

Nutrition, metabolism and colorectal cancer

G. Misciagna · M. G. Caruso · M. Trevisan

Published online: 19 February 2008
© Springer-Verlag 2008

Abstract Colorectal cancer and myocardial infarction are associated at population level and in autoptic studies. Furthermore, they share many blood variables: cholesterol, triglycerides and HDL cholesterol, fructosamine, glycated haemoglobin and glycated apolipoprotein B. These blood variables are intermediates between dietary, mainly saturated fats and high glycemic index and load diets, and colorectal cancer and myocardial infarction. Blood intermediate variables can be used in dietary trials as outcomes, and even to throw light on the pathogenesis of both diseases.

Keywords Diet · Glycated protein · Cancer · Cardiovascular disease

Introduction

Mortality for colorectal cancer (CRC) and for myocardial infarction (MI) are associated at population level [39]. Correa et al. [7] found in an autopsy study on 842 autopsies, that the most extensive atherosclerotic involvement of the aorta was in subjects with adenomatous polyps of the colon, and even more in subjects with adenomatous and

hyperplastic polyps together. Furthermore, Stemmerman [35] in an autopsy study on 288 autopsies found that the degree of the atherosclerosis of the coronary arteries and aorta was positively and significantly related not only to the presence of adenomatous polyps, but also to their size, multiplicity and degree of atypia as well.

MI and CRC can share a common cause, a common intermediate factor or both. In this review we explore the possibility that MI and CRC not only share some common cause, but also some common intermediate factors.

Metabolism, myocardial infarction and colorectal cancer

It is known that MI is associated with high blood cholesterol, LDL cholesterol and triglycerides and low HDL cholesterol [22], however these associations are weaker and even uncertain in old people [29]. Furthermore, MI is associated with the metabolic syndrome and with diabetes [15].

In non-diabetic subjects, MI is associated with HbA1c [16], as well as with fructosamine, an index of glycated proteins in the blood, at least in women [4], and with glycated apolipoprotein B [28].

Several studies have evaluated the association between serum cholesterol and colorectal adenomatous polyps or carcinoma in situ [1, 2, 8, 13, 19, 20, 24, 40]. Most but not all of these studies found an association of colorectal adenoma or cancer in situ with serum cholesterol. Serum triglycerides were associated with colorectal adenoma [25, 32], and with colorectal cancer in situ [40]. CRC was found associated with the metabolic syndrome [6, 37]. CRC and adenomas are associated with diabetes or prediabetes [14, 17, 18, 21, 23, 30, 33, 38, 41]. We found that fructosamine is associated with colorectal adenoma [27], as well as

G. Misciagna (✉)
Laboratory of Epidemiology, IRCCS De Bellis,
Castellana Grotte, Bari 70013, Italy
e-mail: gmisciag@libero.it

M. G. Caruso
Laboratory of Biochemistry, IRCCS De Bellis,
Castellana Grotte, Bari 70013, Italy

M. Trevisan
University of Nevada, Health Sciences System,
Las Vegas, NV, USA

glycated apolipoprotein B with colorectal adenoma and cancer (Misciagna et al., unpublished data).

Diet, myocardial infarction and colorectal cancer

The association of both MI and CRC with blood lipids and non enzymatic glycated serum proteins also in non diabetic subjects allows to study the effects of diet on MI and CRC through the effects of diet on these intermediate variables. Cholesterol, triglycerides and HDL cholesterol are influenced by both saturated fats and sugars in the diet [5, 9], glycated haemoglobin is influenced by saturated fats in the diet [3, 11, 12], fructosamine by glycemic index and load [26], as well as glycated apolipoprotein B (Misciagna et al., unpublished data). All these results show that MI and CRC are associated with a diet rich in saturated fats and at high glycemic index and load.

Conclusions

The results of many epidemiological studies show that MI and CRC share many intermediate variables: cholesterol, cholesterol HDL, triglycerides, glycated haemoglobin and apolipoprotein B, fructosamine. Furthermore, using the relationship of diet with these intermediate blood variables, it is possible to deduce that dietary saturated fats, glycemic index and load are associated with CRC and MI. The discovery of blood intermediate variables between diet and MI and CRC can open the way to trials of the effects of diet on these variables, to add evidence to the results of the observational epidemiological studies on diet and cardiovascular diseases or colorectal cancer.

Myocardial infarction and colorectal cancer share some dietary causes and intermediate variables, do they share also some pathogenetic mechanisms ?

Glycated ApoB has been found in the macrophages of the arterial wall, in the fatty streaks of atherosclerotic vessels [36]. In fact, macrophages prefer glycated, oxidized or glyco-oxidized lipoproteins for their scavenger receptors, not the normal ones [34].

It is known that neoplastic cells behave like a macrophage and have a strong phagocytic activity [10, 31], so may be colorectal cancer too, like the macrophages of the arterial wall in atherosclerosis, “eats” glycated lipoprotein.

References

1. Bayerdorffer E, Mannes GA, Richter WO, et al (1993) Decreased high-density lipoprotein cholesterol and increased low-density cholesterol levels in patients with colorectal adenomas. *Ann Int Med* 118:481–487
2. Bird CL, Ingles SA, Frankl HD, Lee ER, Longnecker MP, Haile RW (1996) Serum lipids and adenoma of the left colon and rectum. *Cancer Epidemiol Biomark Prev* 5:607–612
3. Boeing H, Weisgerber UM, Jeckel A, Rose HJ, Kroke A (2000) Association between glycated hemoglobin and diet and other lifestyle factors in a non diabetic population: cross-sectional evaluation of data from the Potsdam cohort of the EPIC Study. *Am J Clin Nutr* 71:1115–1122
4. Browner WS, Pressman AR, Lui LY, Cummings SR (1999) Association between serum fructosamine and mortality in elderly women: the study of osteoporotic fractures. *Am J Epidemiol* 149:471–475
5. Chong MF, Fielding BA, Frayn KN (2007) Metabolic interaction of dietary sugars and plasma lipids with a focus on mechanisms and de novo lipogenesis. *Proc Nutr Soc* 66:52–59
6. Colangelo LA, Gapstur SM, Gann PH, Dyer AR, Liu K (2002) Colorectal cancer mortality and factors related to the insulin resistance syndrome. *Cancer Epidemiol Biomark Prev* 11: 385–391
7. Correa P, Strong JP, Johnson WD, Pizzolato P, Haenszel W (1982) Atherosclerosis and polyps of the colon. Quantification of precursors of coronary heart disease and colon cancer. *J Chronic Dis* 35:313–320
8. Demers RY, Neale AV, Demers P, et al (1988) Serum cholesterol and colorectal polyps. *J Clin Epidemiol* 41:9–13
9. Denke MA (2006) Dietary fats, fatty acids, and their effects on lipoproteins. *Curr Atheroscler Rep* 8:466–471
10. Fais S (2007) Cannibalism: a way to feed on metastatic tumors. *Cancer Lett* 258:155–164
11. Gulliford MC, Ukoumunne OC (2001) Determinants of glycated haemoglobin in the general population: association with diet, alcohol and cigarette smoking. *Eur J Clin Nutr* 55:615–623
12. Harding AH, Sargeant LA, Welch A, et al (2001) Fat consumption and HbA1c levels. *Diabetes Care* 24:1911–1916
13. Houghton J, Lardieri GG, Zauber P, Kim KH, Cable G (2000) Effect of cholesterol levels on villous histology in colonic adenomas. *Dig Dis Sci* 45:896–899
14. Hu FB, Manson JE, Liu S, et al (1999) Prospective study of adult onset diabetes mellitus (type 2) and risk of colorectal cancer in women. *J Natl Cancer Inst* 91:542–547
15. Hu G, Qiao Q, Tuomilehto J (2005) Metabolic syndrome, diabetes, and coronary heart disease. In: Qiao Q, Tuomilehto J, Marmot M, Elliott P (eds) *Coronary heart disease epidemiology*. 2nd edn. Oxford University Press, New York pp 311–330
16. Khaw KT, Wareham N, Bingham N, Luben R, Welch A, Day N (2004) Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. *Ann Intern Med* 141:413–420
17. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N (2004) Preliminary communication: glycated hemoglobin, diabetes, and incident colorectal cancer in men and women: a prospective analysis from the European prospective investigation into cancer-Norfolk study. *Cancer Epidemiol Biomarkers Prev* 13:915–919
18. Kono S, Honjo S, Todoroki I, et al (1998) Glucose intolerance and adenomas of sigmoid colon in Japanese men. *Cancer Causes Control* 9:441–446
19. Kono S, Imanishi K, Shinchi K, Yanai F (1993) Serum lipids and left-sided adenomas of the large bowel: An extended study of self-defense official in Japan. *Cancer Causes Control* 4:117–121
20. Kono S, Ikeda N, Yanai F, Yamamoto M, Shigematsu T (1990) Serum lipids and colorectal adenoma among male self defence officials in northern Kyushu, Japan. *Int J Epidemiol* 19:274–278
21. La Vecchia C, Negri E, Decarli A, Franceschi S (1997) Diabetes mellitus and colorectal cancer risk. *Cancer Epidemiol Biomark Prev* 6:1007–1010

22. Law MR, Rodgers A (2005) Lipids and cholesterol. In: Marmot M, Elliott P (eds) *Coronary heart disease epidemiology*. 2nd edn. Oxford University Press, New York, pp 174–186
23. Levine W, Dyer AR, Shekelle RB, Schoenberger JA, Stamler J (1990) Post-load plasma glucose and cancer mortality in middle-aged men and women. 12-year follow up findings of the Chicago heart association detection project in industry. *Am J Epidemiol* 131:254–262
24. Mannes GA, Maier A, Thieme C, Wiebecke B, Paumgartner G (1986) Relation between the frequency of colorectal adenoma and the serum cholesterol level. *N Engl J Med* 315:1634–1638
25. McKeown-Eyssen GE, and the Toronto Polyp Prevention Group (1996) Insulin resistance and the risk of colorectal neoplasia. *Cancer Epidemiol Biomark Prev* 5:235–247
26. Misciagna G, De Michele G, Cisternino AM, Guerra V, Logroscino G, Freudenheim JL (2005) Dietary carbohydrates and glycosylated proteins in the blood in non diabetic subjects. *J Am Coll Nutr* 24:22–29
27. Misciagna G, De Michele G, Guerra V, Cisternino AM, Di Leo A, Freudenheim JL, INTEROSP Group (2004) Serum fructosamine and colorectal adenomas. *Eur J Epidemiol* 19:425–432
28. Misciagna G, Logroscino G, De Michele G, Guerra V, Cisternino AM, Caruso MG, Trevisan M (2007) Glycosylated apolipoprotein B and myocardial infarction. *Nutr Metab Cardiovasc Dis* 17:6–12
29. Ravnskov U (2000) The cholesterol myths. *New Trends Publishing*, Washington DC, pp 47–95
30. Sandhu MS, Luben R, Khaw KT (2001) Self reported noninsulin dependent diabetes, family history, and risk of 431 prevalent colorectal cancer: population based, cross sectional study. *Gut* 42:804–805
31. Sato K, Tsuchihara K, Fujii S, Sugiyama M, Goya T, Atomi Y, Ueno T, Ochiai A, Esumi H (2007) Autophagy is activated in colorectal cancer cells and contributes to the tolerance to nutrient deprivation. *Cancer Research* 67:9677–9684
32. SchoenBird CL, Ingles SA, Frankl HD, Lee ER, Longnecker MP, Haile RW (1996) Serum lipids and adenoma of the left colon and rectum. *Cancer Epidemiol BiomarkPrev* 5:607–612
33. Smith GD, Egger M, Shipley MJ, Marmot MG (1992) Postchallenge glucose concentration, impaired glucose tolerance, diabetes, and cancer mortality in men. *Am J Epidemiol* 136:1110–1114
34. Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL (1989) Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med* 320:915–924
35. Stemmerman GN, Heilbrun LK, Nomura AMY, Yano K, Hayashi T (1986) Adenomatous polyps and atherosclerosis: an autopsy study of Japanese men in Hawaii. *Int J Cancer* 38:789–794
36. Stitt AW, He C, Friedman S, Scher L, Rossi P, Ong L, et al (1997) Elevated AGE-modified ApoB in sera of euglycemic, normolipidemic patients with atherosclerosis: relationship to tissue AGEs. *Mol Med* 3:617–627
37. Trevisan M, Liu J, Muti P, Misciagna G, Menotti A, Fucci F, RIFLE Group (2001) Markers of insulin resistance and colorectal cancer mortality. *Cancer Epidemiol Biomark Prev* 10:937–941
38. Will JC, Galuska DA, Vinicor F, Calle EE (1998) Colorectal cancer: another complication of diabetes mellitus? *Am J Epidemiol* 147:816–825
39. Wynder EL, Shigematsu T (1967) Environmental factors of cancer of the colon and rectum. *Cancer* 20:1520–1561
40. Yamada K, Araki S, Tamura M, et al (1998) Relation of serum total cholesterol, serum triglycerides and fasting plasma glucose to colorectal carcinoma in situ. *Int J Epidemiol* 27:794–798
41. Zeliniuch-Jacquotte A, Shore RE, Riboli E (2000) Serum C peptide, insulin-like growth factor (IGF)-I, IGF-binding proteins, and colorectal cancer risk in women. *J Natl Cancer Inst* 92:1592–1600