.33)	4.07 (0.43)	< 0.001
PV (mPa.s)	1.44 (0.08)	1.41 (0.08)	1.43 (0.09)	1.42 (0.08)	0.014

Data are expressed as means (SD) or median (interquartile range) or percentage.
P value was calculated by one-way ANOVA test or Kruskal–Wallis *H* or chi-square test.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GGT, gamma-glutamyl transpeptidase; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; PV, plasma viscosity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WBV, whole blood viscosity.

as elevated total mortality.[7,8]

informed consent from all subjects. The study protocol was

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Bone 56 (2013) 343–346

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Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

Whole blood viscosity is negatively associated with bone mineral density in postmenopausal women with osteoporosis

Zong-yan Teng [a], Li-chun Pei [a], Ying Zhang [a], Ying Li [a,b], Rui-tao Wang [a,*]

[a] Department of Geriatrics, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, China
[b] International Physical Examination and Healthy Center, the Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, China

Osteoporosis (OP) is associated with cardiovascular disease. Moreover, osteoporosis has been shown to be an independent predictor of cardiovascular mortality.

In conclusion, The findings show that WBV is elevated in osteoporosis and negatively correlated with BMD.

nant of bone mass, but exercise with loading of the bone also has a major impact on bone mass. The association between osteoporosis with carotid atherosclerosis, peripheral arterial disease, cardiovascular disease, and stroke has been well documented [1–4]. Furthermore, recent studies show that osteoporosis is an independent predictor of cardiovascular mortality [5,6].

Altered hemorheological parameters have also been shown to play a crucial role in atherogenesis. Many cardiovascular risk factors, including ageing, obesity, carotid intima-media thickness, are associated with changes in hemorheological parameters [7–9]. Moreover, increased viscosity is observed in metabolic syndrome, hypertension, diabetes, ischemic heart disease, and stroke [10–13]. A recent study confirmed that whole blood viscosity (WBV) is a predictor of cardiovascular events. Sedentary lifestyle can easily result in slowing down of blood flow and increasing plasma or whole blood viscosity. Recent studies

* Corresponding author at: Department of Geriatrics, The Second Affiliated Hospital, Harbin Medical University, NO.246 Xuefu ST, Nangang District, Harbin, 150086, China. Fax: +86 451 86605725.
E-mail address: wangruitao2200@gmail.com (R. Wang).

http://dx.doi.org/10.1016/j.bone.2013.07.001

Materials and methods

Study population

The study enrolled 481 postmenopausal women with similar education background and income from the International Physical Examination and Healthy Center of our hospital between Jan. 2009 to Dec. 2010 [16]. This is a case-control study and there are 318 patients and 163 controls. They were matched for type 2 diabetes and hypertension. Informed consent was obtained from every subject. The study protocol was approved by the Ethics Committee of the Second Hospital of Harbin Medical University, China.

Clinical characteristics

Clinical data including medical history, lifestyle behaviors and medication use were recorded for each participant. Regular leisure-time physical activity was defined as participation in moderate or vigorous activity for 30 minutes or more per day at least 3 days a week. All the subjects underwent physical examination which included anthropometric and

Blood Viscosity in Subjects With

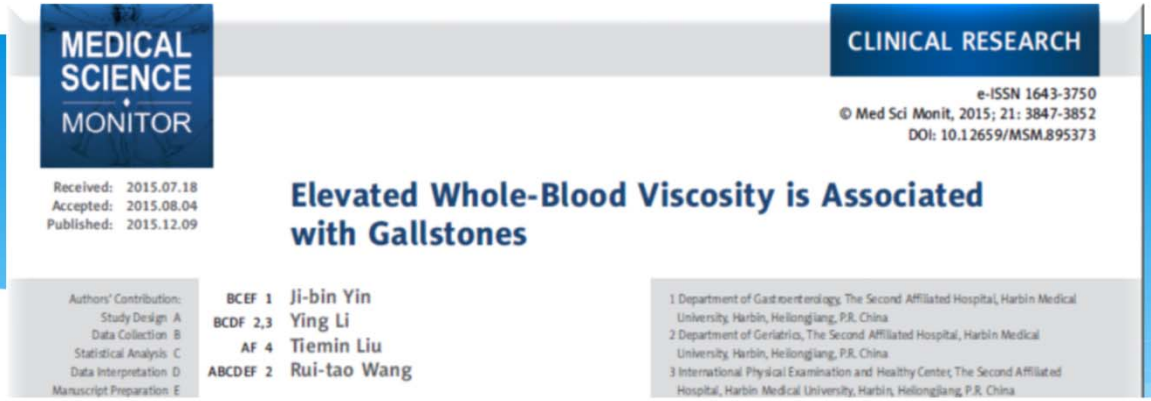
Concetta Irace, Claudio Carallo,

Enrolled subjects were divided into three groups according to blood glucose: group A, blood glucose <90 mg/dL; group B, blood glucose ranging from 90 to 99 mg/dL; and group C, blood glucose ranging from 100 to 125 mg/dL.

Hematocrit ($P < 0.05$) and BV (P between 0.01 and 0.001) were significantly higher in groups B and C compared with group A.

The current study shows a direct relationship between BV and blood glucose in nondiabetic subjects. It also suggests that, even within glucose values considered completely normal, individuals with higher blood glucose levels have increased BV comparable with that observed in subjects with prediabetes.

overloaded to pump blood in the vascular bed, and the blood itself, more viscous, can damage the vessel wall. Furthermore, according to Poiseuille's law (1), BV is



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CLINICAL RESEARCH

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Elevated Whole-Blood Viscosity is Associated with Gallstones

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E

BCEF 1 Ji-bin Yin
BCDF 2,3 Ying Li
AF 4 Tiemin Liu
ABCDEF 2 Rui-tao Wang

1 Department of Gastroenterology, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, P.R. China
2 Department of Geriatrics, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, P.R. China
3 International Physical Examination and Healthy Center, The Second Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, P.R. China

Among 849 enrolled patients, 421 (49.6%) had gallstone disease. Compared with control subjects, whole-blood viscosity (WBV) levels were increased in patients with gallstones.

We found that whole-blood viscosity at low shear rate was independently associated with gallstones. Whether control of hyperviscosity would reduce the risk of developing gallstones deserves further investigation.


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King Saud University

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ORIGINAL ARTICLE

Blood viscosity as a sensitive indicator for paclitaxel induced oxidative stress in human whole blood

Whole-blood samples were collected from healthy volunteers and co-incubated with PTX, CrEL or their combination then compared with control blood samples. After a 24 h incubation time, the whole-blood viscosity (WBV), erythrocyte sedimentation rate (ESR), levels of whole-blood malondialdehyde (MDA), protein carbonyl content (PCC) and reduced glutathione (GSH) were determined. Moreover, plasma nitrite and plasma sialic acid (SA) values were measured.

The present study demonstrates that PTX-induced oxidative stress is associated with an increase of WBV.

at high shear rates, while at low shear, the viscosity reflects erythrocytes aggregability (Simmonds et al., 2013). Additionally, blood rheological parameters are affected by blood

http://dx.doi.org/10.1016/j.jsps.2014.04.006

Research article

Serum bilirubin and lipoprotein-a: How are these associated with whole blood viscosity?

E. U. Nwose[1,2], R. S. Richards[1], P. Bwititi[3], E. Butkowski[4]

[1]School of Community Health, Charles Sturt University, Albury, NSW, Australia, [2]Institute of Clinical Pathology & Medical Research, Nepean Hospital Pathology, Kingswood, NSW, Australia, [3]School of Biomedical Sciences, Charles Sturt University, Wagga Wagga, NSW, Australia, [4]Institute of Clinical Pathology & Medical Research, South West Pathology, Albury, NSW, Australia

Background: It has been demonstrated that oxidative stress can induce red blood cell rigidity and haemolysis, which in turn can cause hyperviscosity and hyperbilirubinaemia, respectively. However, haemolysis may be associated with a low level of haemoglobin, which reduces whole blood viscosity (WBV). Bilirubin can behave as antioxidant or oxidant, and one uncharted course for diagnostic pathology

This pilot study suggests that hyperbilirubinaemia and hyperviscosity are associated and positively correlated. Consideration of whether serum bilirubin (as an indirect index of oxidative stress) can be used in combination with WBV (as index of macrovascular effect of oxidative stress) to assess oxidative damage is recommended

Introduction

In clinical diagnostic practice, bilirubin measurement is an important component of the test panel for liver functions. Total bilirubin is commonly used for monitoring of patients with anaemia who are suspected of disorders associated with haemolysis. Hyperbilirubinaemia has been associated with circadian rhythm and oxidative stress.[1] Circadian rhythm has been linked to several physiological processes including antioxidant activities *vis-à-vis* oxidative stress and blood viscosity.[2-4] Interestingly, and typical of paradoxical properties of antioxidants, bilirubin can behave as an antioxidant or oxidant depending on its concentration.[5] Particularly, bilirubin at low concentration is an antioxidant in neonatal jaundice,[5] but during haemolysis it is possible that bilirubin free radicals such as lumirubin may be generated;[6,7] thereby conferring oxidant properties on bilirubin.

The concept of bilirubin being associated with oxidative stress is interesting with potential for its use in laboratory medicine diagnosis, because it is an established routine laboratory index. Given that oxidative stress may be associated with serum bilirubin level on one hand, and exacerbates whole blood viscosity (WBV) on the other, it is worth investigating whether bilirubinaemia could be associated with WBV. Further, evidence of oxidative stress and a concomitant demonstration of any of the effective vascular events including increase in WBV is necessary to establish oxidative damage.[8] If bilirubinaemia is associated with WBV; it would be worth investigating how or whether the two parameters are correlated, given the antioxidant and pro-oxidant properties of

Correspondence to: E. U. Nwose, Institute of Clinical Pathology & Medical Research, Nepean Hospital Pathology, Derby Street, Kingswood, NSW 2747, Australia. Email: nwoseeu@hotmail.com

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DOI:10.3233/CH-131706
IOS Press

Plasma viscosity, ADMA and oxLDL values were significantly higher in subjects with dyslipidemia than in subjects with normolipidemia. Plasma NOx concentration was decreased in dyslipidemic subjects compared to the normo-lipidemic subjects.

Our results demonstrated that the rheological impairment of dyslipidemic patients was related with endothelial dysfunction and this was a possible cause of both micro and macrovascular complications. Therefore, as plasma viscosity is also a sensitive parameter, it can add useful information about the diagnosis and treatment of various disorders, and it should be utilized more frequently in clinical medicine.

develop further understanding of CVD process to pinpoint new areas named as hemorheology for targeted

*Corresponding author: Dr. Meltem Ercan, İstanbul University, Cerrahpasa Medical Faculty, Biophysics Department, Fatih-Kocamustafa Paşa-İstanbul/Türkiye. Tel.: +90 212 4143069; Fax: +90 212 4143069; E-mails: meltem@istanbul.edu.tr, melat65@yahoo.com.

Viscosity Calculation

Viscosity	**High shear rate: WBV (208 Sec^{-1})** **[0.12 X h] + [0.17 X (p - 2.07)]**	**16-18 (males)** **15.5 – 17.5 (females)**
Example	[0.12 X 147] + [0.17 X (7.3 - 2.07)] = 18.5	

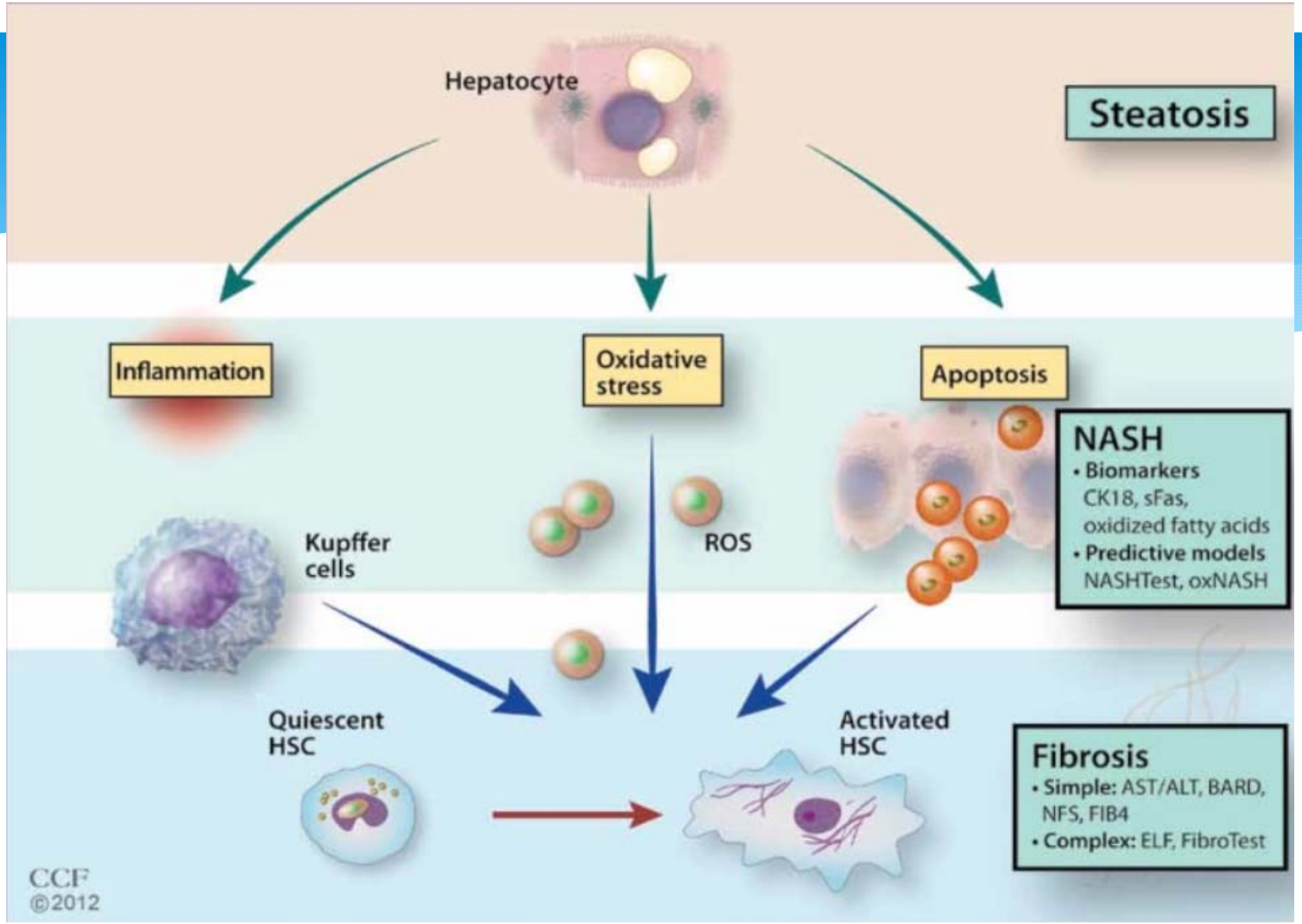
Liver Disease

Why be concerned about the liver?

* Associated with obesity, insulin resistance and diabetes
* Also associated with sub-clinical depression and sub-clinical anxiety
* Associated with cognitive impairment and even loss of self-esteem
* Also associated with chronic pain

Why use blood chemistry calculations?

* 30% of the population has fatty liver
* 90% of the obese population has fatty liver
* Liver enzymes (AST, ALT) fail to detect fatty liver most of the time
* Liver biopsy only evaluates 1/50,000th of total liver mass
  * Prone to error due to "patchy" histological changes
  * Expensive, invasive


Hepatocyte
Steatosis
Inflammation
Oxidative stress
Apoptosis
NASH
• Biomarkers
CK18, sFas,
oxidized fatty acids
• Predictive models
NASHTest, oxNASH
Kupffer cells
ROS
Quiescent HSC
Activated HSC
Fibrosis
• Simple: AST/ALT, BARD, NFS, FIB4
• Complex: ELF, FibroTest
CCF
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Fatty Liver Index

* Uses triglycerides, BMI, GGT and waist circumference

BMC Gastroenterology

BioMed Central

Research article

Open Access

The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population

Giorgio Bedogni[1], Stefano Bellentani[2], Lucia Miglioli[2], Flora Masutti[1], Marilena Passalacqua[2], Anna Castiglione[1] and Claudio Tiribelli*[1]

Address: [1]Centro Studi Fegato (Liver Research Center), AREA Science Park, Basovizza, Trieste, and Department of Biochemistry, Biophysics and Macromolecular Chemistry, University of Trieste, Trieste, Italy and [2]Nutrition and Liver Center, AUSL Modena, Carpi Hospital, Carpi, Modena, Italy

216 subjects with and 280 without suspected liver disease were studied. FL was diagnosed by ultrasonography

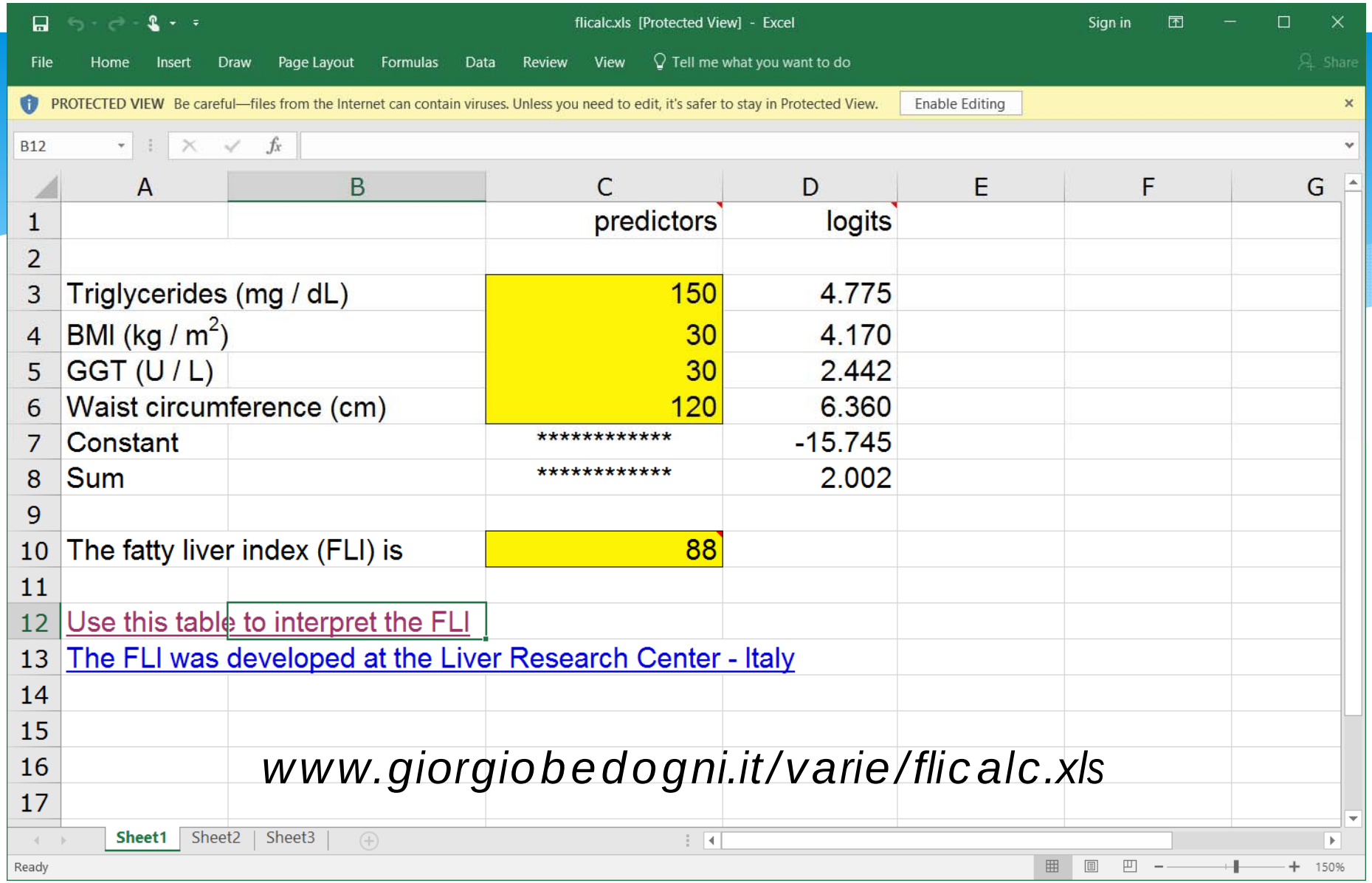
An algorithm based on BMI, waist circumference, triglycerides and GGT had an accuracy of 0.84 (95%CI 0.81-0.87) in detecting FL. We used this algorithm to develop the "fatty liver index" (FLI), which varies between 0 and 100. A FLI < 30 (negative likelihood ratio = 0.2) rules out and a FLI > or = 60 (positive likelihood ratio = 4.3) rules in fatty liver.

epidemiologic studies. Validation of FLI in external populations is needed before it can be employed for these purposes.

Fatty Liver Index

$$FLI = (e^{0.953*\log e\ (triglycerides\ +0.139*BMI+0.718*\log e\ (GGT)+0.053*waist\ circumference-15.745)}/(1+e^{0.953*\log e\ (triglycerides)+0.139*BMI\ +0.718*\log e(GGT\ +0.053*waist\ circumference-15.745)})*100$$

* <30 rules out fatty liver
* >60 rules in hepatosteatosis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Share
PROTECTED VIEW Be careful—files from the Internet can contain viruses. Unless you need to edit, it's safer to stay in Protected View.
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B12
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1 predictors logits
2
3 Triglycerides (mg / dL) 150 4.775
4 BMI (kg / m2) 30 4.170
5 GGT (U / L) 30 2.442
6 Waist circumference (cm) 120 6.360
7 Constant ********** -15.745
8 Sum ********** 2.002
9
10 The fatty liver index (FLI) is 88
11
12 Use this table to interpret the FLI
13 The FLI was developed at the Liver Research Center - Italy
14
15
16 www.giorgiobedogni.it/varie/flicalc.xls
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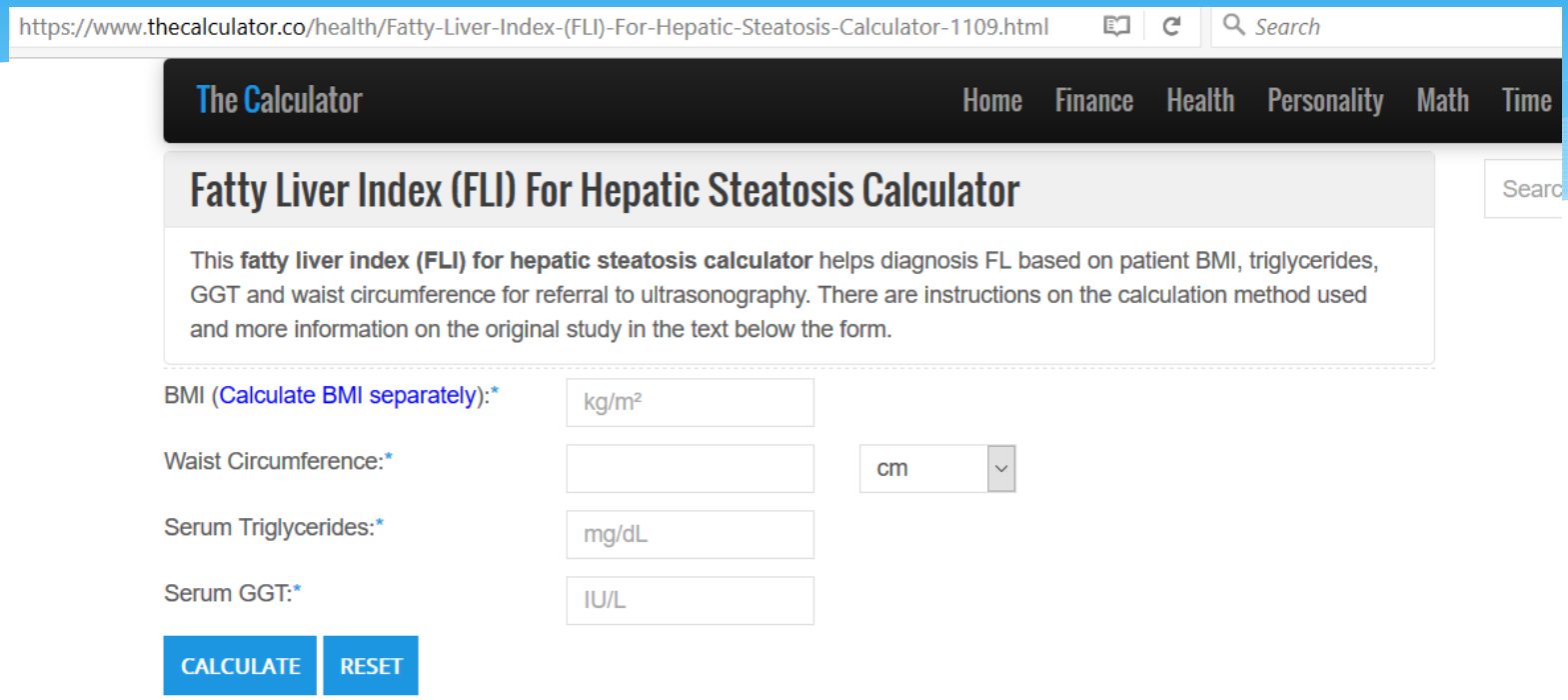
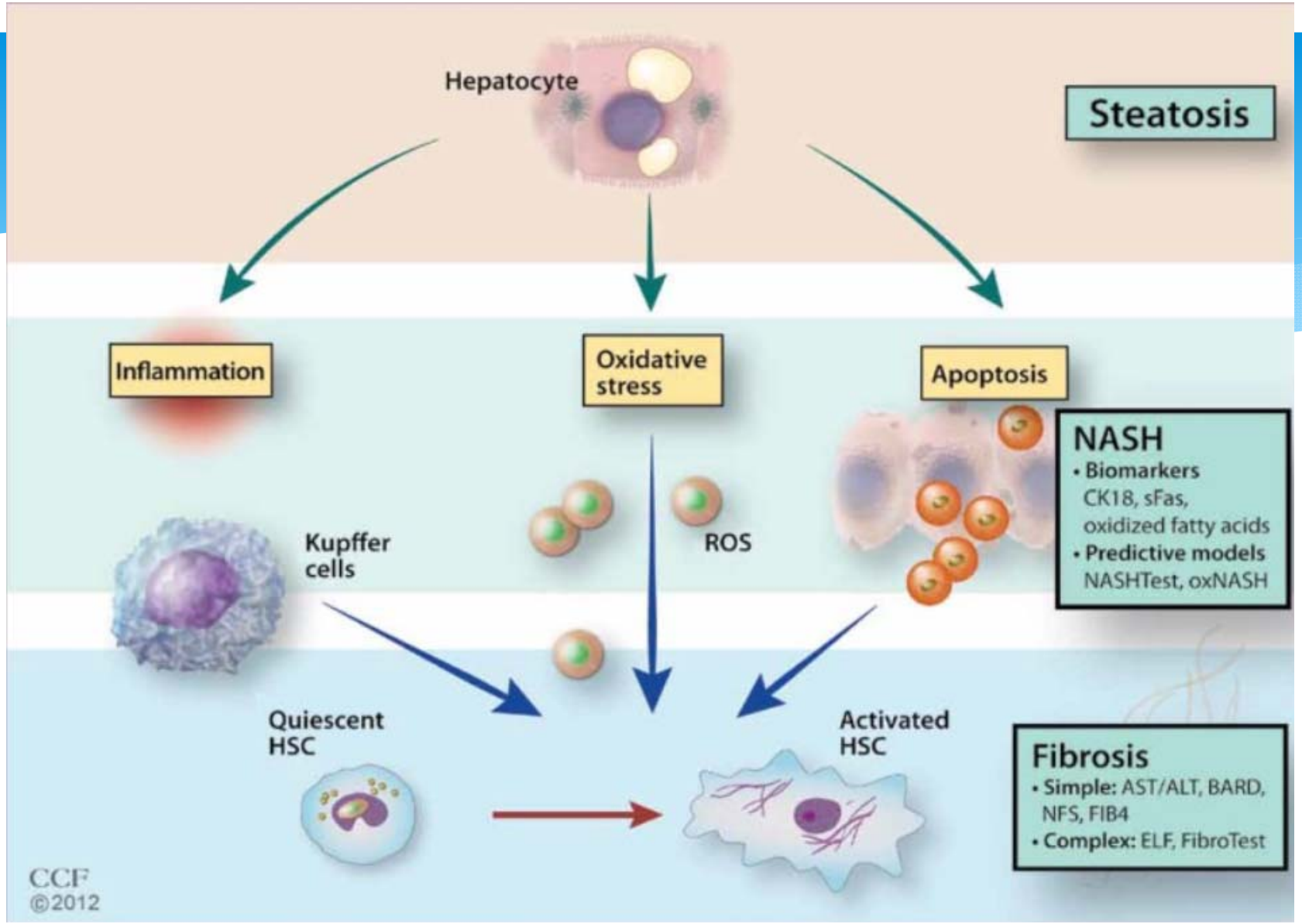


* https://www.thecalculator.co/health/Fatty-Liver-Index-(FLI)-For-Hepatic-Steatosis-Calculator-1109.html

Table 1 Clinical and metabolic characteristics of subjects according to the presence of FLI ≥40)

Variables	All subjects ($n = 448$)	Group A ($n = 208$) (FLI <40)	Group B ($n = 240$) (FLI ≥40)	p value
Age (years), median (IQR)	62.54 (56.77–70.15)	63.92 (54.80–68.65)	68.37 (59.22–70.70)	0.07
LUTS, n (%)				<0.01
Mild	144 (32.1 %)	88 (42.3)	56 (23.3)	
Moderate	216 (48.2 %)	104 (50.0)	112 (46.7)	
Severe	88 (19.6 %)	16 (7.7)	72 (30.0)	
MetS, n (%)	216 (48.2 %)	40 (19.2)	176 (73.3)	<0.01
IPSS, median (IQR)	14.50 (6.00–19.75)	17.00 (6.00–18.00)	19.00 (11.00–23.00)	<0.01
IPSS-storage, median (IQR)	5.00 (2.00–8.75)	5.00 (2.00–8.00)	7.0 (4.00–10.00)	<0.01
IPSS-voiding, median (IQR)	9.00 (4.25–11.009)	9.00 (5.00–11.75)	10.00 (7.00–12.00)	<0.01
IIEF-5, median (IQR)	19.00 (10.00–23.00)	18.00 (8.50–23.00)	16.00 (11.00–21.00)	<0.01
ED (IIEF-5 <22), n (%)	334 (76.8)	144 (69.2)	200 (83.3)	<0.01
PSA (ng/ml), median (IQR)	2.03 (0.74–4.75)	3.31 (0.88.7.20)	3.10 (1.38–4.70)	0.56
Total prostate volume (cc), median (IQR)	36.25 (30.00–58.50)	34.00 (25.00–50.00)	50.00 (30.00–68.00)	<0.01
Waist circumference (cm), median (IQR)	99.00 (92.00–104.75)	91.00 (86.25–98.75)	102.00 (98.00–105.00)	<0.01
Hip circumference (cm), median (IQR)	98.50 (94.00–103.00)	95.00 (91.00–97.00)	101.00 (96.00–103.00)	<0.01
BMI (kg/m^2), median (IQR)	26.51 (24.54–29.23)	24.00 (23.04–25.71)	27.43 (26.64–30.12)	<0.01
Glucose (mg/dl), median (IQR)	93.00 (86.00–102.75)	93.00 (85.75–101.75)	95.00 (89.00–104.00)	<0.01
Cholesterol (mg/dl), median (IQR)	193.50 (169.25–221.50)	203.00 (174.00 (242.75)	190.00 (169.00–215.00)	0.22
HDL-C (mg/dl), median (IQR)	40.50 (34.25–49.75)	47.00 (33.00–56.00)	42.00 (39.25–55.00)	<0.01
LDL-C (mg/dl), median (IQR)	127.20 (102.85–153.15)	135.40 (112.00–176.40)	118.40 (97.20–141.20)	0.31
Tryglicerides (mg/dl), median (IQR)	118.50 (75.25–163.00)	70.00 (50.25–120.00)	142.00 (101.00–164.00)	<0.01
SBP (mmHg), median (range)	125.00 (120.00–140.00)	125.00 (120.00–140.00)	125.00 (120.00–140.00)	0.25
DPB (mmHg), median (IQR)	80.00 (70.00–85.00)	80.00 (66.25–83.75)	75.00 (70.00–85.00)	0.16
Insulin (mUI), median (IQR)	6.95 (4.62–9.85)	6.40 (4.60–7.90)	8.60 (4.60–10.80)	<0.01
HOMA index, median (IQR)	1.63 (1.08–2.30)	1.50 (1.06–1.75)	1.98 (1.08–2.44)	<0.01
HOMA ≥3, n (%)	56 (12.5 %)	8 (3.8)	48 (20.0)	0.03
Total testosterone (mg/dl), median (IQR)	4.31 (3.56–5.80)	4.69 (4.20–6.00)	4.26 (3.31–5.74)	<0.05
Estradiol (mg/dl), median (IQR)	16.90 (11.40–24.10)	20.30 (7.10–22.70)	16.10 (11.40–21.80)	0.56
AST (U/l), median (IQR)	21.00 (18.00–28.00)	21.00 (18.00–27.00)	24.00 (18.00–28.00)	<0.01
ALT(U/l), median (IQR)	25.00 (17.25–30.00)	23.00 (22.00–27.00)	26.00 (16.00–40.00)	<0.01
GGT (U/l), median (IQR)	20.00 (13.00–28.00)	14.00 (11.00–26.00)	21.00 (16.00–28.00)	<0.01
NAFLD, n (%)	206 (45.98 %)	58 (27.88)	148 (61.67)	<0.01
Fatty liver grade, n (%)				<0.01
Grade 0	242 (52.02)	150 (72.12)	92 (38.33)	
Grade 1	152 (33.93)	46 (22.12)	91 (37.92)	
Grade 2	30 (6.70)	10 (4.81)	42 (17.50)	
Grade 3	24 (5.36)	2 (0.96)	15 (6.25)	


Hepatocyte
Steatosis
Inflammation
Oxidative stress
Apoptosis
NASH
• Biomarkers
CK18, sFas,
oxidized fatty acids
• Predictive models
NASHTest, oxNASH
Kupffer cells
ROS
Quiescent HSC
Activated HSC
Fibrosis
• Simple: AST/ALT, BARD, NFS, FIB4
• Complex: ELF, FibroTest
CCF
©2012

NAFLD fibrosis score

* Validated calculation to identify level of fibrosis in NAFLD
* Age, BMI, hyperglycemia (fasting glucose levels ≥ 110 mg/dL or previously diagnosed T2DM), platelet count, albumin and AST/ALT ratio

* NAFLD
  * Simple steatosis or non-alcoholic fatty liver
  * NASH (steatosis, inflammation, hepatocellular ballooning)
    * With or without fibrosis
  * Cirrhosis
  * Hepatocellualr carcinoma

NAFLD fibrosis score calculation

Non-Alcoholic Fatty Liver Disease	−1.675 + 0.0373 x age + 0.0943 x BMI + 1.13 x IFG or diabetes (yes = 1, no = 0) + 0.99 x (AST/ALT) ratio − 0.013 x platelet − 0.66 x albumin	Low risk of fibrosis: < −1.455 Intermediate risk of fibrosis: −1.455–0.676 High risk of fibrosis: >0.676
Example	−1.675 + 0.0373 x 38 + 0.0943 x 26 + 1.13 x IFG or diabetes (yes = 1, no = 0) + 0.99 x (28/21) ratio − 0.013 x 163 − 0.66 x 4.6 = -1.6408 (If "yes" = -0.5108)	

Fibrosis-4 (FIB-4)

* Age, AST, ALT and platelet count
* FIB-4 outperformed the following calculations for the diagnosis of advanced fibrosis :
  * NAFLD fibrosis score
  * APRI
  * age/platelet index
  * AST/ALT ratio
  * BARD score
  * Nippon score
* Thought to distinguish NASH from simple steatosis

Fibrosis-4 (FIB-4)

* (Age[years] × AST[U/L])/(platelet $X\sqrt{}$ALT[U/L])

NASH

* Fib4 score < 1.30 = F0-F1 (80% positive predictive value)
* Fib4 score > 2.67 = F3-F4 (90% negative predictive value)

Hep C

* FIB-4 < 1.45: absence of cirrhosis
* FIB-4 between 1.45 - 3.25: inconclusive
* FIB-4 > 3.25: cirrhosis

Predictive Values of FIB-4 Index Scores for Advanced Fibrosis (stage 3–4)*

	Low cutoff point (<1.30)	Indeterminate (1.30–2.67)	High cutoff point (>2.67)	Total
Total	327	163	51	541
No advanced fibrosis	294	112	10	416
Advanced fibrosis	33	51	41	125
Sensitivity	74%		33%	
Specificity	71%		98%	
Positive predictive value	43%		80%	
Negative predictive value	90%		83%	
Interpretation	Absence of advanced fibrosis		Presence of advanced fibrosis	

* Shah, Amy G, Alison Lydecker, Karen Murray, Brent N. Tetri, Melissa J. Contos, and Arun J. Sanyal. 2009. "USE OF THE FIB4 INDEX FOR NON-INVASIVE EVALUATION OF FIBROSIS IN NONALCOHOLIC FATTY LIVER DISEASE." *Clinical Gastroenterology and Hepatology : The Official Clinical Practice Journal of the American Gastroenterological Association* 7 (10): 1104–12. doi:10.1016/j.cgh.2009.05.033.

Fibrosis-4 (FIB-4)

NASH	(Age[years] × AST[U/L])/(platelet X√ALT[U/L])	Fib4 score < 1.30 = F0-F1 Fib4 score > 2.67 = F3-F4
Example	(45 × 36)/(250 X√36) = 1.08	

Original article

A novel model using mean platelet volume and neutrophil to lymphocyte ratio as a marker of nonalcoholic steatohepatitis in NAFLD patients: multicentric study

NASH patients had an increased N/L ratio compared with non-NASH cases (2.6±1.1 and 1.9±0.7 fl, respectively, P<0.001).

The N/L ratio correlated positively with NAFLD activity score, proinflammatory cytokines, and CRP (P<0.001).

In addition, patients with advanced fibrosis (F3-4) had an N/L ratio (2.5±1.1) comparable with that of patients with early fibrosis (F1-2) (1.8±0.9) (P<0.001).

N/L Ratio statistically significant at a cut-off of 2.4

- Neutrophils of 65 and Lymphocytes of 27 (65/27 = 2.4)

Correspondence to Ahmed Abdel-Razik, MD, Tropical Medicine Department, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt
Tel: +20 100 790 1009; fax: +20 507 735 222;
e-mail: ahmedabdelrazik76@gmail.com
Received 22 July 2015 Accepted 17 August 2015

carcinoma patients [10]. This ratio incorporates data on two different immune pathways – the lymphocytes that expound the regulatory pathway and the neutrophils that are responsible for continuous inflammation [11].

DOI: 10.1097/MEG.0000000000000486

Calculating RBC Lifespan

* Red Blood Cell Survival (days) = 100/[reticulocytes (percent)/reticulocyte life span (days)]

* Helpful in determining accuracy of hemoglobin A1C
  * Longer-lived RBC, leads to more hemoglobin, and thus a falsely elevated HbA1C (false positive)
  * Shorter-lived RBC, leads to less hemoglobin, and thus a falsely decreased HbA1C (false negative)

Reticulocyte Count

* Reticulocytes are early red blood cells that are formed in the bone marrow, enter the blood stream and, after 1-2 days become fully matured red blood cells.
* They do not contain a nucleus, but rather have nucleic acid remnants, which are not found in fully formed red blood cells.
* Reticulocytes tend to be elevated in blood loss and/or hemolytic anemia but normal, or even low, in anemia of nutrient deficiency
  * Poor RBC production due to low nutrient deficiency – they cannot make more
  * But respond rapidly to nutrient supplementation by increasing production
    * Thus reticulocytes can be helpful in seeing if nutrient supplementation is working or not

Reticulocyte count - Increased

Cause	Reason	Additional Inquiry
Hemolytic anemia	Breakdown of red blood cells leads to low oxygen state, which is sensed by the kidneys and increases EPO production	
Blood loss	Same	Client history.

Reticulocyte count - Decreased

Cause	Reason	Additional Inquiry
Untreated nutrient deficiency anemia (iron, B12)	Nutrient deficiency leads to poor RBC production, despite attempts by the body to increase production	Evaluate nutrient-related markers.
Anemia of inflammation	Inflammation suppresses the ability to make more red blood cells.	Evaluate other inflammatory markers.
Alcoholism	Causes nutrient deficiency	History

Calculating RBC Lifespan

Reticulocyte count: 0.8%
Hematocrit: 45

Correction of Reticulocyte Count	
Hematocrit (%)	Reticulocyte Life Span (RLS)
36-45	1.0
26-35	1.5
16-25	2.0
<15	2.5

Adapted from Harrisons Principles of Internal Medicine, 18th edition.

Thus your equation would look like this:

100/[0.8/1] = 125 days

Summary

* Osmolarity (dehydration)
* Viscosity
* Liver dysfunction
  * Fatty liver
  * Fibrosis
* RBC Lifespan

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