Coronary artery bypass graft surgery and primary percutaneous coronary intervention choices in patients with similar coronary anatomy: A computer-based simulation examines the sex gap

Brandon M Meyers MD MSc, Tasnim Vira MD, Chi-Ming Chow MD MSc FRCPC, Beth L Abramson MD MSc FRCPC

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BACKGROUND: Sex differences (or a 'sex gap') exist in the rates of cardiac revascularization. It was evaluated whether physician preference contributes to this difference.

OBJECTIVES: To obtain information on how cardiac specialists manage male and female patients being evaluated for coronary artery disease.

METHODS: A computer-based patient simulation program was developed. Six sex-matched clinical vignettes (three pairs) with uninterpreted coronary angiograms were shown to specialists, who were blinded to the purpose of the study. The sex-matched scenarios were balanced with respect to symptoms, comorbidities and coronary anatomy. Physicians were surveyed on management and rationale.

RESULTS: Fifty physicians were surveyed, consisting mainly of cardiologists from tertiary cardiac centres in Ontario. Among the three sex-matched pairs, the frequencies at which percutaneous coronary intervention (including drug-eluting stents), bypass surgery and medical therapy were chosen did not differ across sexes. The means for men and women, respectively, were 47% and 50% for percutaneous coronary intervention, 32% and 26% for bypass surgery, and 21% and 24% for medical treatment.

CONCLUSIONS: In the present pilot study, cardiac specialists chose similar rates of medical, interventional and surgical procedures independent of a patient's sex. Although large registry trials show that sex differences in management exist, the present data suggest that cardiac specialist preference is less likely to be a factor if coronary angiography was performed. Further research is required to explore the causes of sex discrepancies in cardiac care.

Key Words: *Computer simulation; Myocardial ischemia; Sex bias*

Un logiciel de simulation analyse le fossé sexuel entre le pontage aortocoronarien et l'angioplastie coronarienne percutanée primaire en présence de caractéristiques anatomiques coronariennes similaires

HISTORIQUE : Des différences liées au sexe s'observent quant aux taux d'application des interventions de revascularisation cardiaque. Les auteurs ont voulu vérifier si les préférences des médecins contribuaient à ce « fossé sexuel ».

OBJECTIF : Obtenir des données sur la façon dont les spécialistes traitent les patients et les patientes qu'ils voient pour coronaropathie.

MÉTHODES : Un logiciel de simulation de cas a été mis au point. Six cas cliniques assortis selon le sexe (trois paires) présentant des coronarographies non interprétées ont été soumis à des spécialistes dans le cadre d'un protocole à l'insu aux fins de l'étude. Les scénarios assortis selon le sexe étaient équilibrés sur le plan des symptômes, des morbidités et des spécificités anatomiques des coronaires. On a demandé aux médecins quels traitements ils choisiraient et pourquoi.

RÉSULTATS : On a ainsi interrogé cinquante médecins, principalement des cardiologues de centres de soins cardiaques tertiaires de l'Ontario. Entre les trois paires de cas assortis, la fréquence à laquelle l'intervention coronarienne percutanée (y compris avec pose d'endoprothèse à élution de médicament), la chirurgie cardiaque et le traitement médicamenteux ont été choisis n'a pas différé selon le sexe. Chez les hommes et les femmes, les moyennes ont été respectivement de 47 % et 50 % pour l'intervention coronarienne percutanée, de 32 % et 26 % pour le pontage coronarien et de 21 % et 24 % pour le traitement médicamenteux.

CONCLUSION : Dans la présente étude pilote, des spécialistes de la cardiologie ont choisi dans une même proportion et indépendamment du sexe des patients le traitement médicamenteux, l'intervention coronarienne percutanée et le pontage aortocoronarien. Bien que de grands essais basés les registres fassent état de différences liées au sexe lors de la prise en charge des patients, les données actuelles donnent à penser que la préférence des spécialistes est moins susceptible d'entrer en ligne de compte si une coronarographie a été effectuée. Des recherches plus approfondies s'imposent pour expliquer les différences observées quant à la façon de soigner les patients selon leur sexe.

Women comprise an increasing proportion of patients with coronary artery disease (CAD) (1). The degree of clinically and anatomically significant CAD has been progressively rising in women (2). Shaw et al (3) noted that because female deaths currently surpass male deaths in raw numbers, the older notion of CAD as a "male's disease" could be relabelled a "female's affliction". For nearly two decades, numerous investigators have attempted to determine sex differences in CAD that still exist in North America (4,5).

Since the 1990s, the notion of a sex bias was discussed in the cardiac literature and the term 'Yentl syndrome' was proposed to describe the situation (6). There is a large body of sex research in the cardiac field, with conflicting results. A sex gap could theoretically occur at

any point of the management pathway, from initial diagnosis to referral to investigations and management (7). The influence of race and sex were examined in a decision analysis with hypothetical patients presenting to a primary care physician with chest pain (8). Women were perceived to have a lower probability of CAD, and were less likely to be referred for cardiac catheterization despite identical clinical histories. A retrospective chart review of myocardial infarction patients found that men were not referred for cardiac catheterization at higher rates, except when there were equivocal indications for the procedure (9). However, recent data from a large registry (4) suggest that sex differences in management still exist. The reason for sex differences in care is less clear. A recent study suggests that women and

Division of Cardiology, St Michael's Hospital, University of Toronto, Toronto, Ontario

Correspondence: Dr Beth L Abramson, University of Toronto, St Michael's Hospital, 30 Bond Street, 6-039 Queen Wing, Toronto, Ontario M5B 1W8.

Telephone 416-864-5424, fax 416-864-5974, e-mail abramsonb@smh.toronto.on.ca

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TABLE 1
Simulated patient characteristics

Case	Social history	Age, years	Sex	Symptoms	Noninvasive testing	Medical history	Diagnostic catheterization reason	Angiography details
A	Retired	78	Male	CCS class II chronic angina	None	Diabetes Prostatism	Pre-op (transurethral resection of prostate)	80% CX 99% RCA
	Retired	77	Female	SOBOE with occasional atypical chest pain	None	Diabetes Osteoarthritis	Pre-op (knee surgery)	80% CX 99% RCA
B	Stockbroker	58	Male	CCS class II angina	6.5 min stress test: Bruce 1 mm ST depression and chest pain Perfusion imaging: Moderate-intensity reversible ischemia (anterior and inferior territories)	Dyslipidemia	Catheterization for diagnosis	95% long LAD 80% RCA
	Housewife	60	Female	Dyspnea	7 min stress test: Bruce 1 mm ST depression and SOBOE Perfusion imaging: Moderate-intensity reversible ischemia (anterior and lateral territories)	Fibromyalgia	Catheterization for diagnosis	90% LAD 90% CX
C	Retired; lives in Florida in winter	75	Male	Chest pain intermittently while golfing	Stress test positive at 5 min	Hip replacement Long-standing smoker	Catheterization for diagnosis; returned from Florida for management opinion	3-vessel disease
	Retired teacher	78	Female	Atypical chest pain	Stress test submaximal heart rate but ECG positive and reproduced pain at 5 min	Depression Hypertension Smoker	Catheterization for diagnosis	3-vessel disease

CCS Canadian Cardiovascular Society; CX Circumflex artery; ECG Electrocardiogram; LAD Left anterior descending artery; Pre-op Preoperative; RCA Right coronary artery; SOBOE Shortness of breath on exertion

men may approach decision making differently, but other possibilities, such as physician preference, need to be explored (10).

There is evidence that cardiac revascularization rates also differ between sexes, although the data are conflicting. Multiple studies examining revascularization rates (11-16) have found that coronary artery bypass graft surgery (CABG) is used less often in women, and percutaneous coronary intervention (PCI) is used at lower or the same rates in women as in men. In contrast, Bickell et al (17) found that CABG was used less often in women when surgery offered little benefit over medical treatment, suggesting that these CABG rates may represent a more appropriate referral pattern. In agreement with this, several studies found no differences in revascularization rates after adjusting for degree of CAD and left ventricular function (18,19).

Reasons for this possible sex gap in cardiac care have not been well explored. Results from the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines (CRUSADE) database (20) in patients with acute coronary syndrome confirm that contemporary cardiac catheterization rates are lower in women. They suggest that angioplasty rates may be similar between men and women who are known to have significant angiographic coronary disease. However, CABG rates and total revascularization rates were not compared.

We examined causes of a potential sex gap, and assessed the decision-making process of cardiac specialists. An interactive computer program with hypothetical clinical vignettes was developed, including uninterpreted coronary catheterization films. The objective of the present study was to assess cardiac specialists' management of male and female patients being evaluated for CAD matched for coronary anatomy, symptoms and comorbidities.

METHODS

Survey instrument

An interactive computer-based patient simulation program was developed using Macromedia Authorware (version 7.01, Adobe Systems Inc, USA). The program incorporated patient characteristics, clinical history and coronary angiograms. Six sex-matched

clinical scenarios consisting of three pairs of male and female cases were developed. Four cases consisted of two-vessel disease and two cases consisted of three-vessel disease. Within the sex-matched scenarios, patient age, comorbidities and degree of CAD were controlled for (Table 1). Reported symptoms were matched, accounting for the possible discrepancy of presentation between sexes (21). For example, in scenario B, the male patient had Canadian Cardiovascular Society class II angina, whereas the female patient reported dyspnea. Clinical vignettes were presented to ensure that the matched scenarios did not appear consecutively.

Angiography films

Angiography films were created by selecting the vessels of interest from studies performed at St Michael's Hospital (Toronto, Ontario). The chosen films were matched for grading of lesions. The cardiologists involved with the study (CMC and BLA) reviewed the selected films. To create the films for the simulated patients, several studies from multiple patients were combined to acquire the views required for each case.

An attempt was made to match the coronary anatomy within the clinical sets. However, to eliminate any possibility of bias, the angiograms were switched within a single sex-matched scenario for one-half of the study participants. Except for the required changes in the clinical history, no other variables were altered. To control for left ventricular function, the same ventriculogram (grade 1) was used repeatedly for all cases.

The original films were converted from a digital imaging and communications in medicine (DICOM) format, into a QuickTime movie format using MacAngioview (Wil Lapointe, USA) (best quality conversion, uncompressed format) and were then incorporated into the survey program. The angiograms could be viewed in a continuous loop fashion or frame by frame for greater detail. There were five to 10 angiogram views per case, with the left ventriculogram being the final film.

Data collection

To blind physicians to the purpose of the present study, physicians were told that they were evaluating a new teaching tool. After consent

TABLE 2
Physician characteristics: Demographic data of the sample

Characteristic	n	%
Age, years		
<30	2	4
30–39	15	30
40–49	12	24
50–59	18	36
≥60	3	6
Male sex	45	90
Years in practice		
Resident	7	14
<5	13	26
5–9	1	2
10–14	4	8
15–19	8	16
≥20	17	34
Specialty		
Cardiology	46	92
Cardiac surgery	4	8
Type of practice		
Nonteaching site	3	6
Teaching hospital	47	94
Cardiac facilities on-site (yes)		
Catheterization/intervention	44	88
Cardiac surgery on-site	44	88
Physician practice (yes)		
Perform catheterization	19	38
View films for decision-making*	41	82

*In addition to the 19 who perform catheterization, 22 physicians view coronary angiograms for patient management in everyday practice

was obtained, physicians were asked for demographic data, including age, sex, years in practice, specialty, type of practice, type of cardiac facilities on site, and whether the physician performed cardiac catheterization and/or viewed catheterization films for making decisions. Physicians also selected, from a list, the top three factors they used in deciding whether the simulated patient should be treated with CABG, PCI or medically.

The physician then reviewed the six cases and determined the optimal treatment for the patient. The options were medical therapy initially; PCI (specifying vessel[s]): plain old balloon angioplasty, bare-metal stent or drug-eluting stent [DES]; or CABG (specifying vessel[s]). In the results, plain old balloon angioplasty was combined with bare-metal stent data because it comprised less than 1% of all PCI selections. The rationale for the treatment decision was then selected from a list. Most physicians took approximately 30 min to complete the study.

Study participants

Practicing cardiologists, cardiac surgeons and cardiovascular surgeons in the Greater Toronto Area were mailed a contact letter informing them about the present study. Following the mailing, the physicians were phoned to find out whether they were interested in participating. The same approach was used to contact physicians in the Ottawa, Ontario, region. In addition, data collection was conducted at the Canadian Cardiovascular Society 2004 meeting in Calgary, Alberta; this sample also included cardiology residents and fellows.

Statistics

SPSS version 11 (SPSS Inc, USA) was used for all statistical analyses. Initially, a χ^2 analysis was used for each of the three scenarios with the following factors: vessel (left anterior descending [LAD], circumflex [CX] or right coronary artery [RCA]) and management (medical, PCI, DES or CABG). Because there were no significant differences, a post hoc analysis was performed in which all scenarios were collapsed

TABLE 3
Rate of medical therapy and revascularization decisions of physicians by case

	Vessel					
	LAD		CX		RCA	
	Men	Women	Men	Women	Men	Women
Scenario A, n (%)						
CABG			3 (6)	4 (8)	3 (6)	4 (8)
PCI			24 (48)	26 (52)	27 (54)	27 (54)
Medical therapy	20 (40)	19 (38)				
Scenario B, n (%)						
CABG	12 (24)	9 (18)	4 (8)	3 (6)	8 (16)	6 (12)
PCI	12 (24)	19 (38)	16 (32)	25 (52)	13 (26)	9 (18)
Medical therapy	6 (12)	8 (16)				
Scenario C, n (%)						
CABG	33 (66)	26 (52)	33 (66)	25 (50)	30 (60)	25 (50)
PCI	12 (24)	14 (28)	11 (22)	14 (28)	10 (20)	14 (28)
Medical therapy	5 (10)	9 (18)				
Total CABG, %	45	35	40	32	41	35
Total PCI, %	43	47	51	65	50	50
Total medical therapy, %	21	24				

Medical therapy reflects no intervention. CABG Coronary artery bypass graft surgery; CX Circumflex artery; LAD Left anterior descending artery; PCI Percutaneous coronary intervention; RCA Right coronary artery

into one analysis examining the vessel and management. Binary regression was performed on all variables to determine any correlations.

RESULTS

The study sample consisted of 50 physicians (45 men and five women); 46 physicians were cardiologists and four were cardiac surgeons. Nearly all (n=47) practiced at an academic centre. The majority of physicians either performed cardiac catheterization or viewed catheterization films in everyday practice for treatment decisions (Table 2).

Physicians were asked to select the three most important factors to consider when making treatment decisions. Overall, the most frequent selections were the location of disease (27%), the extent of disease within the vessel (21%) and patient comorbidities (16%). Patient sex was not selected by any as a factor. For the simulated patient scenarios, the most commonly selected reasons for treatment decisions included 'anatomy' (22%), 'studies or personal experience indicated good outcome' (21%) and 'the intended treatment followed expert-opinion guidelines' (19%). Reasons selected less frequently included 'patient quality of life' (14%), 'patient age' (10%), 'degree of CAD suggests medical therapy' (6%) and 'comorbidities influencing intervention' (2%).

Treatment decisions did not differ between male and female cases in any of the three clinical scenarios (Table 3). The mean noninterventional (medical) management rates for all scenarios were 21% and 24% for men and women, respectively. Although these rates varied between the different scenarios, there was no sex effect ($P>0.05$).

Management recommendations for rates of revascularization (PCI, DES or CABG) did not differ between sexes ($P>0.05$) for any vessel within each scenario (Table 3). When vessel revascularization was examined by combining all scenarios, no sex effects were observed. However, binary regression of those who had PCI in the LAD found that women were more likely than men to receive PCI (95% CI 1.1 to 4.2; $P<0.05$). For all other revascularization procedures and vessels, there were no significant correlations. Overall, rates of all forms of PCI were 47% for men and 50% for women; CABG rates were 32% for men and 26% for women (all $P>0.05$).

No sex differences were found among choice of intervention based on the age of the physician, years of practice or whether the physician performed cardiac catheterization. However, if the physician did perform catheterization, they were twice as likely to use PCI or DES in all

vessels (combined 95% CI 1.3 to 5.8; all $P < 0.005$), and this was predominantly in physicians younger than 50 years of age. As might be expected, these same physicians were 50% less likely to use CABG for CX and RCA vessels (combined 95% CI 0.2 to 0.7, $P < 0.005$; LAD 95% CI 0.4 to 1.3, $P > 0.05$).

DISCUSSION

We explored whether patient sex influences the decisions of cardiac specialists when treating patients with CAD. In the present pilot study, we found that cardiac specialists chose medical therapy alone, PCI and CABG at similar rates for the male and female scenarios. To our knowledge, the present report describes the first decision analysis to examine treatment selection based on angiographically proven CAD. Pertinent details of the clinical history were provided, and the sex-matched scenarios were balanced for symptoms, results of noninvasive testing and comorbidities, so theoretically, there should have been no differences in management.

In the real world, differences between male and female patients exist. Women are usually older and have more comorbidities when they present with CAD (22,23). Vaccarino et al (4) recently reported that sex differences have remained unchanged over time in an analysis of a national myocardial infarction registry. They found a higher rate of CABG in men and PCI in women in a contemporary cohort, which may reflect differing patient characteristics. In contrast, a post hoc analysis of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial (24) found that women were less likely to undergo any revascularization procedure, but there was no difference in revascularization rates after adjustment for the lower prevalence of significant CAD in women. Despite this, women were more likely to have refractory angina and repeat hospitalization.

In the current study, when specialists made treatment decisions based on clinical scenarios and angiography results matched for age and comorbidities, we found no evidence that patient sex influenced the decisions of physicians. However, given the small sample size, the subgroup analysis that showed a higher rate of PCI usage in the LAD for women requires further investigation. Our sample physicians reported that anatomy (location and extent of disease) was the main factor in decision making in everyday practice and for the scenarios, which is consistent with the literature (16). Our results are in agreement with several studies showing similar findings in clinical practice. In a prospective cohort analysis of Canadian data (18), CABG and PCI rates were nearly identical between sexes (revascularization RR 0.98 [95% CI 0.94 to 1.03]) after adjusting for several factors not typically collected in administrative databases, including extent of CAD and ejection fraction. Before this adjustment, there were sex differences for CABG and PCI rates. Several recent studies failed to find evidence of a sex gap in revascularization rates, but female sex tends to confer poorer mortality and morbidity at follow-up in both old and new data. The Euro Heart Survey (19) found a reduced revascularization rate in women, but after adjustment, only a trend remained (revascularization OR 0.71 [95% CI 0.48 to 1.04]). However, the authors reported poorer outcomes at one year in women. In contrast, Miller et al (25) reported lower rates of revascularization in women, but sex was not an independent predictor of revascularization. A single-centre retrospective study (26) found lower rates of both PCI and CABG in women, and at two years of follow-up, there was a higher incidence of cardiovascular death and myocardial infarction in women. Recent Canadian data indicate that following a myocardial infarction, women are at increased mortality risk (7). A possible contributing factor was that women were less likely to be seen by a cardiologist or undergo invasive investigations or revascularization.

Consistent with decision making regarding revascularization, we found no differences in the number of men and women recommended for initial medical management. Although some data (19,21,27) suggest sex differences in medical management, we did not collect detailed information on this topic because it was not the focus of the study.

The CRUSADE trial (20) showed that while men were more likely to be catheterized, among patients who were catheterized, there was no sex difference in revascularization rates. However, the CRUSADE trial examined non-ST elevation myocardial infarction acute coronary syndrome patients, who may be different from the chronic stable CAD patient population examined in our study. The fact that coronary artery diameter differs between men and women may have traditionally played a role in outcomes, and therefore, referral for PCI (28). However, with newer technologies, sex differences and outcomes are less important and therefore, differences in luminal diameter between men and women should not be driving care (28).

The issue of sex discrepancies in cardiac care has been studied extensively in the past decade. If the differences reported in some studies are not due to systematic bias on the basis of sex, other factors must exist. At the time of revascularization, women have higher perioperative risk and comorbidities (22,23). Some cohort studies found that women were older and at higher surgical risk for CABG, but recent registries report similar mortality following CABG (22,29) and PCI in women (23,30). Current studies and guidelines suggest that women should not be denied revascularization (31). As Vaccarino et al (4) recently suggested, differences between sexes (and among races) may reflect some unmeasured characteristic or health care factor that has remained stable over time. Our data suggest that decisions made by the cardiac specialist once an angiogram is performed are unlikely to be influenced by patient sex. Therefore, further research is required to identify these unmeasured variables that may account for discrepancies in cardiac care.

There are limitations to the current study. Our sample consisted of physicians primarily from academic centres in Toronto and Ottawa. This may affect the ability to generalize our results, but is likely to be representative of physicians in high-volume North American centres. Given the length of time required to complete this interactive survey, our sample is not large. The possibility exists that we were underpowered to detect differences in patient management, such as PCI usage in the LAD. However, the main purpose of the present pilot study was to generate discussion about this controversial area and look at potential factors that affect decision making rather than evaluate practice patterns per se. The selection rates of modern technologies need to be studied in larger registries and database surveillance of both male and female patients.

SUMMARY

We examined the influence of sex on the decisions of cardiac specialists when evaluating clinical scenarios with angiographic data. We did not find that patient sex influenced management. Our results suggest that the well-established sex gap is likely not accounted for solely by cardiac specialist preference. There are likely other factors contributing to the sex gap in cardiac care that will require further exploration.

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