Inverse association between gastroesophageal reflux and blood pressure: results of a large community based study

Murray, L., McCarron, P., McCorry, R. B., Anderson, L., Lane, A. J., Johnston, B. T., Davey Smith, G., & Harvey, R. F. (2008). Inverse association between gastroesophageal reflux and blood pressure: results of a large community based study. *BMC Gastroenterology, 8*, 1-4. [10]. https://doi.org/10.1186/1471-230x-8-10

Published in:
BMC Gastroenterology

Queen's University Belfast - Research Portal:
Link to publication record in Queen's University Belfast Research Portal

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

Open Access
This research has been made openly available by Queen's academics and its Open Research team. We would love to hear how access to this research benefits you. – Share your feedback with us: http://go.qub.ac.uk/oa-feedback

Download date: 12. Oct. 2023
Background:
In a cross-sectional community based study, as part of a randomised controlled trial of eradication of Helicobacter pylori infection, the association between blood pressure and symptoms of gastro-oesophageal reflux was examined.

Methods:
Linear regression was used to examine the association between systolic and diastolic blood pressure and the frequency of heartburn and acid regurgitation in 4,902 of 10,537 participants aged 20–59 years.

Results:
In multivariable analyses, adjusted mean systolic blood pressure was 4.2 (95% confidence interval 1.5 to 7.0) mm Hg lower in participants with daily acid regurgitation compared to those with less frequent symptoms. Similarly, for diastolic blood pressure, a reduction of 2.1 (0.0 to 4.3) mm Hg was observed.

Conclusion:
People who experience daily symptoms of gastro-oesophageal reflux have lower blood pressure than people with less frequent or no symptoms. It is possible that factors influencing nitric oxide concentrations both at the lower oesophageal sphincter and within the vasculature may be involved. This hypothesis requires confirmation.

Trials registration number: ISRCTN44816925
scribed for upper gastrointestinal conditions other than gastro-oesophageal reflux and Barrett’s oesophagus. We hypothesised that the association we observed may be due to individuals with reduced lower oesophageal sphincter (LOS) pressure, (a risk factor for gastro-oesophageal reflux and Barrett’s oesophagus) also having low vascular tone and blood pressure, resulting in reduced stroke risk. To investigate this, we examined whether blood pressure is associated with symptoms of gastro-oesophageal reflux.

Methods
From 1996 to 1998, 10,537 individuals, aged 20–59 years, registered with seven general practices in Southwest England were enrolled in a community based randomised controlled trial of eradication of *Helicobacter pylori* (*H. pylori*). The trial obtained ethics approval from Frenchay Hospital LREC (reference number: 95/83 20/01/1996) and participants provided written informed consent. Participants provided information on the frequency of dyspeptic symptoms experienced in the previous three months, including heartburn ("a burning or ache behind the sternum not due to heart trouble") and acid regurgitation ("a very sour or acid tasting fluid at the back of the throat") using a validated questionnaire [3]. In addition, blood pressure, height, and weight were measured and data on antihypertensive medication, smoking history, alcohol and coffee consumption, and adult social class (derived from current occupation) were collected. The current analysis is based on all participants who tested positive for *H. pylori* infection (n = 1,634) and a computer generated random sample of *H. pylori* negative participants (n = 3,268) to give a *H. pylori* negative to positive ratio of 2:1

Linear regression was used to examine the association between systolic and diastolic blood pressure and the frequency of heartburn and acid regurgitation (daily vs. less frequent). Analyses took account of the clustered nature of the data (by general practice), and the increased sampling frequency. Analyses took account of the clustered nature of *H. pylori* pressure, (a risk factor for gastro-oesophageal reflux and Barrett’s oesophagus) also having low vascular tone and blood pressure, resulting in reduced stroke risk. To investigate this, we examined whether blood pressure is associated with symptoms of gastro-oesophageal reflux.

**Results**
One hundred and seven (2.5%) and 66 (1.6%) of the 4,227 participants with complete data experienced daily heartburn or acid regurgitation respectively. Participants experiencing either daily acid regurgitation or heartburn symptoms were heavier, and smoked more cigarettes than people with less frequent symptoms, while those with daily heartburn consumed more alcohol and were more likely to come from manual social class (Table 1). In age and sex-adjusted analyses, restricted to individuals not receiving antihypertensive medication (258 excluded), participants with daily acid regurgitation had lower mean systolic and diastolic blood pressure than individuals who had less frequent or no acid regurgitation (Table 2). Controlling for potential confounders strengthened these associations. There was no association between daily heartburn or the other dyspeptic symptoms and blood pressure.

**Discussion**
We found an inverse association between experiencing daily acid regurgitation and blood pressure. This was a large, population based study, whose participants were representative of the total sample. A wide age range of both sexes were studied producing novel findings. Weaknesses, however, include the fact the study was symptom based with no direct information regarding the underlying endoscopic diagnosis. Some researchers suggest that for heartburn a more complete ‘word picture’ than we used is required to avoid misreporting this symptom [4]. Misclassification may therefore have contributed to the weak relationship seen between blood pressure and heartburn. Moreover, as few participants in our study had daily reflux symptoms, our results need to be viewed as preliminary. However, there are several emerging strands of evidence to support a causal relationship between gastro-oesophageal reflux and low blood pressure. Firstly, this finding is consistent with our previous observation of lower stroke mortality in patients with Barrett’s oesophagus in a separate cohort from Northern Ireland [1]. Secondly, patients with gastro-oesophageal reflux disease have been shown to have decreased sympathetic function, with blunting of blood pressure responses to stress [5]. Thirdly, recent research into nitric oxide (NO) provides a mechanistic link between gastro-oesophageal reflux and low blood pressure. NO functions as the major non-adrenergic non-cholinergic neurotransmitter in the autonomic nervous system [6] and NO-mediated action appears to be crucial in governing LOS pressure [7]. Patients with gastro-oesophageal reflux have elevated levels of serum nitrate compared to controls [8] and infusion...
of a NO synthase blocker has been seen to induce both raised resting LOS tone and, in keeping with the well known vasodilatory effects of NO, raised blood pressure [9].

**Conclusion**

We suggest that factors influencing the endogenous production of NO underlie the observed association between symptoms of gastro-oesophageal reflux and blood pressure. Confirmation of these findings, and further investigation of the pathophysiological role that NO may play in gastro-oesophageal reflux, and possibly Barrett’s oesophagus, are warranted.

**Competing interests**

The author(s) declare that they have no competing interests.

**Authors’ contributions**

LM, and RH were involved in planning and obtaining funding for the Bristol Helicobacter project. JAL managed the project. LM proposed the hypothesis for this paper. LM and PMcC carried out the analyses and wrote the initial draft of the paper. All the authors commented critically on the initial draft, and contributed to the final version of the paper. LM is the guarantor.

**Table 1: Characteristics of participants with and without acid regurgitation or heartburn**

| Symptom, frequency | Acid regurgitation, n (%) | Heartburn, n (%) |
|--------------------|--------------------------|-----------------|
|                    | No (98.4)                | Yes (1.6)       |
| All participants   | 4161                     | 66 (1.6)        |
| Males              | 4120 (97.5)              | 107 (2.5)       |
| Mean age (SD)      | 45.6 (8.9)               | 45.5 (9.0)      |
| Receiving antihypertensives | 255 (6.1)           | 255 (6.1)       |
| Mean BMI (SD)      | 26.7 (4.4)               | 26.8 (4.4)      |
| Cigarettes         |                          |                 |
| Never              | 2204 (53.0)              | 2183 (53.0)     |
| Ever               | 987 (23.7)               | 976 (23.7)      |
| Current, <20/day   | 597 (14.4)               | 589 (14.3)      |
| Current, = 20/day  | 373 (9.0)                | 372 (9.0)       |
| Alcohol (units/wk) |                          |                 |
| None               | 659 (15.8)               | 651 (15.8)      |
| 1–9                | 1966 (47.2)              | 1955 (47.4)     |
| 10–19              | 883 (21.2)               | 877 (21.3)      |
| ≥ 20               | 653 (15.7)               | 637 (15.5)      |
| Cigarettes         |                          |                 |
| Never              | 801 (19.2)               | 792 (19.2)      |
| 1–4                | 2209 (53.1)              | 2182 (53.0)     |
| ≥ 5                | 1151 (27.7)              | 1146 (27.8)     |
| Non-manual social class | 2667 (64.1)         | 2653 (64.4)     |
| Mean systolic BP (SD) | 119.8 (21.7)      | 119.8 (21.8)    |
| Mean diastolic BP (SD) | 75.6 (19.2)          | 75.6 (19.3)     |

Data shown relate to 4227 participants with complete data

**Table 2: Association between blood pressure and frequency of acid regurgitation and heartburn**

| Symptom, frequency | Acid regurgitation, n (%) | Heartburn, n (%) |
|--------------------|--------------------------|-----------------|
|                    | Mean difference in systolic blood pressure (mm Hg) (95% CI), p | Mean difference in diastolic blood pressure (mm Hg) (95% CI), p |
|                    | Age and sex adjusted     | Fully-adjusted2 | Age and sex adjusted | Fully-adjusted2 |
| Daily              | -2.5 (-4.2 to -0.8), 0.012 | -0.9 (-2.9 to 1.2), 0.34 | -2.1 (-4.3 to 0.0), 0.053 |
| Less frequently    | 1.00 (reference group)   | 1.00            | 1.00                  |
| Heartburn          | 1.7 (-3.7 to 7.1), 0.48  | -0.6 (-1.3 to 2.5), 0.46 | -0.9 (-2.8 to 1.1), 0.32 |

1 Number of participants for whom full data available

2 Adjustment for age, sex, BMI, antihypertensive medication, smoking, coffee and alcohol intake, and social class
Acknowledgements
We thank the participants in the Bristol Helicobacter Project and the general practitioners and Health Centre staff; the nursing team of Lynne Bradshaw, Julie Watson, Tina Critchley, Jo Lee, Carol Everson-Coombe, Penny Nettlefield and Joanne Smith; Judy Millward, Helen Davies, Amy Hawkins and Sarah Pike for secretarial support and Erwin Brown, Paul Thomas, Nick Pope and Phil Hedges of the Microbiology Department and Peter Spurr, Martin Bullock and Fiona Greenwood of the Pharmacy Department, Frenchay Hospital, for help with the 10,537 breath tests.

Funding: This study was funded jointly by the South and West Regional Research and Development Directorate and GlaxoSmithKline UK. The Department of Social Medicine is the lead centre for the MRC Health Services Research Collaboration.

References
1. Anderson LA, Murray LJ, Murphy SJ, Fitzpatrick DA, Johnston BT, Watson RG, McCarron P, Gavin AT: Mortality in Barrett’s oesophagus: results from a population based study. Gut 2003, 52:1081-4.
2. Bateman DN, Colins-Jones D, Hartz S, Langman M, Logan RF, Mant J, Murphy M, Paterson KR, Rowsell R, Thomas S, Vessey M, SURVEIL (Study of Undetected Reactions, Vigilance Enquiry into Links) Group: Mortality study of 18,000 patients treated with omeprazole. Gut 2003, 52(7):942-6.
3. Kennedy T, Jones R: The prevalence of gastro-oesophageal reflux symptoms in a UK population and the consultation behaviour of patients with these symptoms. Aliment Pharmacol Ther 2000, 14:1589-94.
4. Carlsson R, Dent J, Bolling-Sternevald E, Johnsson F, Junghard O, Lauritsen K, Riley S, Lundell L: The usefulness of structured questionnaire in the assessment of symptomatic gastroesophageal reflux disease. Scand J Gastroenterol 1998, 33:1023-9.
5. Campo SM, Capria A, Antonucci F, Martino G, Ciamati A, Rossini PM, Bologna E, Cannata D: Decreased sympathetic inhibition in gastroeosphageal reflux disease. Clinical Autonomic Research 2001, 11:45-51.
6. Bredt DS: Endogenous nitric oxide synthesis: biological functions and pathophysiology. Free Radical Research 1999, 31:577-90.
7. Tomita R, Tanjoh K, Fujisaki S, Fukuzawa M: Physiological studies on nitric oxide in the lower esophageal sphincter of patients with reflux esophagitis. Hepatogastroenterology 2003, 50:110-4.
8. Kassim SK, El Touny M, El Guinaidy M, El Moghni MA, El Mohsen AA: Serum nitrites and vasoactive intestinal peptide in patients with gastroesophageal reflux disease. Clin Biochem 2002, 35:641-6.
9. Konturek JW, Thor P, Lukaszyk A, Gabryelewicz A, Konturek SJ, Domshke W: Endogenous nitric oxide in the control of esophageal motility in humans. J Physiol Pharmacol 1997, 48:201-9.

Pre-publication history
The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-230X/8/10/prepub