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## Gender differences in symptoms of myocardial ischaemia

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### Aims

Better understanding of symptoms of myocardial ischaemia is needed to improve timeliness of treatment for acute coronary syndromes (ACS). Although researchers have suggested sex differences exist in ischaemic symptoms, methodological issues prevent conclusions. Using percutaneous coronary intervention (PCI) balloon inflation as a model of myocardial ischaemia, we explored sex differences in reported symptoms of ischaemia.

### Methods and Conclusions

Patients having non-emergent PCI, but not haemodynamic instability or left bundle branch block or non-acute coronary occlusion, were prospectively recruited. Pre-procedure, descriptions of pre-existing symptoms were obtained using open-ended questioning. Inflation was maintained for 2 min or until moderate discomfort or clinical instability occurred. During inflation, subjects were exhaustively questioned about their symptoms. Concurrent ECG data were collected. The final sample was 305 [39.7% women; mean age 63.9 ( $\pm$  10.6)]. No sex differences were found in rates of chest or typical ischaemic discomfort, regardless of ischaemic status. Women were significantly more likely to report throat/jaw discomfort [odds ratio: 2.91; 95% confidence interval: 1.58–5.37] even after statistical adjustment for clinical and demographic variables.

### Conclusion

This prospective study with ECG-affirmed ischaemia found no statistically significant differences in women's and men's rates of chest and other typical symptoms during ischaemia, although women were more likely to experience throat and jaw discomfort. Currently both popular press and some patient education materials suggest women experience myocardial ischaemia differently from men. Steps to ensure women and health professionals are alert for the classic symptoms of myocardial ischaemia in women, as well as men, may be warranted.

Observational studies have previously suggested sex-based differences in symptoms of myocardial ischaemia.<sup>1–10</sup> Failure to efficiently recognize ischaemic symptoms in women could partly explain delays in presentation,<sup>11–14</sup> diagnosis, and lower rate of treatment to guidelines observed in women.<sup>8</sup>

Diagnosis of ischaemia using clinical history is limited by a patient's recall of symptom characteristics, their inherent subjectivity, and by biases among care providers. Electrocardiographic verification of ischaemia for described episodes is usually unavailable. Even when obstructive coronary artery disease is conclusively documented, attributing index symptoms to the ischaemic substrate can be imprecise. Thus, there remains uncertainty as to

whether reported sex-based differences in ischaemic symptoms are due to biological differences, gender differences, patient or provider bias, flawed research methods, or other factors.

Few researchers have prospectively characterized sex-specific symptoms during objective ischaemia.<sup>15,16</sup> Our objective, therefore, was to determine the nature of symptoms provoked by discrete episodes of ischaemia produced by transient coronary occlusion during percutaneous coronary intervention (PCI) and to determine, in this controlled setting, whether sex differences exist.<sup>17–20</sup> To achieve this we employed a standardized balloon inflation protocol and concurrent questionnaire administration during routine PCI.

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## Methods

### Design and subjects

Beginning in October 2003, potentially eligible patients at two university-affiliated centres in Vancouver, Canada were screened, including those undergoing scheduled elective (required within 4 months) or urgent (required during current hospitalization) but not emergent (immediately) PCI, or coronary angiography with provisional PCI. In the latter case, final eligibility required that a PCI was performed. Exclusions were (i) emergent PCI [evolving myocardial infarction (MI) or refractory ischaemia]; (ii) baseline occlusion of the target lesion [Thrombolysis in Myocardial Infarction (TIMI) grade 0 or 1 flow] (iii) haemodynamic or electrical instability, or (iv) inability to converse in English. Participants were informed that the intent was to examine ischaemic symptoms provoked by PCI, but were blinded to the sex-specific nature of the analysis, to avoid reporting bias, and gave written, informed consent.

### Assessment of symptoms

Before entering the catheterization laboratory, subjects were questioned using a standardized tool regarding the intensity (on a 0–10 scale), location and quality of all symptoms they attributed to their heart that had led to their angiography or PCI referral ('baseline' symptoms). Overlapping patient-reported descriptors were later grouped using clinical and etymological knowledge (e.g. 'across chest' and 'front of chest' became 'chest discomfort'; 'heartburn', 'indigestion' became 'epigastrium/indigestion/heartburn'). Analysis employed the commonly used taxonomy for ischaemic symptoms. Typical symptoms were defined as either: chest, arm(s), shoulder, jaw, back or epigastric discomfort; shortness of breath; diaphoresis; weakness; indigestion; nausea or vomiting; dizziness or lightheadedness; fear or restlessness.<sup>21–23</sup>

The PCI proceeded in standard fashion, except balloon inflation was prolonged to a maximum of 2 min so as to produce symptomatic and/or electrocardiographic ischaemia. Throughout balloon inflation, subjects were re-questioned about active symptoms using the same tool. Inflation was terminated before 2 min for greater than moderate symptom severity, or insipient electrical or haemodynamic instability.

### Assessment of ischaemia

A multi-lead ECG recording (leads I, II, III, aVR, aVF, and either V<sub>2</sub> or V<sub>3</sub>) was obtained at baseline, immediately before balloon inflation, and immediately preceding balloon deflation, and the duration of balloon inflation was recorded. ST-segment deviation was measured manually in at least six ECG leads, including a precordial lead. Ischaemia was defined as any ST deviation of 1 mm or more in any lead.<sup>21</sup>

### Statistics

Descriptive statistics were used to characterize the sample, number of symptoms, and the frequency of reporting symptoms. The Mann–Whitney *U* test was used to compare the number of symptoms reported because of positive skewness. Bivariate analysis for sex differences in each reported symptom was conducted using either the  $\chi^2$  or Fisher's exact test. To establish potential symptom predictors (other than sex), each symptom having a sex difference nearing statistical significance ( $\leq 0.25$ )<sup>24</sup> was subjected to further bivariate analysis of its relationship with clinical, demographic, and treatment characteristics: education, immigrant status, body mass index, procedure urgency, Canadian Cardiovascular Society (CCS) classification, procedure indication, renal dysfunction, pre-existing heart failure, pulmonary, liver/gastrointestinal disease, malignancy, hypertension, hyperlipidaemia, diabetes, peripheral vascular disease, cerebrovascular disease, smoking

status, prior MI, prior PCI, prior coronary artery bypass grafting, and medications received within past 24 h [ $\beta$ -blockers, intravenous nitroglycerin, long-acting nitrates, calcium antagonists, lipid-lowering agents, angiotensin-converting enzyme (ACE) inhibitors, aspirin, clopidogrel, glyburide, hormone replacement therapy, anticoagulants, anti-depressants]. Variables nearing significance ( $\leq 0.25$ ) were entered *en bloc* into a multivariate logistic regression model as potential predictors. Step-wise trimming of variables that were non-contributory (significance of  $>0.05$ ) produced the most parsimonious model. To ensure that the final model was reliable, the minimum requirement of 10 events per predictor variable was met.<sup>25</sup>

All analyses were conducted using the Statistical Package for the Social Sciences, version 16.0 (SPSS, Inc., Chicago, IL, USA). Power analysis indicated that, given a prevalence of chest or typical discomfort of 70% in men<sup>26</sup> ( $\alpha = 0.05$ ) a sample of 160 men and 160 women would provide 80% power to detect a statistically significant difference of  $\sim 15\%$  ( $\alpha = 0.05$ ).<sup>27</sup>

## Results

### Sample characteristics

After receiving approval from local research ethics boards, the study was conducted over 51 months, ending in February 2008. Of 820 patients screened, 775 (94.5%) met inclusion criteria, of which 560 (72.3%) consented. Of those, 235 (42%) were ineligible after angiography: (PCI not undertaken,  $n = 140$ ; occluded target,  $n = 95$ ). Twenty subjects were excluded because of incomplete ECG data ( $n = 13$ ), incomplete interview data ( $n = 5$ ), or aborted PCI ( $n = 2$ ), yielding a final sample of 305 participants.

One hundred fifty-eight (51.8%) subjects were exposed to balloon inflation of  $>60$  s and 120 (39.3%) had  $<60$  s [median (Mdn) 38 s, inter-quartile range (IQR) 23.5]; duration data were missing in 27 subjects. Of those with duration  $>60$  s, two men had ventricular arrhythmias converted with a single countershock. There were no sex differences in the rate of complications. Reasons for early deflation were: worsening discomfort (12), worsening ST elevation (15), haemodynamic instability (1), premature ventricular contractions (1), and operator choice (2), but no reason for early deflation was reported in 89 cases. We examined all those who had early deflation but no ischaemia, and found there were no statistically significant sex/gender differences in frequencies. That is, women were not more likely than men to have inappropriate early deflation (i.e. for reasons other than ECG-verified ischaemia). In comparing the participants for whom no reason for early deflation was recorded with those for whom a reason was noted, differences were found only in the procedural urgency rating; those with no reason recorded were more likely to be 'urgent' cases.

Baseline characteristics are provided in *Tables 1* and *2*. Most were Canadian-born (70.5%), and spoke English as their first language (78.7%). Fifty-three per cent had CCS class III or IV angina and 54.5% were undergoing angiography and PCI on an urgent inpatient basis. Women were older [65.8 (SD: 11.6) vs. 62.8 (SD: 9.9) years  $P = 0.02$ ] and were more likely to have a history of hypertension, cerebrovascular disease, or evidence of renal dysfunction.

### Number of reported symptoms

Most subjects (75.7%) reported symptoms during balloon inflation. Women had significantly shorter balloon inflations (63.7 s vs. 73.6;

**Table 1** Baseline characteristics, by sex

Characteristic	All (N = 305)	Women (n = 121)	Men (n = 184)	P-value
Socio-demographic				
Age, mean (SD)	63.9 (10.7)	65.8 (11.6)	62.8 (9.9)	0.02
English as first language [n (%)]	240 (78.7)	94 (77.7)	146 (79.3)	0.73
Immigrant to Canada [n (%)]	90 (29.5)	28 (23.1)	62 (33.7)	0.05
Highest education (%)				
Secondary or less	160 (52.4)	70 (57.9)	90 (48.9)	0.10
Post-secondary	145 (47.6)	51 (42.1)	94 (51.0)	
Clinical				
CCS angina class III or IV [n (%)]	163 (53.4)	63 (52.1)	100 (54.3)	0.46
Urgency of procedure [n (%)]				
Elective	139 (45.6)	55 (45.5)	84 (45.7)	0.97
Urgent	166 (54.4)	66 (54.5)	100 (54.4)	
Indication for procedure [n (%)]				
ACS	131 (43.0)	53 (43.8)	78 (42.4)	0.81
Stable angina/CAD	174 (57.0)	68 (56.2)	106 (57.6)	0.84
Prior MI [n (%)]	109 (35.7)	38 (31.4)	71 (38.6)	0.20
Prior revascularization [n (%)]				
PCI	72 (23.6)	28 (23.1)	44 (23.9)	0.88
CABG	18 (5.9)	5 (4.1)	13 (7.1)	0.28
Diabetes [n (%)]				
Type I	2 (0.7)		2 (1.1)	0.15
Type II	58 (19.0)	20 (16.6)	38 (20.7)	0.37
Hypertension	198 (64.9)	88 (72.7)	110 (59.8)	0.02
Peripheral vascular disease	32 (10.5)	14 (11.6)	18 (9.8)	0.62
Cerebrovascular disease	22 (7.2)	14 (11.6)	8 (4.3)	0.02
eGFR $\leq$ 60 mL/min/1.73 m <sup>2a,b</sup>	68 (22.3)	42 (34.7)	26 (14.1)	<0.001
Hypercholesterolaemia	215 (70.5)	87 (69.6)	128 (71.9)	0.66
Liver/gastrointestinal disease	38 (12.5)	19 (15.7)	19 (10.3)	0.17
Pulmonary disease	18 (5.9)	11 (9.1)	7 (3.8)	0.06
Malignancy	42 (13.8)	18 (14.9)	24 (13.0)	0.20

CCS, Canadian Cardiovascular Society; ACS, acute coronary syndrome; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery.

<sup>a</sup>Calculated using Cockcroft–Gault formula.

<sup>b</sup>Some missing data.

$t = 2.99$ ,  $P = 0.003$ ), but the rate of reporting at least one symptom did not differ significantly between men and women (73.9 vs. 80.2%;  $\chi^2 = 1.61$ ,  $P = 0.21$ ). During the baseline interview, women recalled a greater number of prior ischaemic symptoms than did men (Mdn 4, IQR 3, vs. Mdn 3, IQR 3,  $P = 0.01$ ). However, no difference in the number of symptoms reported during inflation was observed (Mdn 1, IQR 2, vs. Mdn 1, IQR 2,  $P = 0.06$ ) (Supplementary material online, Table S1).

## Location of reported symptoms during inflation

The raw data consisted of 202 unique symptom descriptors. Grouping of similar descriptors yielded 49 symptoms of which 21 were described as the 'main' discomfort.

## Unadjusted sex-specific findings

Chest discomfort was the most commonly reported symptom overall (54.8%) (Table 3). There was no significant difference between men and women in this, whether including only symptoms reported as the 'main' symptom, or all reported symptoms. The overall prevalence of symptoms typical of myocardial ischaemia was 69.8% (Table 4). Analysis, including either only main symptoms, or all reported symptoms, indicated no significant difference between men and women. Two symptoms were statistically significantly more prevalent in women: jaw/teeth/throat or neck discomfort, and reporting *only* non-chest-pain discomfort.

## Adjusted sex-specific findings

Symptoms with fewer than five reports or those not reaching statistical significance of  $<0.25$  in bivariate analysis were not included (Table 5). Adjustment for covariates did not substantially change

**Table 2** Procedural characteristics, by sex

Characteristic	All (N = 305)	Women (n = 121)	Men (n = 184)	P-value
First vessel treated [n (%)]				
Left anterior descending	115 (37.6)	44 (36.3)	71 (38.6)	0.88
Diagonal	8 (2.6)	4 (3.4)	4 (2.2)	0.86
Ramus	8 (2.6)	4 (3.3)	4 (2.2)	0.55
Circumflex	44 (14.4)	13 (10.8)	31 (16.8)	0.13
Obtuse marginal	27 (9.0)	10 (8.3)	17 (9.1)	0.97
Right coronary	100 (32.9)	45 (37.1)	55 (29.8)	0.24
Posterior descending	3 (1.0)	1 (0.8)	2 (1.1)	0.82
% Stenosis				
Pre-PCI, mean (SD) (n = 299)	83.0 (15.8)	82.0 (16.5)	83.7 (15.3)	0.37
Post-PCI, mean (SD) (n = 292)	4.0 (10.5)	4.6 (9.7)	3.5 (11.1)	0.41
TIMI flow grade [n (%)] (n = 275)				
Pre-PCI				
3	248 (81.3)	106 (87.6)	142 (77.2)	0.29
Post-PCI				
3	270 (88.5)	112 (92.6)	158 (85.9)	0.35
Balloon inflation duration (s), mean (SD)	71.9 (31.8)	63.7 (37.1)	77.6 (40.8)	<0.01

PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

**Table 3** Prevalence of chest discomfort, main or ever-reported symptom, during balloon inflation

Sex	Chest discomfort as main symptom [n (%)] (95% CI)	P-value	Chest discomfort ever-reported [n (%)] (95% CI)	P-value
All (N = 305)	167 (54.8) (45.4–65.5)	0.66	177 (58.0) (45.4–65.5)	0.60
Women (n = 121)	64 (52.9) (45.4–65.5)		68 (56.2) (45.4–65.5)	
Men (n = 184)	103 (56.0) (45.4–65.5)		109 (59.2) (45.4–65.5)	

CI, confidence interval.

the finding for jaw/teeth/throat or neck discomfort [adjusted odds ratio (OR) 2.91; 95% confidence interval (CI) 1.58–5.37], but female sex was no longer predictive of reporting *only* non-chest pain discomfort (adjusted OR: 1.76; 95% CI: 0.91–3.40) after adjustment for co-variables, specifically immigration status, co-morbid peripheral vascular, renal or liver/gastrointestinal disease, and prior use of clopidogrel. Restricting the analysis to subjects with ECG-confirmed ischaemia (n = 245) did not change the findings substantially, although after adjustment, female sex was a stronger predictor of jaw/teeth/throat or neck discomfort (adjusted OR: 4.55; 95% CI: 2.31–8.98) than in the whole sample, and remained a significant predictor of reporting *only* non-chest discomfort (adjusted OR: 2.11; 95% CI: 1.09–4.09). Factors that decreased the odds of reporting chest or typical symptoms were: co-morbid peripheral vascular disease, increasing age, and current clopidogrel therapy. Having immigrated to Canada increased the odds of reporting chest discomfort. Factors that increased the odds of reporting *only* non-chest

discomfort were peripheral vascular disease and current clopidogrel therapy. Increased reporting of jaw/teeth/throat or neck discomfort was associated with peripheral vascular disease and current clopidogrel, whereas decreased reporting of jaw/teeth/throat or neck discomfort was predicted by having been an immigrant to Canada.

## Discussion

This study is the first to prospectively examine sex-specific ischaemic cardiac symptoms caused by intentional transient reduction in regional coronary blood flow. We found no statistically significant differences in the frequency of ischaemia-induced chest discomfort or other typical ischaemic symptoms among women vs. men. However, women were significantly more likely to report throat, jaw and neck discomfort. No differences in frequency of back discomfort, a commonly cited sex difference, were found.

**Table 4** Prevalence of 'typical' symptoms, main or ever-reported, during balloon inflation

Sex	'Typical' <sup>a</sup> symptoms as main symptom [n (%)] (95% CI)	P-value	'Typical' symptoms ever-reported [n (%)] (95% CI)	P-value
All (N = 305)	199 (65.2) (55.53–75.14)	0.47	212 (69.5) (55.53–75.14)	0.82
Women (n = 121)	76 (62.8) (55.53–75.14)		85 (70.2) (65.91–84.49)	
Men (n = 184)	123 (66.8) (55.53–75.14)		127 (69.0) (55.53–75.14)	

CI, confidence interval.

<sup>a</sup>Chest, arm(s), shoulder, jaw, back or epigastric discomfort; shortness of breath; diaphoresis; weakness; indigestion; nausea and/or vomiting; dizziness and/or lightheadedness; fear or restlessness.**Table 5** Association of sex with selected symptoms reported during balloon inflation (men as referent)

Discomfort or symptom	Sex		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	Women (%) (n = 121)	Men (%) (n = 184)		
Localized discomfort				
Chest	69 (57.0)	111 (60.3)	0.87 (0.55–1.40)	1.21 (0.71–2.06) <sup>A, IMGR, PVD, CRB, CABG, GI, CLP</sup>
Arms (either/both)	11 (9.1)	17 (9.2)	0.98 (0.44–2.18)	— <sup>b</sup>
Throat, jaw/teeth or neck	48 (38.0)	32 (17.4)	2.64 (1.53–4.57)	2.91 (1.58–5.37) <sup>A, IMMIG, CCS, PVD, CLP</sup>
Back/intrascapular	5 (4.1)	7 (3.8)	1.09 (0.34–3.52) <sup>a</sup>	— <sup>b</sup>
Epigastric/indigestion	2 (1.7)	3 (1.6)	1.01 (0.17–6.16) <sup>a</sup>	— <sup>c</sup>
Non-localized symptoms				
Diaphoresis	4 (3.3)	3 (1.6)	2.06 (0.45–9.38) <sup>a</sup>	— <sup>c</sup>
SOB	3 (2.5)	0	—	— <sup>c</sup>
Weakness	2 (1.7)	2 (1.1)	1.53 (0.21–11.01) <sup>a</sup>	— <sup>c</sup>
Nausea/vomiting	2 (1.7)	6 (3.3)	0.50 (0.09–2.51) <sup>a</sup>	— <sup>c</sup>
Dizziness	2 (1.7)	1 (0.5)	3.08 (0.28–34.30) <sup>a</sup>	— <sup>c</sup>
Restlessness/fear	0	0	—	— <sup>c</sup>
Grouped symptoms				
Only non-chest discomfort	29 (24.0)	27 (14.7)	1.83 (1.02–3.29)	1.76 (0.91–3.40) <sup>IMGR, PVD, GI, CLP</sup>
Any 'typical' symptoms	85 (70.2)	127 (69.0)	1.06 (0.64–1.75)	1.63 (0.89–2.96) <sup>PVD, CRB, PCI, LL</sup>
No discomfort	24 (19.8)	48 (26.1)	0.70 (0.40–1.22)	0.63 (0.35–1.14) <sup>A, LL</sup>

OR, odds ratio; CI, confidence interval; SOB, shortness of breath.

Significant co-variables: <sup>A</sup>age; <sup>CCS</sup>Canadian Cardiovascular Society class <sup>CLP</sup>clopidogrel; <sup>CRB</sup>cerebrovascular disease; <sup>GI</sup>GI/liver disease; <sup>IMGR</sup>immigrant; <sup>LL</sup>lipid-lowering therapy; <sup>PCI</sup>prior percutaneous coronary intervention; <sup>PVD</sup>peripheral vascular disease.<sup>a</sup>Exact Fisher CI (expected cell frequency <5).<sup>b</sup>Adjusted analyses not reported if unadjusted  $P \geq 0.25$ .<sup>c</sup>Adjusted analysis not undertaken for event rates <10.

## Sex differences in rates of chest discomfort or typical symptoms not found

Chest discomfort is the most widely recognized symptom of myocardial ischaemia, relied upon by both health professionals and the public.<sup>26,28–30</sup> Sex-based differences in this symptom could have broad clinical and public health implications.

The similarity we observed between men and women in the frequency of chest discomfort and typical symptoms differs from some previous reports. A review of studies relying upon symptom recall found fewer women presented with chest discomfort than did men.<sup>26</sup> However, several recent symptom-recall

studies, using both prospective and retrospective methods, have yielded no sex differences in this symptom<sup>31–37</sup> and others, after adjusting for age, have found no sex differences in chest discomfort.<sup>1,3–5,7,38,39</sup> Importantly, most of the aforementioned studies used retrospective review of health records or non-open-ended questionnaires (only allowing a pre-specified list of responses) administered days to weeks after the event. Closed, checklist-style questionnaires may favour reporting of more classical symptoms, and might discourage reporting symptoms not thought (by either patient or provider) to be typical. We note that, of 14 studies using open methods,<sup>33,34,36,40–42</sup> all found no sex differences, whereas only two of eight studies using closed methods<sup>35,37</sup> found no differences.

Our prospective design, using consistent, iterative interrogation of symptoms during ischaemic episodes, eliminates recall bias. Our open-ended questioning may have aided more complete symptom reporting, thereby reducing sex/gender differences.<sup>43</sup> Finally, collection of electrocardiographic data during coronary occlusion to verify ischaemia overcomes another previously cited limitation.

Collateral flow, ischaemic pre-conditioning, and prior infarction may mitigate the development of ischaemia during temporary obstruction of coronary flow during balloon angioplasty. Therefore, we examined our findings within the subgroup of 245 patients with electrocardiographically evident ischaemia during balloon inflation. Men and women did not differ with respect to ST changes, and there were no statistically significant sociodemographic or clinical differences between those with and without electrocardiographic ischaemia, though others have reported that ischaemia during PCI is more frequent and causes greater ST deviation in women.<sup>44,45</sup> Our findings of no sex differences in objective ischaemia may be due to the shorter inflation times to which the women were exposed. Notably though, our findings of no sex differences in chest or other typical symptoms were unchanged by this narrower analysis.

## Women report greater number of symptoms

Our observation at baseline that women recall more previous symptoms than men is concordant with the findings from studies in which data are based solely upon recall. Moreover, the differential we observed between recalled and prospectively triggered symptoms implies that women are more likely to report symptoms that are not actually part of their true ischaemic symptom array. It is possible though that the statistically significantly greater number of reported symptoms by women at baseline would have also been evident during balloon inflation if women had been exposed to inflations of equal duration. It has been previously suggested that women with ACS report more symptoms than men,<sup>40,42,46</sup> although such analyses have been infrequent. However, others have reported no differences.<sup>32,41,47,48</sup> Psychosocial factors [e.g. socially prescribed gender roles, including the gender of the interviewer (research assistants in this study were predominantly women), different coping mechanisms, higher levels of anxiety, and higher prevalence of depression] may influence women's tendency to report higher pain intensity,<sup>49</sup> and may similarly explain the greater number of reported symptoms. Open- vs. closed-ended questioning, as mentioned, may also affect the number of symptoms reported.

## Other symptoms

Throat, jaw, and neck discomfort were reported more by women, which is consistent with many previous studies.<sup>2,26,34–37,46,48,50,51</sup> The observation that women have greater vagal activity than men,<sup>52</sup> and that the jaw area is innervated by the vagus nerve<sup>53,54</sup> may be clues to the mechanism underlying this observation.

As noted, women had shorter mean duration of balloon inflation than men and so were less likely to have had the full opportunity to develop ischaemia and symptoms. Consequently, it is possible that with longer duration, differential symptom profiles would have

emerged. Further study is warranted to ascertain whether this is the case.

## Limitations

We did not measure gender in this study, though it is acknowledged that gender (e.g. socially or culturally prescribed experiences of 'femaleness' or 'maleness'),<sup>55</sup> as opposed to sex (biological characteristics such as anatomy)<sup>56</sup> differences may explain some of the observed differences. We may have had insufficient statistical power to detect some sex differences. However, the upper bounds of the odds ratio confidence intervals for chest pain were not large, suggesting that such differences, if present, are small, difficult to detect, and unlikely to be relevant in the assessment and management of individual patients. Studying a cohort referred for angiogram may have introduced biases, because those not referred may have had a higher prevalence of atypical symptoms.<sup>57</sup> The duration of ischaemia induced during PCI is shorter than that of ACS or STEMI,<sup>21</sup> and longer-lasting ischaemia might have elicited different or more symptoms. No measures of depression or anxiety were incorporated in the study, which have both been shown to be positively associated with pain.<sup>49</sup> Because we did not systematically collect data about reasons for early balloon deflation, the extent to which other differences may have been present in this subset, and been a source of bias, is unknown. Finally, although our questionnaire possesses strong content-related validity, evidence for other types of validity has not yet been established.

## Conclusions

In this sample of patients undergoing non-emergent PCI, no statistically significant differences were found between men and women in the prevalence of reporting chest or most other typical symptoms. However, the findings revealed that women reported throat and jaw discomfort significantly more often than men. These findings add to the evidence that women report the typical symptoms of myocardial ischaemia with similar frequency to men. Efforts to emphasize differences between men's and women's symptoms of ischaemic heart disease, although well-intentioned, may be misguided.

## Supplementary material

Supplementary material is available at *European Heart Journal* online.

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