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BRIEF ARTICLE

Physical activity, obesity and gastroesophageal reflux disease in the general population

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Abstract

AIM: To clarify the association between physical activity and gastroesophageal reflux disease (GERD) in nonobese and obese people.

METHODS: A Swedish population-based cross-sectional survey was conducted. Participants aged 40-79 years were randomly selected from the Swedish Registry of the Total Population. Data on physical activity, GERD, body mass index (BMI) and the covariates age, gender, comorbidity, education, sleeping problems, and tobacco smoking were obtained using validated questionnaires. GERD was self-reported and defined as heartburn or regurgitation at least once weekly, and having at least moderate problems from such symptoms. Frequency of physical activity was categorized into three groups: (1) "high" (several times/week); (2) "intermediate" (approximately once weekly); and (3) "low" (1-3 times/mo or less). Analyses were stratified for participants with "normal weight" (BMI < 25 kg/m²), "overweight" (BMI 25 to \leq 30 kg/m²) and "obese" (BMI > 30 kg/m²). Multivariate logistic regression was used to calculate odds ratios (ORs) with 95% confidence intervals (CIs), adjusted for potential confounding by covariates.

RESULTS: Of 6969 eligible and randomly selected individuals, 4910 (70.5%) participated. High frequency of physical activity was reported by 2463 (50%) participants, GERD was identified in 472 (10%) participants, and obesity was found in 680 (14%). There were 226 (5%) individuals with missing information about BMI. Normal weight, overweight and obese participants were similar regarding distribution of gender and tobacco smoking status, while obese participants were on average slightly older, had fewer years of education, more comorbidity, slightly more sleeping problems, lower frequency of physical activity, and higher occurrence of GERD. Among the 2146 normal-weight participants, crude point estimates indicated a decreased risk of GERD among individuals with high frequency of physical activity (OR: 0.59, 95% CI: 0.39-0.89), compared to low frequency of physical activity. However, after adjustment for potential confounding factors, neither intermediate (OR: 1.30, 95% CI: 0.75-2.26) nor high (OR: 0.99, 95% CI: 0.62-1.60) frequency of physical activity was followed by decreased risk of GERD. Sleeping problems and high comorbidity were identified as potential confounders. Among the 1859 overweight participants, crude point estimates indicated no increased or decreased risk of GERD among individuals with intermediate or high frequency of physical activity, compared to low frequency. After adjustment for confounding, neither intermediate (OR: 0.75, 95% CI: 0.46-1.22) nor high frequency of physical activity were



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followed by increased or decreased risk of GERD compared to low frequency among nonobese participants. Sleeping problems and high comorbidity were identified as potential confounders for overweight participants. In obese individuals, crude ORs were similar to the adjusted ORs and no particular confounding factors were identified. Intermediate frequency of physical activity was associated with a decreased occurrence of GERD compared to low frequency of physical activity (adjusted OR: 0.41, 95% CI: 0.22-0.77).

CONCLUSION: Intermediate frequency of physical activity might decrease the risk of GERD among obese individuals, while no influence of physical activity on GERD was found in non-obese people.

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Key words: Physical exercise; Gastroesophageal reflux disease; Population-based study; Risk factor; Body mass index; Obesity

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a public health concern defined by troublesome and frequent symptoms of heartburn or regurgitation^[1,2], affecting up to 20% of the adult population in the western world^[3]. GERD is associated with a negative impact on health-related quality of life (HRQL), increased risk of esophageal adenocarcinoma, and great costs for patients and society^[3-8]. Established risk factors for GERD are overweight, tobacco smoking, low socioeconomic status, and heredity^[9-15], while the potential role of physical activity is complex and intriguing. Intense physical activity is known to trigger reflux symptoms^[16], but physical activity has many positive effects on health in general, and some data indicate that high physical activity might also prevent GERD in a longterm perspective^[17,18]. Two population-based studies have assessed associations between physical activity and reflux; our twin study from Sweden indicated that high physical activity at work was related to an increased risk of GERD, while recreational physical activity decreased this risk^[17], and our nested case-control study from Norway has suggested a protective effect of physical activity on the risk of GERD^[18]. Few studies have addressed this issue and the available results are partly conflicting, thus, more research is required before any preventive effect of physical activity on GERD can be established. Obesity is strongly linked with both physical activity and GERD, therefore, for this study, we aimed to test the hypothesis that the association between frequency of physical activity and GERD differs between non-obese and obese people^[11]. The occurrence of GERD and frequency of physical activity might change with time, therefore, we conducted a cross-sectional study assessing both variables at the same time, enabling us to investigate whether a higher frequency of physical activity is associated with an increased risk of GERD in an unselected general population.

MATERIALS AND METHODS

Design

A population-based, cross-sectional study was performed between April and June 2008 in Sweden. Participants aged 40-79 years were randomly selected from the Swedish Registry of the Total Population; a registry that contains information of all Swedish residents regarding vital status, gender, age, place of residence, with a maximum of 2 wk delay. Eligible individuals received a postal questionnaire assessing physical activity, body weight, height, and GERD, together with socio-demographic variables, concurrent disease, and lifestyle factors. By completing and returning the questionnaires, participants consented to their data being used for research purposes. Up to two reminder letters were sent to non-responders. Participants were not offered any inducement for participation.

Study variables

Physical activity: The questionnaire assessed physical activity by asking "How often do you perform a physically demanding activity lasting at least 30 min? For example running, cycling, swimming". Frequency of physical activity was categorized into three groups: (1) "high" (several times per week); (2) "intermediate" (approximately once per week); and (3) "low" (1-3 times per month, or less often).

GERD: Information regarding GERD was collected on a 5-point Likert scale for frequency and symptom severity. In line with the implementation of the Montreal definition of GERD^[19], individuals were categorized as having GERD or not (yes or no). Participants were categorized as having GERD if they reported heartburn or regurgitation occurring at least once a week, and having at least moderate problems from such symptoms. Participants reporting use of medications for heartburn or regurgitation at least once weekly were also included in the group fulfilling the criteria for GERD, irrespective of symptom severity.

Covariates: The socio-demographic information included

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Table 1 Characteristics of 4910 study participants, randomly selected from the Swedish general population, and stratified into normal weight $n (\%)^1$

| | BMI < 25 (kg/m ²) | BMI 25 to \leq 30 (kg/m ²) | BMI > 30 (kg/m ²) | | |
|--------------------------------|----------------------------------|--|----------------------------------|--|--|
| Gender | 2146 (46) | 1859 (40) | 680 (15) | | |
| Male | 885 (41) | 1110 (60) | 340 (50) | | |
| Female | 1261 (59) | 749 (40) | 340 (50) | | |
| Age | | | | | |
| (yr) (mean \pm SD) | 58 ± 10 | 57 ± 11 | 59 ± 10 | | |
| Years of formal educ | ation | | | | |
| $\leqslant 9$ | 628 (29) | 682 (37) | 295 (43) | | |
| 10-12 | 798 (37) | 550 (30) | 204 (30) | | |
| > 12 | 653 (30) | 585 (31) | 163 (24) | | |
| No. of diseases | | | | | |
| None | 1226 (57) | 810 (44) | 225 (33) | | |
| 1 | 546 (25) | 553 (30) | 193 (28) | | |
| 2 | 228 (11) | 269 (14) | 118 (17) | | |
| At least 3 | 146 (7) | 227 (12) | 144 (21) | | |
| Sleeping problems | | | | | |
| Not at all | 1295 (60) | 1159 (62) | 383 (56) | | |
| A little | 545 (25) | 467 (25) | 168 (25) | | |
| Quite a bit | 214 (10) | 163 (9) | 89 (13) | | |
| Very much | 69 (3) | 52 (3) | 33 (5) | | |
| Current tobacco smo | oking | | | | |
| No | 1762 (82) | 1576 (85) | 584 (86) | | |
| Yes | 384 (18) | 282 (15) | 96 (14) | | |
| Physical activity ² | | | | | |
| Low | 446 (21) | 495 (27) | 219 (32) | | |
| Intermediate | 432 (20) | 473 (25) | 176 (26) | | |
| High | 1236 (58) | 869 (47) | 265 (39) | | |
| Gastroesophageal re | flux disease ³ | | | | |
| No | 2009 (94) | 1668 (90) | 569 (84) | | |
| Yes | 137 (6) | 190 (10) | 111 (16) | | |

¹Two hundred and twenty-six persons had missing information about body mass index. Percentages not adding up to 100 are explained by missing data in some variables; ²Low: 1-3 times per month or less often; Intermediate: approximately once per week; and High: several times per week; ³Definition of GERD^[19]. heartburn or regurgitation occurring at least once a week and at least having intermediate problems from heartburn or regurgitation. Persons reporting use of medications for heartburn or regurgitation at least once weekly were also included in the group fulfilling the criteria for GERD, irrespective of their severity of the problem. GERD: Gastroesophageal reflux disease.

gender, age, years of formal education, and marital status. The questionnaire further assessed diseases confirmed by a physician (yes or no), including angina, heart failure, atrial fibrillation, myocardial infarction, hypertension, stroke, chronic obstructive pulmonary disease, asthma, diabetes, rheumatoid arthritis, osteoarthritis, kidney failure requiring dialysis, chronic pain, depression under treatment, and cancer. Data on sleeping problems during the past week were assessed with the validated EORTC QLQ-C30^[20] questionnaire. Tobacco smoking was assessed by asking if the person had been smoking during the past 3 mo (yes or no). For calculation of body mass index (BMI), the questionnaire assessed adult height and current weight, and participants were categorized as normal weight (BMI < 25 kg/m²), overweight (BMI 25 to ≤ 30 kg/m²) or obese $(BMI > 30 \text{ kg/m}^2).$

Statistical analysis

Sample characteristics were described by standard de-

scriptive statistics. In order to examine the associations between frequency of physical activity and presence of GERD, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression with multivariate adjustment for potential confounders. Analyses were stratified for participants with normal weight (BMI $< 25 \text{ kg/m}^2$), overweight (BMI 25 to $\leq 30 \text{ kg/m}^2$), or obese (BMI > 30 kg/m²). Potential confounders were: (1) gender (male or female); (2) age (as a continuous variable); (3) education level (< 9 years, 10-12 years, or > 12 years); (4) number of concurrent diseases (0, 1, 2) or > 2); (5) sleeping problems ("none", "a little", "quite a bit" or "very much"); and (6) current tobacco smoking (yes or no). A weighting factor was applied to ensure that the characteristics of the study sample conformed to independently estimated national distributions by age, gender and region. The statistical package STATA 12 for Windows (STATA Corp, College Station, Texas, United States) and SAS (SAS Institute, Cary, NC, United States) were used for the analyses.

RESULTS

Study participants

Of 6969 eligible individuals, 4910 (70.5%) participated. Some characteristics of the participants are presented in Table 1. High physical activity was reported by 2463 (50%) of all participants, GERD was identified in 472 (10%) participants, and obesity was found in 680 (14%) of the participants. Missing information about BMI was found in 226 individuals. Normal weight, overweight and obese participants were similar regarding distribution of gender and tobacco smoking status, while obese participants were on average slightly older, had fewer years of education, a greater number of comorbidities, slightly more sleeping problems, lower frequency of physical activity, and higher occurrence of GERD.

Frequency of physical activity and GERD in normal weight participants

Among normal weight participants (BMI < 25 kg/m^2), crude point estimates indicated a decreased risk of GERD among individuals with high frequency of physical activity (OR: 0.59, 95% CI: 0.39-0.89), compared to low frequency of physical activity. After adjustment for confounding variables, neither intermediate (OR: 1.30, 95% CI: 0.75-2.26) nor high (OR: 0.99, 95% CI: 0.62-1.60) frequency of physical activity was followed by a decreased risk of GERD compared to low frequency of physical activity among normal weight participants (Table 2). Sleeping problems and a high number of comorbidities were identified as potential confounders, since they had a major impact in the multivariable model.

Frequency of physical activity and GERD in overweight participants

Among overweight participants (BMI 25 to $\leq 30 \text{ kg/m}^2$), crude point estimates indicated no increased or decreased



| Table 2 Association between frequency of physical exercise and occurrence of gastroesophageal reflux disease | | | | | | | | | | | |
|--|--------------------------|---|----------|--------------------------|---------|----------|--------------------------|---------|--|--|--|
| | Normal wei | $\label{eq:Risk} Risk \ of \ GERD^1 \\ Normal \ weight \ (BMI \ < \ 25 \ kg/m^2) \qquad \qquad Overweight \ (BMI \ 25 \ to \ \leqslant \ 30 \ kg/m^2) \qquad \qquad Obese \ (BMI \ > \ 30 \ kg/m^2) \\ \end{array}$ | | | | | | | | | |
| | п | n = 2146 (46%) | | n = 1859 (40%) | | | n = 680 (15%) | | | | |
| | OR (95% CI) ² | P value | n (%) | OR (95% CI) ² | P value | n (%) | OR (95% CI) ² | P value | | | |
| Physical activity ³ | | | | | | | | | | | |
| Low | Reference | | 495 (27) | Reference | | 219 (33) | Reference | | | | |
| Intermediate | 1.30 (0.75-2.26) | 0.35 | 869 (47) | 0.74 (0.46-1.22) | 0.24 | 176 (27) | 0.41 (0.22-0.77) | 0.01 | | | |
| High | 0.99 (0.62-1.60) | 0.98 | 473 (25) | 1.34 (0.90-2.00) | 0.15 | 265 (40) | 0.83 (0.50-1.35) | 0.45 | | | |

¹Definition of GERD^[19]: Self-reported heartburn or regurgitation occurring at least once a week and at least having moderate problems from heartburn or regurgitation. Persons reporting use of medications for heartburn or regurgitation at least once weekly were also included in the group fulfilling the criteria for GERD, irrespective of their severity of the problem; ²Adjusted for gender, age, education level, number of diseases, sleeping problems and tobacco smoking; ³Low = 1-3 times per month or less often, Intermediate = approximately once per week, and High = several times per week. Association between frequency of physical exercise and occurrence of gastroesophageal reflux disease in normal weight people in a random sample of 4910 people from the Swedish general population (226 participants had missing information on BMI). Presented as OR: with 95% CI. GERD: Gastroesophageal reflux disease; BMI: Body mass index; CI: Confidence interval; OR: Odds ratio.

risk of GERD among individuals with intermediate or high frequency of physical activity, compared to low frequency of physical activity. After adjustment for confounding variables, neither intermediate (OR: 0.75, 95% CI: 0.46-1.22) nor high frequency of physical activity were followed by an increased or decreased risk of GERD compared to low frequency of physical activity among overweight participants (Table 2). Identified potential confounders were sleeping problems and a high number of comorbidities, because they had a major impact in the multivariate model.

Frequency of physical activity and GERD in obese participants

In obese individuals (BMI > 30 kg/m^2), crude ORs were similar to the adjusted ORs and no particular confounding factors were identified. Intermediate frequency of physical activity was associated with a decreased occurrence of GERD compared to low frequency of physical activity (adjusted OR: 0.41, 95% CI: 0.22-0.77). A nonsignificantly decreased risk of GERD was found among obese individuals with high frequency of physical activity compared to low frequency of physical activity (adjusted OR: 0.83, 95% CI: 0.50-1.35).

DISCUSSION

This study indicated that intermediate frequency of physical activity was associated with a lower occurrence of GERD among obese individuals, while no such association was found among normal weight or overweight individuals.

The strengths of the present study include the population-based design with random selection of participants, the high participation rate, and the large sample size. Moreover, symptoms of GERD were measured with a well-validated questionnaire^[21], fulfilling the consensus criteria for GERD^[1]. Furthermore, it was possible to adjust the results for several potential confounding factors. Limitations include an inherent uncertainty about the accuracy of self-reported data and lack of validation of the assessment of frequency of physical activity, BMI, as well as information about previous surgical interventions for GERD. Also, because this was a cross-sectional study, it is not possible to know if participants with a self-detected association between reflux and physical exercise may have changed their behavior, resulting in reverse causality.

The decreased risk of GERD in people participating in physical activity is in line with previous populationbased studies assessing an association between physical activity and GERD within the general population^[17,18]. However, none of the previous studies conducted stratified analyses for BMI categories; meaning that the decreased risk of GERD limited to obese individuals is a first-time observation.

A potential biological mechanism underlying increased risk of reflux among obese persons is through increased extrinsic gastric compression by surrounding adipose tissue and anatomical disruption of the gastroesophageal junction^[8,22]. This is also thought to be the mechanism when physical activity triggers reflux symptoms^[16]. It has also been argued that physical exercise might cause GERD by decreasing the gastrointestinal blood flow and changing the esophagogastric motor function. On the other hand, physical activity might strengthen striated muscles in the diaphragmatic crurae and thereby reinforce the antireflux barrier^[16,23-25]. Furthermore, both intensity and type of physical exercise might pose different risks for GERD^[16,23,26]. Should the present results be confirmed in future research, the findings from this study might be important for the prevention and treatment of GERD and its complications.

In conclusion, this large population-based study indicates decreased occurrence of GERD in obese people who report intermediate frequency of physical activity, while no influence of frequency of physical activity on GERD was identified in non-obese people.

COMMENTS

Background

Gastroesophageal reflux disease (GERD) is a public health concern defined by



troublesome and frequent symptoms of heartburn or regurgitation, affecting up to 20% of the adult population in the western world. Established risk factors for GERD are overweight, tobacco smoking, low socioeconomic status, and heredity, while the potential role of physical activity is complex and intriguing.

Research frontiers

GERD is very common and bothersome for people experiencing this disease. All types of risk factors and possible treatments and interventions to reduce symptoms are of relevance.

Innovations and breakthroughs

Two population-based studies have assessed associations between physical activity and reflux; the twin study from Sweden indicated that high physical activity at work was related to an increased risk of GERD, while recreational physical activity decreased this risk, and the nested case-control study based on data from Norway suggested a protective effect of physical activity on the risk of GERD.

Applications

To summarize the actual application values, the implications for further application and modification, or the perspectives of future application of the outcome of the study. Further studies are necessary to determine the direction of causation between physical exercise and GERD in obese patients.

Terminology

GERD is defined by troublesome and frequent symptoms of heartburn or regurgitation. Body mass index (BMI), is calculated by dividing height in meters by the square root of weight in kilograms.

Peer review

The study was well-designed and the results add to current knowledge about GERD and its relieving and aggravating factors.

REFERENCES

- 1 **Vakil N**, van Zanten SV, Kahrilas P, Dent J, Jones R. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; **101**: 1900-1920; quiz 1943
- 2 Vakil N, Malfertheiner P, Salis G, Flook N, Hongo M. An international primary care survey of GERD terminology and guidelines. *Dig Dis* 2008; **26**: 231-236
- 3 **Dent J**, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005; **54**: 710-717
- 4 **el-Serag HB**, Sonnenberg A. Associations between different forms of gastro-oesophageal reflux disease. *Gut* 1997; **41**: 594-599
- 5 **El-Serag HB**. Time trends of gastroesophageal reflux disease: a systematic review. *Clin Gastroenterol Hepatol* 2007; **5**: 17-26
- 6 Lagergren J, Bergström R, Lindgren A, Nyrén O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med 1999; 340: 825-831
- 7 Pandeya N, Webb PM, Sadeghi S, Green AC, Whiteman DC. Gastro-oesophageal reflux symptoms and the risks of oesophageal cancer: are the effects modified by smoking, NSAIDs or acid suppressants? *Gut* 2010; **59**: 31-38
- 8 **Dean BB**, Crawley JA, Schmitt CM, Wong J, Ofman JJ. The burden of illness of gastro-oesophageal reflux disease: impact on work productivity. *Aliment Pharmacol Ther* 2003; **17**: 1309-1317
- 9 **Cameron AJ**, Lagergren J, Henriksson C, Nyren O, Locke GR, Pedersen NL. Gastroesophageal reflux disease in mono-

zygotic and dizygotic twins. Gastroenterology 2002; 122: 55-59

- 10 De Ceglie A, Fisher DA, Filiberti R, Blanchi S, Conio M. Barrett's esophagus, esophageal and esophagogastric junction adenocarcinomas: the role of diet. *Clin Res Hepatol Gastroenterol* 2011; 35: 7-16
- 11 El-Serag H. Role of obesity in GORD-related disorders. *Gut* 2008; **57**: 281-284
- 12 Lagergren J. Body measures in relation to gastro-oesophageal reflux. *Gut* 2007; **56**: 741-742
- 13 Jansson C, Nordenstedt H, Johansson S, Wallander MA, Johnsen R, Hveem K, Lagergren J. Relation between gastroesophageal reflux symptoms and socioeconomic factors: a population-based study (the HUNT Study). *Clin Gastroenterol Hepatol* 2007; 5: 1029-1034
- 14 El-Serag H. The association between obesity and GERD: a review of the epidemiological evidence. *Dig Dis Sci* 2008; 53: 2307-2312
- 15 Nordenstedt H, Lagergren J. Environmental factors in the etiology of gastroesophageal reflux disease. *Expert Rev Gastroenterol Hepatol* 2008; **2**: 93-103
- 16 Jozkow P, Wasko-Czopnik D, Medras M, Paradowski L. Gastroesophageal reflux disease and physical activity. Sports Med 2006; 36: 385-391
- 17 Zheng Z, Nordenstedt H, Pedersen NL, Lagergren J, Ye W. Lifestyle factors and risk for symptomatic gastroesophageal reflux in monozygotic twins. *Gastroenterology* 2007; 132: 87-95
- 18 Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Lifestyle related risk factors in the aetiology of gastro-oesophageal reflux. *Gut* 2004; 53: 1730-1735
- 19 Flook N, Jones R, Vakil N. Approach to gastroesophageal reflux disease in primary care: Putting the Montreal definition into practice. *Can Fam Physician* 2008; 54: 701-705
- 20 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85: 365-376
- 21 **Löfdahl HE**, Lane A, Lu Y, Lagergren P, Harvey RF, Blazeby JM, Lagergren J. Increased population prevalence of reflux and obesity in the United Kingdom compared with Sweden: a potential explanation for the difference in incidence of esophageal adenocarcinoma. *Eur J Gastroenterol Hepatol* 2011; **23**: 128-132
- 22 **El-Serag HB**, Ergun GA, Pandolfino J, Fitzgerald S, Tran T, Kramer JR. Obesity increases oesophageal acid exposure. *Gut* 2007; **56**: 749-755
- 23 Clark CS, Kraus BB, Sinclair J, Castell DO. Gastroesophageal reflux induced by exercise in healthy volunteers. *JAMA* 1989; 261: 3599-3601
- 24 **Soffer EE**, Merchant RK, Duethman G, Launspach J, Gisolfi C, Adrian TE. Effect of graded exercise on esophageal motility and gastroesophageal reflux in trained athletes. *Dig Dis Sci* 1993; **38**: 220-224
- 25 Pandolfino JE, Bianchi LK, Lee TJ, Hirano I, Kahrilas PJ. Esophagogastric junction morphology predicts susceptibility to exercise-induced reflux. *Am J Gastroenterol* 2004; 99: 1430-1436
- 26 Schoeman MN, Tippett MD, Akkermans LM, Dent J, Holloway RH. Mechanisms of gastroesophageal reflux in ambulant healthy human subjects. *Gastroenterology* 1995; 108: 83-91

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