

EDITORIAL

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“The metabolic syndrome... is dead”: These reports are an exaggeration

Alexander Tenenbaum^{1,2,3*}, Enrique Z Fisman^{1,2}

Abstract

The debates continue over the validity of the metabolic syndrome concept. The continuous increment of the obesity pandemic is almost worldwide paralleled by rising rates of metabolic syndrome prevalence. Then, it seems obvious that these debates drove the need for further investigations as well as a deeper cooperation between relevant national and international organizations regarding the issue. Instead, part of the scientific community elected to totally “dismiss” the concept of the metabolic syndrome. Meanwhile, *the best available evidence* from three consecutive large meta-analyses has systematically shown that people with metabolic syndrome are at increased risk of cardiovascular events. The most recent and largest of them included near one million patients (total n = 951,083). The investigators concluded that the metabolic syndrome is associated with a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality rates. One of the ways to hit the metabolic syndrome is an utterly simplistic view on this concept as a predictive tool only. Of course, the presence of the metabolic syndrome possesses a definite predictive value, but first of all it is a widely accepted concept regarding a biological condition based on the complex and interrelated pathophysiological mechanisms starting from excess central adiposity and insulin resistance. Therefore, it is completely unfair to compare it with statistically constructed predictive tools, including stronger prognostic variables even unrelated to each other from the biological point of view. For example, in the criteria for metabolic syndrome (in contrast to Framingham score) age and cholesterol - presumably low density lipoprotein - cholesterol (LDL-C) - levels are not included, as well as a variety of strong predictors used in other risk-stratification scores: previous myocardial infarction, heart failure, smoking, family history, etc. However, the metabolic syndrome identifies additional important residual vascular risk mainly associated with insulin resistance and atherogenic dyslipidemia (low high density lipoprotein-cholesterol (HDL-C), high triglycerides, small, dense LDL-C). Therefore, the metabolic syndrome could be a useful additional contributor in estimation of global cardiovascular risk beyond age, high LDL-C or other standard risk factors. The components of the metabolic syndrome have partially *overlapping* mechanisms of pathogenic actions mediated through common metabolic pathways. Therefore their total combined effect could be less than the summed of the individual effects. The concept that the metabolic syndrome is a consequence of obesity and insulin resistance, provides a useful “life-style changes” approach for prevention and treatment: caloric restriction, weight-loss and increased physical activity. The next step could theoretically be pharmacological interventions such as metformin, acarbose, fibrates, weight-loss drugs (currently only orlistat is practically available) and perhaps glucagon-like peptide-1 agonists. A third step should probably be kept for bariatric surgery.

The diagnostic criteria for the metabolic syndrome are not ideal. Controversy continues over the validity of its naming, as well as disagreement over its relevance as a practical clinical tool. One of the important questions which still remain open is its predictive value: does the metabolic syndrome forecast cardiovascular events,

diabetes or disease progression any better than the sum of its components?

The continuous increment of the obesity pandemic is almost worldwide paralleled by rising rates of metabolic syndrome prevalence. Then, it seems obvious that these debates drove the need for further investigations as well as a deeper cooperation between relevant national and international organizations aiming to improve and unify the terms [1,2]. Surprisingly, part of the scientific community

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elected to totally “dismiss” the concept of the metabolic syndrome instead [3-5].

Meanwhile, *the best available evidence* from three consecutive large meta-analyses systematically had shown that people with metabolic syndrome are at increased risk of cardiovascular events [6-8]. The most recent and largest of them [8] included near one million patients (total n = 951,083). The investigators concluded that the metabolic syndrome is associated with a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality rates. The meta-analysis showed that the point estimates for cardiovascular risk were consistently higher in women vs. men. A very important finding of this study demonstrated that cardiovascular risk was still high in patients with the metabolic syndrome but without diabetes.

The prognostic importance of the metabolic syndrome, compared with that of the sum of its individual components has repeatedly been challenged [5,9,10]. For example, in a cohort study of 2,815 patients [9], the risk of cardiovascular disease (CVD) mortality associated with the metabolic syndrome (HR: 2.53; 95% CI: 1.74 to 3.67) was similar to the risk associated with impaired fasting glucose (HR: 2.87; 95% CI: 1.96 to 4.20). However, it seems that most of the published reports indicate that the syndrome predicts cardiovascular events or/and diabetes independently from other conventional risk factors [11-16]. Our group has shown that metabolic syndrome is a strong independent predictor of mortality and morbidity in patients with acute coronary syndrome [16]. It should be specifically pointed out that patients with hyperglycemia and metabolic syndrome had higher mortality rates compared with patients with the same hyperglycemia but without metabolic syndrome (for example 30-day mortality rates respectively 8.3% vs. 2.5%, $p < 0.05$)!

This situation resembled the old and long-lasting discussion regarding clinical significance of insulin resistance: over the past years it has been recognized that insulin resistance is an independent risk factor for the development of type 2 diabetes mellitus, whereas its association with major cardiovascular events remained controversial. We have previously demonstrated the independent association of insulin resistance with major cardiovascular events and mortality [17]. After multivariable adjustments, measurable effect of insulin resistance was somewhat attenuated but remained significant. Similarly, insulin resistance was associated with >2-fold increased age-adjusted risk for the development of diabetes in nondiabetic subjects. After adjustment for multiple potential confounders, the prediction conferred by the insulin resistance for new diabetes was substantially attenuated, mainly after inclusion of body mass index in the model, remaining yet strongly significant. Consequently, insulin resistance and body mass

index are most likely associated with diabetes development by partially (but not completely) reciprocated mechanisms.

One of the ways to hit the metabolic syndrome is an utterly simplistic view on this concept as a predictive tool only. Of course, the presence of the metabolic syndrome possesses a definite predictive value, but first of all it is a widely accepted concept regarding a biological condition based on the complex and interrelated pathophysiological mechanisms starting from excess central adiposity and insulin resistance. Therefore, it is completely unfair to compare it with statistically constructed predictive tools, including stronger prognostic variables even unrelated to each other from the biological point of view. For example, in the criteria for metabolic syndrome (in contrast to Framingham score) age and cholesterol (presumably LDL-C) levels are not included, as well as a variety of strong predictors used in other risk-stratification scores: previous myocardial infarction, heart failure, smoking, family history, etc. However, the metabolic syndrome identifies additional important residual vascular risk mainly associated with insulin resistance and atherogenic dyslipidemia (low HDL-C, high triglycerides, small dense LDL-C). Therefore, the metabolic syndrome could be a useful additional contributor in estimation of global cardiovascular risk beyond age, high LDL-C or other standard risk factors.

Moreover, even critics of the metabolic syndrome concept should agree that obesity, dysglycemia, dyslipidemia and hypertension coexist more frequently than predicted by chance. These common chronic conditions (and components of the metabolic syndrome) have partially *overlapping* mechanisms of pathogenic actions mediated through common metabolic pathways. Therefore their total combined effect could be less than the summed of the individual effects.

People with the metabolic syndrome usually pass through the phases of excessive adipogenesis (obesity), nuclear peroxisome proliferator-activated (PPAR) receptors modulation, insulin resistance, hyperinsulinemia, impaired glucose postprandial and fasting levels [2,18-22]. Fasting glucose is presumed to remain normal or borderline as long as insulin hypersecretion can compensate for insulin resistance. The fall in insulin secretion (due to pancreatic beta cells stress and damage) leading to hyperglycemia occurs as a late phenomenon and, in fact, separates the patients with metabolic syndrome from those with or without overt diabetes.

Development of insulin resistance in consequence of excess central adiposity has been considered to be key event in the origin and progression of the metabolic syndrome. It represents a complex interaction of maladaptive characteristics related to impaired insulin action at target organs and external factors such as genetics

and environment. It is likely that the molecular factors that underlie insulin resistance (mediated in part via nuclear PPAR) contribute for many of the clinical components of the metabolic syndrome, although the precise associations remain still weakly understood [2,21,23-26].

Emerging multiple areas of metabolic syndrome research interests include nowadays heterogeneous topics like as adiponectin, angiotensinogen, resistin, and leptin secretion [27-29], nonalcoholic fatty liver disease and liver steatosis [30-32], hyperuricemia [33], genetic predisposition [34,35]; the role of inflammation, interleukins and high-sensitivity C-reactive protein [36-39]; age and gender specific profiles [40,41], the possible ways for treatment optimization [42-47] and several additional matters.

The concept that the metabolic syndrome is a consequence of obesity and insulin resistance, provides a useful "life-style changes" approach for prevention and treatment: caloric restriction, weight-loss and increased physical activity. The next step could theoretically be pharmacological interventions such as metformin, acarbose, fibrates, weight-loss drugs (currently only orlistat is practically available) and perhaps glucagon-like peptide-1 agonists [48-52]. A third step should probably be kept for bariatric surgery [53,54].

In conclusion, currently available evidences strongly support the evolving concept of the metabolic syndrome as an important clustering of the cardiovascular risk factors and diabetes. Resembling Mark Twain's renowned saying [55], the reports of its death are an exaggeration. The recognition, prevention, and treatment of the metabolic syndrome and its underlying risk factors should become an important approach for the reduction of cardiovascular disease burden in the general population. However, future problem-oriented research is needed to improve and unify the diagnostic criteria for the syndrome, its genetic and environmental basis and the optimal medical management.

Abbreviations

CVD: cardiovascular disease; LDL-C: low density lipoprotein - cholesterol, HDL-C:high density lipoprotein-cholesterol; PPAR: peroxisome proliferator-activated receptor.

Acknowledgements

This work was supported in part by the Cardiovascular Diabetology Research Foundation (RA 58-040-684-1), Holon, Israel.

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Authors' contributions

Both authors have equally contributed in the conception and drafting of the manuscript and read and approved its final version.

Competing interests

The authors declare that they have no competing interests.

Received: 25 January 2011 Accepted: 27 January 2011

Published: 27 January 2011

References

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr, International Diabetes Federation Task Force on Epidemiology and Prevention, National Heart Lung, Blood Institute; American Heart Association, World Heart Federation, International Atherosclerosis Society, International Association for the Study of Obesity: **Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.** *Circulation* 2009, **120**:1640-1645.
2. Eckel RH, Alberti KG, Grundy SM, Zimmet PZ: **The metabolic syndrome.** *Lancet* 2010, **375**:181-183.
3. Kahn R, Buse J, Ferrannini E, Stern M: **The metabolic syndrome: time for a critical appraisal. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes.** *Diabetologia* 2005, **48**:1684-1699.
4. Kahn R: **Metabolic syndrome—what is the clinical usefulness?** *Lancet* 2008, **371**:1892-1893.
5. Sattar N, McConnachie A, Shaper AG, Blauw GJ, Buckley BM, de Craen AJ, Ford I, Forouhi NG, Freeman DJ, Jukema JW, Lennon L, Macfarlane PW, Murphy MB, Packard CJ, Stott DJ, Westendorp RG, Whincup PH, Shepherd J, Wannamethee SG: **Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies.** *Lancet* 2008, **371**:1927-1935.
6. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, Montori VM: **Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies.** *J Am Coll Cardiol* 2007, **49**:403-414.
7. Galassi A, Reynolds K, He J: **Metabolic syndrome and risk of cardiovascular disease: a meta-analysis.** *Am J Med* 2006, **119**:812-819.
8. Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, Rinfret S, Schiffrin EL, Eisenberg MJ: **The metabolic syndrome and cardiovascular risk. A systematic review and meta-analysis.** *J Am Coll Cardiol* 2010, **56**:1113-1132.
9. Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP, San Antonio Heart Study: **National Cholesterol Education Program versus World Health Organization metabolic syndrome in relation to all-cause and cardiovascular mortality in the San Antonio Heart Study.** *Circulation* 2004, **110**:1251-1257.
10. Haring R, Wallaschofski H, Nauck M, Felix SB, Schmidt CO, Dörr M, Sauer S, Wilking G, Völzke H: **Total and Cardiovascular Disease Mortality Predicted by Metabolic Syndrome is Inferior Relative to its Components.** *Exp Clin Endocrinol Diabetes* 2010, **118**:685-691.
11. Sundstrom J, Riserus U, Byberg L, Zethelius B, Lithell H, Lind L: **Clinical value of the metabolic syndrome for long term prediction of total and cardiovascular mortality: prospective, population based cohort study.** *BMJ* 2006, **332**:878-82.
12. Simons LA, Simons J, Friedlander Y, McCallum J: **Does a diagnosis of the metabolic syndrome provide additional prediction of cardiovascular disease and total mortality in the elderly? The Dubbo Study.** *Med J Aust* 2007, **186**:400-403.
13. Guzder RN, Gatling W, Mullee MA, Byrne CD: **Impact of metabolic syndrome criteria on cardiovascular disease risk in people with newly diagnosed type 2 diabetes.** *Diabetologia* 2006, **49**:49-55.
14. Kasai T, Miyauchi K, Kurata T, Okazaki S, Kajimoto K, Kubota N, Daida H: **Impact of metabolic syndrome among patients with and without diabetes mellitus on long-term outcomes after percutaneous coronary intervention.** *Hypertens Res* 2008, **31**:235-241.
15. Dohi T, Miyauchi K, Kasai T, Kajimoto K, Kubota N, Tamura H, Yokoyama T, Kojima T, Yokoyama K, Kurata T, Daida H: **Impact of metabolic syndrome on 10-year clinical outcomes among patients with acute coronary syndrome.** *Circ J* 2009, **73**:1454-1458.

16. Feinberg MS, Schwartz R, Tanne D, Fisman EZ, Hod H, Zahger D, Schwammethal E, Eldar M, Behar S, Tenenbaum A: **Impact of the metabolic syndrome on the clinical outcomes of non-clinically diagnosed diabetic patients with acute coronary syndrome.** *Am J Cardiol* 2007, **99**:667-672.
17. Tenenbaum A, Adler Y, Boyko V, Tenenbaum H, Fisman EZ, Tanne D, Lapidot M, Schwammethal E, Feinberg MS, Matas Z, Motro M, Behar S: **Insulin resistance is associated with increased risk of major cardiovascular events in patients with preexisting coronary artery disease.** *Am Heart J* 2007, **153**:559-565.
18. Tenenbaum A, Motro M, Schwammethal E, Fisman EZ: **Macrovascular complications of metabolic syndrome: an early intervention is imperative.** *Int J Cardiol* 2004, **97**:167-172.
19. Hayden MR, Tyagi SC: **Intimal redox stress: accelerated atherosclerosis in metabolic syndrome and type 2 diabetes mellitus.** *Atherosclerosis*. *Cardiovasc Diabetol* 2002, **1**:3.
20. Porte D Jr, Kahn SE: **Beta-cell dysfunction and failure in type 2 diabetes: potential mechanisms.** *Diabetes* 2001, **50**(Suppl. 1):S160-3.
21. Tenenbaum A, Fisman EZ, Motro M: **Metabolic syndrome and type 2 diabetes mellitus: focus on peroxisome proliferator activated receptors. (PPAR).** *Cardiovasc Diabetol* 2003, **2**:4.
22. Tenenbaum H, Behar S, Boyko V, Adler Y, Fisman EZ, Tanne D, Lapidot M, Schwammethal E, Feinberg M, Matas Z, Motro M, Tenenbaum A: **Long-term effect of bezafibrate on pancreatic beta-cell function and insulin resistance in patients with diabetes.** *Atherosclerosis* 2007, **194**:265-271.
23. Nesto RW: **Correlation between cardiovascular disease and diabetes mellitus: current concepts.** *Am J Med* 2004, **116**(Suppl 5A):11S-22S.
24. Reaven GM: **Role of insulin resistance in human disease (syndrome X): an expanded definition.** *Annu Rev Med* 1993, **44**:121-131.
25. Jadhav S, Petrie J, Ferrell W, et al: **Insulin resistance as a contributor to myocardial ischaemia independent of obstructive coronary atheroma: a role for insulin sensitisation?** *Heart* 2004, **90**:1379-13 83.
26. Cleland SJ, Petrie JR, Small M, Elliott HL, Connell JM: **Insulin action is associated with endothelial function in hypertension and type 2 diabetes.** *Hypertension* 2000, **35**:507-511.
27. Comuzzie AG, Tejero ME, Funahashi T, Martin LJ, Kissebah A, Takahashi M, Kihara S, Tanaka S, Rainwater DL, Matsuzawa Y, MacCluer JW, Blangero J: **The genes influencing adiponectin levels also influence risk factors for metabolic syndrome and type 2 diabetes.** *Hum Biol* 2007, **79**:191-200.
28. Hiuge A, Tenenbaum A, Maeda N, Benderly M, Kumada M, Fisman EZ, Tanne D, Matas Z, Hibuse T, Fujita K, Nishizawa H, Adler Y, Motro M, Kihara S, Shimomura I, Behar S, Funahashi T: **Effects of peroxisome proliferator-activated receptor ligands, bezafibrate and fenofibrate, on adiponectin level.** *Arterioscler Thromb Vasc Biol* 2007, **27**:635-641.
29. Cornier MA, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, Van Pelt RE, Wang H, Eckel RH: **The metabolic syndrome.** *Endocr Rev* 2008, **29**:777-822.
30. Steinvil A, Shapira I, Ben-Bassat OK, Cohen M, Vered Y, Berliner S, Rogowski O: **The association of higher levels of within-normal-limits liver enzymes and the prevalence of the metabolic syndrome.** *Cardiovasc Diabetol* 2010, **9**:30.
31. Tilg H, Moschen A: **Update on nonalcoholic fatty liver disease: genes involved in nonalcoholic fatty liver disease and associated inflammation.** *Curr Opin Clin Nutr Metab Care* 2010, **13**:391-396.
32. Kawamoto R, Tabara Y, Kohara K, Miki T, Kusunoki T, Takayama S, Abe M, Katoh T, Ohtsuka N: **High-sensitivity c-reactive protein and gamma-glutamyl transferase levels are synergistically associated with metabolic syndrome in community-dwelling persons.** *Cardiovasc Diabetol* 2010, **9**:87.
33. Borges RL, Ribeiro AB, Zanella MT, Batista MC: **Uric acid as a factor in the metabolic syndrome.** *Curr Hypertens Rep* 2010, **12**:113-119.
34. Junyent M, Arnett DK, Tsai MY, Kabagambe EK, Straka RJ, Province M, An P, Lai CQ, Parnell LD, Shen J, Lee YC, Borecki I, Ordovas JM: **Genetic variants at the PDZ-interacting domain of the scavenger receptor class B type I interact with diet to influence the risk of metabolic syndrome in obese men and women.** *J Nutr* 2009, **139**:842-848.
35. Garaulet M, Madrid JA: **Chronobiology, genetics and metabolic syndrome.** *Curr Opin Lipidol* 2009, **20**:127-134.
36. Trøseid M, Seljeflot I, Arnesen H: **The role of interleukin-18 in the metabolic syndrome.** *Cardiovasc Diabetol* 2010, **9**:11.
37. Kong AP, Chan NN, Chan JC: **The role of adipocytokines and neurohormonal dysregulation in metabolic syndrome.** *Curr Diabetes Rev* 2006, **2**:397-407.
38. Fisman EZ, Tenenbaum A: **The ubiquitous interleukin-6: a time for reappraisal.** *Cardiovasc Diabetol* 2010, **9**:62.
39. Calabro P, Yeh ET: **Intra-abdominal adiposity, inflammation, and cardiovascular risk: new insight into global cardiometabolic risk.** *Curr Hypertens Rep* 2008, **10**:32-38.
40. Regitz-Zagrosek V, Lehmkuhl E, Mahmoodzadeh S: **Gender aspects of the role of the metabolic syndrome as a risk factor for cardiovascular disease.** *Genet Med* 2007, **4**(Suppl B):S162-177.
41. Moebus S, Balijepalli C, Lösche C, Göres L, von Stritzky B, Bramlage P, Wasem J, Jöckel KH: **Age- and sex-specific prevalence and ten-year risk for cardiovascular disease of all 16 risk factor combinations of the metabolic syndrome - A cross-sectional study.** *Cardiovasc Diabetol* 2010, **9**:34.
42. Tenenbaum A, Motro M, Fisman EZ, Tanne D, Boyko V, Behar S: **Bezafibrate for the secondary prevention of myocardial infarction in patients with metabolic syndrome.** *Arch Intern Med* 2005, **165**:1154-1160.
43. Tenkanen L, Manttari M, Kovanen PT, Virkkunen H, Manninen V: **Gemfibrozil in the treatment of dyslipidemia: an 18-year mortality follow-up of the Helsinki Heart Study.** *Arch Intern Med* 2006, **166**:743-748.
44. Zidek W, Naditch-Brülé L, Perlini S, Farsang C, Kjeldsen SE: **Blood pressure control and components of the metabolic syndrome: the GOOD survey.** *Cardiovasc Diabetol* 2009, **8**:51.
45. Tenenbaum A, Fisman EZ, Boyko V, Benderly M, Tanne D, Haim M, Matas Z, Motro M, Behar S: **Attenuation of progression of insulin resistance in patients with coronary artery disease by bezafibrate.** *Arch Intern Med* 2006, **166**:737-741.
46. Tenenbaum A, Motro M, Fisman EZ, Adler Y, Shemesh J, Tanne D, Leor J, Boyko V, Schwammethal E, Behar S: **Effect of bezafibrate on incidence of type 2 diabetes mellitus in obese patients.** *Eur Heart J* 2005, **26**:2032-2038.
47. Hansen BC, Tigno XT, Benardeau A, Meyer M, Sebokova E, Mizrahi J: **Effects of aleglitazar, a balanced dual peroxisome proliferator-activated receptor alpha/gamma agonist on glycemic and lipid parameters in a primate model of the metabolic syndrome.** *Cardiovasc Diabetol* 2011, **10**:7.
48. Sullivan SD, Ratner RE: **Should the Metabolic Syndrome Patient with Prediabetes Be Offered Pharmacotherapy?** *Curr Diab Rep* 2011.
49. Tenenbaum A, Motro M, Fisman EZ, Schwammethal E, Adler Y, Goldenberg I, Leor J, Boyko V, Mandelzweig L, Behar S: **Peroxisome proliferator-activated receptors ligand bezafibrate for prevention of type 2 diabetes mellitus in patients with coronary artery disease.** *Circulation* 2004, **109**:2197-2202.
50. Lukacova-Zib I, Gopalakrishnan G: **Therapeutic options for the prevention of type 2 diabetes mellitus in the metabolic syndrome.** *Mt Sinai J Med* 2010, **77**:524-532.
51. Tenenbaum A, Fisman EZ: **"If it ain't broke, don't fix it": a commentary on the positive-negative results of the ACCORD Lipid study.** *Cardiovasc Diabetol* 2010, **9**:24.
52. Scott R, O'Brien R, Fulcher G, Pardy C, D'Emden M, Tse D, Taskinen MR, Ehnholm C, Keech A, Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Study Investigators: **Effects of fenofibrate treatment on cardiovascular disease risk in 9,795 individuals with type 2 diabetes and various components of the metabolic syndrome: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.** *Diabetes Care* 2009, **32**:493-498.
53. Pontiroli AE, Laneri M, Veronelli A, Frigè F, Micheletto G, Folli F, Adami G, Scopinaro N: **Biliary pancreatic diversion and laparoscopic adjustable gastric banding in morbid obesity: their long-term effects on metabolic syndrome and on cardiovascular parameters.** *Cardiovasc Diabetol* 2009, **8**:37.
54. Lahsen R, Berry M: **Surgical interventions to correct metabolic disorders.** *Br J Diabetes Vasc Dis* 2010, **10**:143-147.
55. Powers R: *Mark Twain: A Life* New York, NY: Free Press; 2005.

doi:10.1186/1475-2840-10-11

Cite this article as: Tenenbaum and Fisman: "The metabolic syndrome... is dead": These reports are an exaggeration. *Cardiovascular Diabetology* 2011 **10**:11.