Dairy consumption and the incidence of hyperglycemia and the metabolic syndrome: results from a french prospective study, Data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR).

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Frédéric Fumeron [1 *], Amel Lamri [1], Charbel Abi Khalil [1 2], Riphed Jaziri [1], Isabelle Porchay-Baldérelli [1], Olivier Lantieri [3], Sylviane Vol [3], Beverley Balkau [4], Michel Marre [1 2]

[1] *Déterminants génétiques du diabète de type 2 et de ses complications vasculaires INSERM : U695 , Université Paris VII - Paris Diderot , Faculte de Medecine Xavier Bichat 16, Rue Henri Huchard 75018 PARIS,FR*

[2] *Service d'endocrinologie, diabétologie et nutrition Assistance publique - Hôpitaux de Paris (AP-HP) , Hôpital Bichat - Claude Bernard , Université Paris VII - Paris Diderot , Paris,FR*

[3] *IRSA, Institut Inter Regional pour la santé IRSA , La Riche,FR*

[4] *CESP, Centre de recherche en épidémiologie et santé des populations INSERM : U1018 , Université Paris XI - Paris Sud , Université de Versailles Saint-Quentin-en-Yvelines , INED , FR*

* Correspondence should be adressed to: Frédéric Fumeron <frederic.fumeron@inserm.fr >

Abstract

Objective

In the French D.E.S.I.R. cohort, cross-sectional analyses have shown that a higher consumption of dairy products and calcium are associated with a lower prevalence of the metabolic syndrome (MetS). We assess the influence of dairy products on 9-year incident MetS and on impaired fasting glycaemia and/or type 2 diabetes (IFG/T2D).

Research Design and Methods

3435 men and women who completed a food frequency questionnaire at baseline and after 3 years were studied. Logistic regression models were used to study associations between the average year 0 and year 3 consumption of milk and dairy products, cheese, and of dietary calcium density, and incident MetS and IFG/T2D after adjusting for 1) sex, age, alcohol, smoking, physical activity, fat intake and 2) additionally for BMI. Associations between dairy products and continuous variables were studied by repeated measures ANCOVA, using the same covariates.

Results

Dairy products other than cheese, and dietary calcium density, were inversely associated with incident MetS and IFG/T2D; cheese was negatively associated with incident MetS. All three parameters were associated with lower diastolic blood pressure, and with a lower BMI gain. Higher cheese intake and calcium density were associated with a lower increase in waist circumference and lower triglyceride levels. Calcium density was also associated with a lower systolic blood pressure and a lower 9-y increase in plasma triglycerides levels.

Conclusion

A higher consumption of dairy products and calcium was associated with a lower 9-year incidence of MetS and IFG/T2D in a large cohort drawn from the general population.

MESH Keywords Adult ; Aged ; Calcium, Dietary ; Dairy Products ; Female ; Humans ; Hyperglycemia ; epidemiology ; Insulin Resistance ; physiology ; Male ; Metabolic Syndrome X ; epidemiology ; Middle Aged ; Prospective Studies ; Questionnaires

The metabolic syndrome (MetS) is a cluster of metabolic disorders, including central obesity, glucose intolerance (impaired fasting glucose, impaired glucose tolerance, type 2 diabetes), dyslipidemia (low HDL cholesterol, high triglyceride levels), high blood pressure. All of its components are risk factors for cardiovascular disease (CVD). Although fats from dairy products are rich in saturated fatty acids, there is no clear evidence that dairy food is associated with a high risk of CVD (1). An explanation is that dairy consumption has been found to be inversely associated with MetS traits in cross-sectional as well as prospective studies. In the French population from the D.E.S.I.R. cohort, cross-sectional analyses have shown that a higher consumption of dairy products or calcium was associated with a lower prevalence of the MetS (2 , 3). In the CARDIA study of young adults, the highest consumption of dairy products was associated with a 70 % reduction in the risk of incident metabolic syndrome over a period of 10 years, when compared to the group with the lowest consumption (4). However, these results were not always found. In an elderly Dutch population from the Hoorn study with a 6.4-year

follow-up, a higher dairy consumption did not protect against weight gain nor development of metabolic disturbances (5). The aim of our study was to assess the influence of dairy products on the nine year cumulative incidence of the MetS and impaired fasting glucose or type 2 diabetes (IFG/T2D) as well as on associated traits, in the French population-based prospective study with a 9-year follow-up, D.E.S.I.R..

Research Design and Methods

Population

The D.E.S.I.R. study (Data from an Epidemiological Study on the Insulin-Resistance syndrome) is a prospective study of 5212 subjects at inclusion (2,576 men and 2,636 women, aged 30 to 65 years), recruited from volunteers who were offered periodic health examinations free of charge by the French Social Security system in 10 health examination centres from the western part of France. They were clinically and biologically evaluated at 3-yearly visits and the final examination was 9 years after inclusion. For the purpose of these analyses, diabetic subjects at entry were excluded. In addition, subjects who declared that they were on a diet and those who did not answer all the questions in the food frequency questionnaire were excluded. In consequence, the 3435 subjects (1710 men, 1725 women) with a food frequency questionnaire at baseline and/or at three years remained for this study. The study was approved by the ethics committee of the Kremlin Bicêtre Hospital, and all participants signed an informed consent.

Measurements

Weight, height, and waist circumferences were measured by trained personnel. Venous blood samples were collected in the morning after subjects had fasted for 12 h. Systolic and diastolic arterial pressures were measured after 5 min of rest in participants in a supine position with a mercury sphygmomanometer adapted for arm size. Two measures of blood pressure were taken, and means were used for the analysis. A detailed description of laboratory measurements including fasting triglycerides, HDL-C, glucose, and insulin is provided elsewhere (6).

In the present work, two definitions for the MetS were used. According to the IDF (International Diabetes Federation) (7), it was defined as waist circumference ≥ 94/80 cm for men/women plus two of the following factors: 1) elevated triglycerides: ≥ 1.70 mmol/l or specific treatment for this lipid abnormality; 2) reduced HDL cholesterol (HDL-C): ≤ 1.03 mmol/l for men and 1.29 mmol/l for women or specific treatment for this lipid abnormality; 3) elevated blood pressure: ≥ 130/85mmHg or treatment of previously diagnosed hypertension; 4) elevated fasting glycemia ≥ 5.6 mmol/l or previously diagnosed type 2 diabetes (treated by glucose lowering drugs and/or fasting glycemia ≥ 7.0 mmol/l). According to the NCEP-ATPIII (8), it was defined as three of the following factors: 1) waist circumference > 102/88 cm for men/women; 2) elevated triglycerides: ≥ 1.70 mmol/l; 3) reduced HDL-C: ≤ 1.03 mmol/l for men and 1.29 mmol/l for women; 4) elevated blood pressure: systolic blood pressure ≥ 130 or diastolic ≥ 85mmHg; 5) elevated fasting glycemia ≥ 6.1 mmol/l.

Type 2 diabetes (T2D) was defined as fasting plasma glucose ≥ 7 mmol/l or treatment by anti-diabetic agents. Impaired fasting glucose (IFG) was defined as fasting plasma glucose between 6.1 and 6.9 mmol/l. Incident cases for MetS and/or IFG/T2D were defined as subjects free of disease at entry who developed the disease at any time during the follow-up.

A 23-item questionnaire was completed by each participant, to determine the frequency and level of consumption of different foods. This questionnaire has been validated by comparison with the dietary history method, with 30 minute interviews by trained dieticians. This validation study enabled the determination of multiple linear regression equations to estimate the main nutrient intakes (including calcium) from the questions on the consumption of different foods (9). Two items concerned dairy products: cheese, milk and other dairy products (except cheese). One portion was defined as 30 g for cheese, and 125 mL for milk or milk products. There were four responses for the intake of dairy products (never; < 1 portion/day; 1–2/day; > 2/day; coded 1,2,3,4) and 3 for cheese intake (0–1 portion/day; 2–3/day; > 3/day; coded 1,2,3). Calcium density of the diet was defined as the amount of calcium ingested per 1000kCal (excluding alcohol).

Statistics

Analyses used the average dietary data from year 0 and year 3 to take into account the variability over time; 212 participants with only one dietary record were also included; their exclusion did not change the results, We categorized the dairy intake and the cheese intake in 4 groups and 3 groups respectively, according to their responses at both questionnaires. The dairy intake groups were defined as group 1 for an average response ≤ 2, group 2 for an average response of 2.5, group 3 for an average response of 3, and group 4 for an average response > 3. The cheese intake groups were defined as group 1 for an average response of 1, group 2 for an average response of 1.5, and group 3 for an average response ≥ 2. These limits were chosen in order to have comparable frequencies in the groups. For calcium, we calculated sex specific quartiles of the mean calcium density at T0 and T3 (3). Multiple logistic regression analysis was used to evaluate associations between the dairy consumption variables, and the odds of developing MetS or IFG/T2D during the 9 year study. Two models were used: in model 1, the covariates were age, sex, alcohol consumption (continuous covariate), smoking (yes/no), physical activity (three classes used as a continuous covariate), fat intake (from the questions on the consumption of meat, fish, pork products, fried foods, butter, cheese and other dairy products); in model 2, the same covariates + BMI as a covariate. To take into account the variation in BMI over the 9 years, we

used as covariate the mean of BMI at entry and at 9 years. Odds ratios indicate the risk of a change from one category to the next, e.g. from one quartile of calcium density to the next quartile. ANCOVA with repeated measures was used to test for the average effect of dairy products and the effects on changes between baseline and the end of the follow-up (9 years), adjusted for age, sex, alcohol, smoking, physical activity, fat intake, BMI. Data were log transformed for skewed variables (insulin levels, serum triglycerides). Results are presented as least squares means adjusted for covariates with the SEM, or as geometric means with 95% CI for skewed variables.

Results

The consumption of dairy products other than cheese and the calcium density of the diet were inversely associated with the incidence of the MetS, whatever the definition, and with the incidence of IFG/T2D during the 9-year follow-up (Table 1). The consumption of cheese was negatively associated with the incidence of the MetS (Table 1). The consumption of dairy products other than cheese was associated with the incidence of T2D alone (multiple adjustment without BMI, model 1: OR = 0.82 [95%CI 0.71–0.92]; *P* = 0.02), but this association was no longer significant after taking BMI into account (model 2, *P* =0.07). Neither cheese nor calcium density were associated with T2D alone (data not shown). No interaction with sex was observed nor with overweight at baseline.

The three dairy parameters were associated with lower 9-year diastolic blood pressure, and with lower BMI gain over this period (online-only appendix Tables A1–A3). Higher cheese intake and calcium density were associated with lower triglyceride levels, and a lower 9-y increase in waist circumference both in men and women (online-only appendix Tables A2-A3). Calcium density was also associated with a lower systolic blood pressure and a lower 9-y increase in plasma triglycerides levels (online-only appendix Tables A3). Few significant interaction effects with sex were observed: time changes in systolic blood pressure for dairy intake (online appendix table A1), and insulin levels for calcium density (online appendix table A3), which were significant only in women. Some adverse effects were observed. Intake of dairy products was associated with lower HDL-C levels in men, but the decrease with time was also lower. Intake of cheese was associated with a higher average BMI, but also with a lower increase with time.

Conclusions

In the DESIR prospective study with a 9-year follow-up, we found that the consumption of dairy products and cheese, and dietary calcium density, were associated with a lower incidence of the MetS. The consumption of dairy products, cheese excluded, and calcium intake, were also associated with a lower incidence of IFG or T2D. When looking at phenotypes associated with the MetS, these parameters were also generally associated with a more beneficial profile during the follow-up, or with a better change in profile over the 9-year period. These results support the hypothesis of beneficial effects of milk products on cardiovascular risk, despite their saturated fat content. In a meta-analysis of prospective studies (10), it was shown that milk and dairy consumption was associated with a lower risk of incident vascular events. This might be explained by beneficial associations with the MetS and associated parameters and/or T2D such as those found in the present study and by other groups. In this respect, Warensjo et al. (11) found, in a prospective study, a negative association between the risk of myocardial infarction and biomarkers of milk fat, which disappeared when adjusted for variables related to the MetS (diabetes, blood pressure, BMI).

Our results are consistent with those obtained in the prospective ARIC study (12) where subjects in the highest quintile of dairy consumption had a 13% lower risk of the MetS when compared to the lowest quintile. In another prospective study CARDIA (4), results were similar, but only in the overweight. As stated in the paper by Lutsey et al. (12), the differences between studies may be due to different methods used, for example definition of outcome, population, age, dietary assessment, and statistical methods. Both D.E.S.I.R. and the ARIC studies were in the middle-aged, but CARDIA study was in young adults, 18 to 30 years.

In prospective studies, for men with a 12 year follow-up (13), as in women with a 10 year follow-up (14), there was a negative association between dairy intake and T2D incidence. In these two studies, the association with dairy was mainly due to low-fat dairy. Unfortunately, we do not have specific data on low-fat or high-fat dairy products in our study, but we believe that our results are in accordance with this differential effect as dairy products included milk which is consumed as 80% low-fat and are associated beneficially with IFG/T2D, while cheese which is high-fat is not significantly associated with IFG/T2D risk. In the Nurses Health Study (15), women who consumed three or more servings per day had an 11% lower risk of type 2 diabetes compared with women who consumed less than one serving per day of dairy food. After adjustment for total vitamin D and calcium intake, this association was attenuated, showing that the association with dairy food was due in large part to these nutrients. In D.E.S.I.R. study, the calcium density of the diet was also very significantly associated with IFG/T2D and the MetS, but since it was not directly measured but only calculated from food intake mainly from dairy variables (therefore very linked to the assessment of dairy intake), we could not adjust for this variable in order to test whether the beneficial effects of dairy were due to calcium in D.E.S.I.R. Unfortunately, we do not have data on vitamin D. Compounds other than calcium and vitamin D may be involved in these associations: peptides, conjugates of linoleic acid (1 , 16 , 17).

Dairy consumption and calcium intake have been described in epidemiological studies to be associated with lower BMI or to lower body weight in intervention studies, in humans as well as in animal models (18 , 19). In our longitudinal study, we did not find an overall association with BMI, but there was a lower gain in BMI and/or waist circumference over the 9-year follow-up. A similar finding was

found in the CARDIA study (4) where high dairy intake appeared to protect from weight gain. In contrast, this result was not found in the Hoorn Study (5). In the French SUVIMAX study, a high consumption of dairy products was associated with a lower weight gain over 6 years, but this result was obtained only in overweight men (20). In the D.E.S.I.R. study, no significant interaction with sex was found for BMI changes, but we observed a significant lower BMI gain only in men (P =0.07, 0.05 and 0.002 for dairy products, cheese and calcium density respectively). The effects on BMI did not explain all of the effects on the MetS, as we adjusted for BMI in all our analyses.

Modest but significant effects on triglycerides were found. Nevertheless, no beneficial effect on HDL-C was observed. These results are very similar to those from the CARDIA study (4). The adjustments that we systematically used: BMI, fat intake, physical activity and alcohol, might have lessened or cancelled these associations. Here we observed a negative association between cheese and triglycerides which has been found sometimes (21 , 22), but not always (23 , 24), in cross-sectional studies.

Dairy consumption has generally been associated with low blood pressure. This was found in the cross-sectional analysis of the Hoorn study (24) but not in the prospective data (5). In our study, only the mean effect was found to be significant, but generally there was no effect on changes. Dairy nutrients, notably calcium, have been shown to have a blood pressure lowering effect. Dairy peptides may also act as angiotensin converting enzyme inhibitors (16)

Consistently with the results concerning the MetS and/or IFG/T2D, we found a negative association between the calcium density of the diet and insulin levels. This association which was detected only in women might be explained by the higher dietary calcium density in women than in men (3). A negative trend was also found with cheese intake (P =0.07). In acute effect, milk intake has been associated with higher insulin levels due to insulin-secretagogue peptides, nevertheless, its chronic effect has rather been linked to an improvement in insulin sensitivity, thus presumably, with lower insulinemia. Dairy foods may beneficially alter adiponectin levels independently of changes in body weight (18). This in turn may increase insulin sensitivity and lower insulin levels. It has also been observed that milk and whey appear insulinotropic as an acute effect but addition of fermented milk (yogurt) lowered post-prandial insulin and glucose as compared to a reference meal alone (17). Moreover whey protein was associated with a 40% lower plasma insulin after 6 weeks in insulin resistant rats (17). Biomarkers of milk fat were also negatively associated with plasma insulin (25).

There was no significant interaction between dairy variables and sex on the risk of the MetS or on IFG/T2D (actually the results were very similar, data not shown), and very few significant interactions were observed for associations with continuous variables.

Our study has several strengths but also some limitations. Among the strengths are the prospective nature of the data and the large number of participants included, who were from the general population, and selected with a 1:1 sex ratio and in age strata. Also we were able to adjust for confounders such as lifestyle factors. The relations we observed with the characteristics of the MetS are modest, but they were obtained after adjustment for lifestyle variables, including physical activity, smoking, alcohol consumption and dietary fat intake. Moreover, the adjustments for BMI show that there may be a specific independent effect of dairy intake on the MetS characteristics. The main limitation of our study concerns the dietary questionnaire. We used a semi-quantitative, very simple, self-questionnaire. Nevertheless, it has been validated by a more sophisticated questionnaire (9) and is suitably short to be well answered in an epidemiological study. As with all food-frequency questions, the accuracy of the responses (under- or over-consumption) is difficult to evaluate. We may have over-evaluated the consumption of calcium with a semi-quantitative questionnaire, but the range of our values is not too far removed from the range of intake observed in the 1998–1999 cross-sectional French Enquete INCA (Individuelle et Nationale sur les Consommations Alimentaires) food consumption survey (3). We have used the same food frequency questionnaire, completed at baseline and at the tree year visit, and using mean values will reduce the variability of the responses. Our questionnaire does not allow the separation of low-fat and high-fat products, or to estimate the effects of the different dairy products. However, we could separate cheese from other dairy products. As already stated, it can be assumed that in France, cheese is high-fat, while the milk included in other dairy products is low fat.

In summary, a higher consumption of dairy products and calcium was associated with a lower incidence of the MetS and IFG/T2D during a 9-year follow-up period, in a large cohort drawn from the French general population. This inverse association was observed with many traits of the metabolic syndrome. These results indicate that dairy product consumption could be associated with a lower cardiovascular risk.

Acknowledgements:

This work has been supported by a grant from Centre de Recherche et d'Information Nutritionnelles (CERIN) - Centre National Interprofessionnel de l'Economie Laitière (CNIEL).

F.F. has received support for travelling to scientific meetings from CNIEL. He has also received honoraria for lectures and reviews of the literature from CNIEL.

The D.E.S.I.R. study has been supported by INSERM contracts with CNAMTS, Lilly, Novartis Pharma and Sanofi-Aventis; by INSERM (Réseaux en Santé Publique, Interactions entre les déterminants de la santé), Cohortes Santé TGIR, the Association Diabète Risque Vasculaire, the Fédération Française de Cardiologie, La Fondation de France, ALFEDIAM, CERIN-CNIEL, ONIVINS, Ardix Medical, Bayer Diagnostics, Becton Dickinson, Cardionics, Merck Santé, Novo Nordisk, Pierre Fabre, Roche, Topcon.

The D.E.S.I.R. Study Group. INSERM U1018: B. Balkau, P. Ducimetière, E. Eschwège; INSERM U367: F. Alhenc-Gelas; CHU D'Angers: Y. Gallois, A. Girault; Bichat Hospital: F. Fumeron, M. Marre; CHU Rennes: F Bonnet; CNRS UMR8090, Lille: P. Froguel; Centres d' Examens de Santé: Alençon, Angers, Caen, Chateauroux, Cholet, Le Mans, Tours; Institute de Recherche Médecine Générale: J. Cogneau; General practitioners of the region; Institute inter-Regional pour la Santé: C. Born, E. Caces, M. Cailleau, O Lantieri, J.G. Moreau, F. Rakotozafy, J. Tichet, S. Vol.

Parts of this study were presented in abstract form at the Société Francophone du Diabète (SFD), Lille, France, 16–19 March 2010, and at the 44th annual meeting of the European Association for the Study of Diabetes, Stockholm, Sweden, 20–24 September 2010.

Footnotes:

Author Contributions: F.F. researched data, wrote manuscript, and reviewed manuscript. A.L., C.A.-L., R.J. and I.P.-B. researched data and contributed to discussion. O.L. and S.V. researched data and reviewed/edited manuscript. B.B. and M.M researched data, contributed to discussion, and reviewed/edited the manuscript.

No other potential conflicts of interest relevant to this article were reported.

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Table 1

Incidence of the metabolic syndrome (MetS) and impaired fasting glucose and type 2 diabetes (IFG/T2D) according to dairy product consumption in the D.E.S.I.R. cohort and odds-ratios

		No incident MetS (IDF)	Incident MetS (IDF)	No incident MetS (NCEP)	Incident MetS (NCEP)	No incident IFG/T2D	Incident IFG/T2D
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Dairy products (except cheese)	Group 1 (low)	430 (69.2)	191 (30.8)	568 (81.5)	129 (18.5)	543 (77.5)	158 (22.5)
	Group 2	423 (75.3)	139 (24.7)	525 (84.1)	99 (15.9)	522 (83.8)	101 (16.2)
	Group 3	960 (81.4)	220 (18.6)	1111 (87.3)	162 (12.7)	1126 (87.0)	169 (13.1)
	Group 4 (high)	525 (81.8)	117 (18.2)	608 (90.7)	62 (9.3)	607 (89.1)	74 (10.9)
Odds-ratios (95% CI) *	unadjusted	0.77 (0.71–0.84); $p<10^{-6}$		0.78 (0.70–0.85); $p<10^{-6}$		0.74 (0.68–0.81); $p<10^{-6}$	
	model 1†	0.86 (0.79–0.94); p=0.001		0.84 (0.76–0.93); p=0.0007		0.83 (0.75–0.92); p=0.0003	
	Model 2 ‡	0.88 (0.79–0.97); p=0.01		0.89 (0.79–1.00); p=0.04		0.85 (0.76–0.94); p=0.001	
Cheese	Group 1 (low)	718 (76.7)	218 (23.3)	847 (85.2)	147 (14.8)	868 (85.5)	147 (14.5)
	Group 2 (medium)	511 (76.5)	157 (23.5)	636 (86.2)	102 (13.8)	639 (85.7)	107 (14.3)
	Group 3 (high)	1109 (79.2)	292 (20.8)	1329 (86.7)	203 (13.3)	1291 (83.9)	248 (16.1)
Odds-ratios (95% CI) *	unadjusted	0.93 (0.84–1.02); p=0.14		0.94 (0.84–1.05); p=0.28		1.07 (0.96–1.19); p=0.23	
	Model 1 †	0.90 (0.80–1.00); p=0.06		0.86 (0.76–0.98); p=0.02		0.94 (0.83–1.07); p=0.37	
	Model 2 ‡	0.88 (0.77–1.00); p=0.05		0.82 (0.71–0.95); p=0.008		0.93 (0.82–1.06); p=0.30	
Calcium density	quartile 1	553 (74.6)	188 (25.4)	668 (82.8)	139 (17.2)	676 (81.8)	150 (18.2)
	quartile 2	576 (75;7)	185 (24.3)	716 (86.6)	111 (13.4)	709 (84.3)	132 (15.7)
	quartile 3	601 (79.7)	153 (20.3)	707 (85.0)	125 (15.0)	696 (84.6)	127 (15.4)
	quartile 4	608 (81.2)	141 (18.8)	721 (90.4)	77 (9.6)	717 (88.5)	93 (11.5)
Odds-ratios (95% CI) *	unadjusted	0.87 (0.81–0.94); p=0.0005		0.84 (0.77–0.92); p=0.0001		0.85 (0.78–0.93); p=0.0003	
	Model 1 †	0.90 (0.82–0.97); p=0.009		0.86 (0.78–0.94); p=0.001		0.91 (0.83–1.00); p=0.05	
	Model 2 ‡	0.86 (0.78–0.95); p=0.002		0.83 (0.75–0.92); p=0.001		0.90 (0.82–0.99); p=0.04	

* Odds ratios calculated by logistic regression indicate the risk for a change from one category to the next.

† Model 1: adjustment for sex, age, smoking, total fat intake, physical activity.

‡ Model 2: same as model 1 plus adjustment for mean BMI (mean of BMI at baseline and at 9 years of follow-up)