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## Atherosclerosis

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## Discussion

## Being constipated: A bad omen for your cardiovascular system?

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## ARTICLE INFO

## Article history:

Received 23 September 2015

Accepted 1 October 2015

Available online xxx

## Keywords:

Cardiovascular disease mortality

Cohort study

Constipation

Defecation frequency

Japan

Constipation is one of the most frequent symptoms reported daily in clinical practice throughout the world [1] and it carries a considerable burden in terms of productivity losses and healthcare utilization [2]. Although constipation is usually perceived as a benign, often self-limited condition [3], chronic constipation may display a more darker side and be associated with potentially life-threatening diseases [4] and increased mortality [5,6]. The latter may be due to several reasons, such as the association with aging, use of drugs and cardiovascular disease. Concerning the latter, there is evidence from a study that constipation is a marker for cardiovascular risk factors and increased cardiovascular risk in postmenopausal women [7]. However, the question whether constipation may be a risk factor for cardiovascular disease in the general population has remained so far unanswered.

In this issue of *Atherosclerosis*, Honkura and colleagues try to give us such an answer, by reporting data on this association in a large sample of more than 40,000 Japanese subjects [8]. The authors demonstrated robustly that constipation, here generically defined as a decreased evacuation frequency, is significantly associated with overall cardiovascular disease mortality, and that this mortality was particularly associated with risk of stroke. Although the data are impressive, some confounding factors must be taken into consideration, factors that could not be evaluated due to the

descriptive nature of the study and its focus on the lifestyle of the subjects. Thus, we do not know whether these constipated patients were consuming drugs directly or indirectly affecting cardiovascular function, whether they had associated conditions (diabetes, thyroid diseases, other endocrine diseases, collagenopathies, etc.) that could worsen or trigger the clinical picture, and which kind of constipation subtype played a major role in this increase of mortality. Moreover, the data collection only referred to defecation frequency, that might still underestimate the actual size of the problem and it was conducted on “recall” questionnaires that may be less precise in the long-term period compared to daily questionnaires [9]. Notwithstanding these limitations, the study is interesting and provides both food for thought on the topic and a starting point to address more specifically these relationships.

How can constipation affect cardiovascular mortality? As the authors emphasized [8], one possible explanation may be due, at least for stroke risk, to the increased intracranial pressure following Valsalva-like manoeuvres, possibly triggering aneurysm rupture [10] or increasing the size of right to left and pulmonary shunts [11]. Indeed, straining at stools is the hallmark of obstructed defecation, the more frequent subtype of constipation reported by patients [12], and it is plausible that chronic daily strain may influence intracranial pressure and cause strokes in predisposed subjects.

On the other hand, it is more difficult to correlate ischemic heart disease with constipation, even though in this instance the role of certain drugs may have played a role. For instance, before their withdrawal from the market, some widely used products for gastroenterological issues have been shown to be associated with adverse cardiovascular events [13,14]. However, some evidence also suggests that Valsalva-like manoeuvres (in this instance, straining at stools) may be associated with electrical abnormalities in patients with myocardial infarction and worsen the prognosis [15]. Interestingly, a relatively dated study showed that only about 70% of nurses practice coronary precautions (including avoidance of Valsalva manoeuvre) concerning acute myocardial infarction [16].

Last, but not least, cardiovascular complications leading to fatal events may be triggered by faecal impaction [17,18]. This frequent clinical problem should be always sought and aggressively treated in patients confined to bed (but also in those with constipation refractory to treatment and in those with “faecal incontinence”) [19,20], and especially in those with cardiovascular problems and the advanced elderly, to avoid serious impairment of the health

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status and quality of life, not to speak of potentially fatal outcomes.

In conclusion, we can broadly state that being constipated represents a risk factor for potentially fatal cardiovascular events and that this symptom should be searched for and treated in all those patients with cardiac disease, to avoid complications. Further studies assessing the relationship between constipation and cardiovascular events, possibly conducted in a more detailed manner to establish firmer correlations between straining at stools and the incidence of such effects are eagerly awaited.

### Conflict of interest statement

None declared.

### References

- [1] G. Bassotti, Understanding constipation treatment: do we need to strain to obtain better results? *Expert Opin. Drug Metab. Toxicol.* 9 (2013) 387–389.
- [2] L. Neri, G. Basilisco, E. Corazzari, V. Stanghellini, G. Bassotti, M. Bellini, I. Perelli, R. Cuomo, LIRS Study Group, Constipation severity is associated with productivity losses and healthcare utilization in patients with chronic constipation, *United Eur. Gastroenterol. J.* 2 (2014) 138–147.
- [3] C. Dennison, M. Prasad, A. Lloyd, S.K. Bhattacharyya, R. Dhawan, K. Coyne, The health-related quality of life and economic burden of constipation, *Pharmacoeconomics* 23 (2005) 461–476.
- [4] A. Guérin, R. Mody, B. Fok, K.L. Lasch, Z. Zhou, E.Q. Wu, W. Zhou, N.J. Talley, Risk of developing colorectal cancer and benign colorectal neoplasm in patients with chronic constipation, *Aliment. Pharmacol. Ther.* 40 (2014) 83–92.
- [5] J.Y. Chang, G.R. Locke 3rd, M.A. McNally, S.L. Halder, C.D. Schleck, A.R. Zinsmeister, N.J. Talley, Impact of functional gastrointestinal disorders on survival in the community, *Am. J. Gastroenterol.* 105 (2010) 822–832.
- [6] N.A. Koloski, M. Jones, R. Wai, R.S. Gill, J. Byles, N.J. Talley, Impact of persistent constipation on health-related quality of life and mortality in older community-dwelling women, *Am. J. Gastroenterol.* 108 (2013) 1152–1158.
- [7] E. Salmoirago-Blotcher, S. Crawford, E. Jackson, J. Ockene, I. Ockene, Constipation and risk of cardiovascular disease among postmenopausal women, *Am. J. Med.* 124 (2011) 714–723.
- [8] Honkura K, Tomata Y, Sugiyama K, Kahio K, Watanabe T, Zhang S, Sugawara Y, Tsuji I. Defecation frequency and cardiovascular disease mortality in Japan: the Ohsaki cohort study. *Atherosclerosis* (in press)
- [9] M. Bellini, A. Bove, M.P. Sormani, E. Battaglia, R. Bocchini, P. Alduini, G. Bassotti, P. Bruzzi, F. Pucciani, Italian Constipation Study Group, The daily diary and the questionnaire are not equivalent for the evaluation of bowel habits, *Dig. Liver Dis.* 42 (2010) 99–102.
- [10] M.H. Vlak, G.J. Rinkel, P. Greebe, J.G. van der Bom, A. Algra, Trigger factors and their attributable risk for rupture of intracranial aneurysms: a case-crossover study, *Stroke* 42 (2011) 1878–1882.
- [11] N.R. Clarke, J. Timperley, A.D. Kelion, A.P. Banning, Transthoracic echocardiography using second harmonic imaging with Valsalva manoeuvre for the detection of right to left shunts, *Eur. J. Echocardiogr.* 5 (2004) 176–181.
- [12] G. Iantorno, M. Cinquetti, A. Mazzocchi, A. Morelli, G. Bassotti, Audit of constipation in a gastroenterology referral center, *Dig. Dis. Sci.* 52 (2007) 317–320.
- [13] E.M. Quigley, Cisapride: what can we learn from the rise and fall of a prokinetic? *J. Dig. Dis.* 12 (2011) 147–156.
- [14] J. Tack, M. Camilleri, L. Chang, W.D. Chey, J.J. Galligan, B.E. Lacy, S. Müller-Lissner, E.M. Quigley, J. Schuurkes, J.H. De Maeyer, V. Stanghellini, Systematic review: cardiovascular safety profile of 5-HT<sub>4</sub> agonists developed for gastrointestinal disorders, *Aliment. Pharmacol. Ther.* 35 (2012) 745–767.
- [15] Y. Balbay, A. Cosgun, R. Jean-Baptiste, A.D. Demir, H. Tikiz, S. Korkmaz, E. Kutuk, Effects of Valsalva maneuver on QT dispersion in patients with ischemic heart diseases, *Angiology* 52 (2001) 735–741.
- [16] B. Riegel, T. Thomason, B. Carlson, I. Gocka, Are nurses still practicing coronary precautions? A national survey of nursing care of acute myocardial infarction patients, *Am. J. Crit. Care* 5 (1996) 91–98.
- [17] A.M. Lofman, J.M. Fessenden, W.H. Ayers 3rd, Fecal impaction: a fatal cause of cardiac tamponade? *Curr. Surg.* 60 (2003) 449–451.
- [18] Z.H. Hussain, D.A. Whitehead, B.E. Lacy, Fecal impaction, *Curr. Gastroenterol. Rep.* 16 (2014) 404.
- [19] G. Bassotti, V. Villanacci, A practical approach to diagnosis and management of functional constipation in adults, *Intern Emerg. Med.* 8 (2013) 275–282.
- [20] G. Bassotti, C. Blandizzi, Understanding and treating refractory constipation, *World J. Gastrointest. Pharmacol. Ther.* 5 (2014) 77–85.