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REPORTS OF ORIGINAL INVESTIGATIONS

Gender differences in mortality following non-cardiovascular surgery: an observational study

Variation de la mortalité après chirurgie non cardiovasculaire en fonction du sexe des patients: une étude observationnelle

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Abstract

Purpose *Although inequality between males and females in cardiovascular surgery is well recognized, few studies have examined the influence of sex on mortality following non-cardiovascular surgery. The objective of the study was to determine whether there are differences in mortality between males and females following non-cardiovascular surgery and to ascertain to what extent preoperative risk factors explain these differences.*

Methods *This was an observational study of 39,433 consecutive non-cardiovascular inpatient surgical cases from non-sex-biased surgical services from 2003 to 2009. Data on the surgical procedure, patient risk factors, and outcomes was retrieved from the institutional Electronic Data Warehouse. The primary outcome was in-hospital mortality within 30 days of surgery. Multivariate analysis using logistic regression was conducted to determine the role of risk factors for mortality.*

Results *The 30-day mortality was 2.76% for males and 1.89% for females (odds ratio, 1.47; 95% confidence interval [CI], 1.29 to 1.69). Logistic regression showed that age, number of Charlson comorbidities, American Society of Anesthesiologists (ASA) classification, and emergent/urgent status were independent predictors of mortality (receiver operating characteristic area, 0.90). After adjustment for these factors, the odds ratio for male mortality was reduced to 1.31 (95% CI, 1.14 to 1.52).*

Conclusion *Males present for non-cardiovascular surgery with a higher ASA classification, with more comorbidities, and more often emergently than females, providing a partial explanation of the observed difference in mortality.*

Résumé

Objectif *Alors que les inégalités entre hommes et femmes sont bien connues dans le domaine de la chirurgie cardiovasculaire, peu d'études se sont intéressées à la mortalité après chirurgie non cardiovasculaire. L'objectif de l'étude était de déterminer s'il y avait des différences en termes de mortalité entre les hommes et les femmes après chirurgie non cardiovasculaire et de définir dans quelle mesure les facteurs de risque préopératoires expliquaient d'éventuelles différences.*

Méthodes *Il s'agit d'une étude observationnelle incluant 39 433 patients consécutifs, hospitalisés dans des services de chirurgie non cardiovasculaires offrant des interventions pour les deux sexes, entre 2003 et 2009. Les données concernant l'intervention chirurgicale, les facteurs de*

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risque des patients et l'évolution ont été extraits du dépôt de données électroniques des établissements. Le critère d'évaluation principal était la mortalité en cours d'hospitalisation dans les 30 jours suivant la chirurgie. Une analyse multifactorielle a été menée au moyen d'un modèle de régression logistique pour déterminer le rôle des facteurs de risque sur la mortalité.

Résultats *La mortalité à 30 jours a été de 2,76 % pour les hommes et de 1,89 % pour les femmes (rapport de cotes: 1,47; intervalle de confiance à 95 % [IC]: 1,29 à 1,69). Le modèle de régression logistique a montré que l'âge, le nombre de comorbidités de Charlson, la classification de l'American Society of Anesthesiologists (ASA) ainsi que le statut d'urgence ou de secours étaient des facteurs prédictifs de mortalité (surface sous la courbe ROC [receiver operating characteristic]: 0,90). Après ajustement pour ces facteurs, le rapport de cotes pour la mortalité masculine a été abaissé à 1,31 (IC à 95 %: 1,14 à 1,52).*

Conclusion *Les hommes se présentent pour une chirurgie non cardiovasculaire avec une classification ASA plus élevée, davantage de comorbidités et plus souvent en urgence que les femmes, ce qui peut expliquer partiellement la différence de mortalité observée dans l'étude.*

Differences between males and females in postoperative outcomes following cardiovascular surgery have been well documented. Several studies have shown increased rates of mortality and complications among females undergoing cardiac revascularization compared with their male counterparts.[1,2] Many hypotheses have been offered to explain these discrepancies between the sexes in cardiac surgery. For instance, some studies have suggested females are more likely to be referred for cardiac revascularization procedures at a later stage of disease compared with males, thus increasing the risk of postoperative complications.[3] Others have suggested that differences in female physiology, specifically smaller coronary vessel size and body surface area, contribute to observed differences in mortality.[4,5] Such discrepancies between the sexes in non-cardiovascular surgery have not been well explored.

Although there is considerable research examining predictors of postoperative mortality following specific non-cardiac surgical procedures, in many of these studies, sex has typically been used as a variable in statistical models in order to adjust for other outcomes. Moreover, studies reporting inequalities between the sexes in outcome among patients undergoing non-cardiovascular surgery have been largely limited to specific surgical procedures. For instance, an association has been found between males and an increase in postoperative mortality in pulmonary resection and hip replacement.[6-8] Males have also been associated with other adverse outcomes following non-cardiovascular surgery, such as increased intensive care unit (ICU) admissions and rates of sepsis.[9] In a study of surgical ICU patients, males were shown to have a poorer prognosis compared with females.[10] Similarly, Schroder *et al*. (1998) found the risk of hospital mortality was more than 2.5 times greater among males than among females in a cohort of matched male and female surgical sepsis patients.[11] In a ten-year series, Boersma *et al.* examined mortality differences between males and females across all categories of non-cardiac surgery, and in 2005, they reported an increased risk of male mortality (2.2% in males *vs* 1.3% in females).[12] Although this study was a validation of the Lee cardiac risk index, Boersma did not analyze the preoperative risk factors by sex.

The purpose of this study was to examine differences between the sexes in postoperative mortality following non-cardiovascular surgery and to determine whether there are differences in preoperative risk factors that might help to explain any discrepancies between the sexes that were observed.

Methods

The study included consecutive patients who underwent non-cardiovascular inpatient surgery from January 2003 to December 2009 at the University Health Network. A full range of adult surgical procedures (with the exception of trauma and labour and delivery) is performed at the University Health Network, which is a quaternary-care teaching hospital affiliated with the University of Toronto (Toronto, ON, Canada). The primary outcome of the study was 30-day in-hospital mortality. For patients who had more than one surgical procedure in the same visit, the first surgery was considered the index surgery.

Data were extracted from the institutional Electronic Data Warehouse (EDW), which contained information on the surgical procedure, patient demographics, results of laboratory tests, medications administered in hospital, International Classification of Diseases 10th revision (ICD-10) codes, and patient outcomes. The ICD-10 codes were used to determine the number of Charlson Comorbidities (CC) for each patient using the method developed by Quan *et al.*[13] Information from the EDW allowed us to determine the surgical service performing the procedure, whether the surgical procedure was emergent/urgent (EU) in nature, whether the patient died in hospital within 30 days of surgery, and the age, sex, and American Society of Anesthesiologists (ASA) physical status classification of the patient. The data from the EDW is fed electronically from various clinical systems in the hospitals. As with any database, there is the potential for errors in data entry; however, these errors would be distributed randomly between males and females. A validation of data from the EDW compared with the patient charts showed an error rate of less than 2%.

The inclusion criteria for this study were all surgical procedures performed from January 1, 2003 to December 31, 2009 (159,459 procedures). Day surgeries (65,619 procedures) were excluded as they are very low risk. For patients who had multiple surgical procedures during the same visit, only the first surgery in the visit (87,857 procedures) was considered the index procedure for the analysis. Cardiac and vascular procedures (19,020 procedures) were excluded as they have well-known but poorly understood differences between the sexes in incidence and outcome, leaving 68,837 procedures. For patients with surgery in multiple visits over the seven-year period (11,376 procedures), only the last surgery was retained. Cadaveric organ donors (100 patients) were excluded as they were brain-dead at the time of surgery. Transplant procedures (1,940 patients) were excluded as they have unique risk factors that distinguish them from other non-cardiovascular procedures. Sex-biased surgical services were excluded; therefore, urology, surgical oncology, and gynecology procedures (13,651 patients) were excluded. Urology procedures are primarily male; surgical oncology procedures are mostly breast surgery and so are primarily female, and gynecology procedures are exclusively female. Procedures from surgical services representing less than 1% of patients (ANAE, ENDO, GEN BREAST, ORAL and RAD ONC GYN) or less than 0.5% mortality (e.g., ophthalmology) were also excluded (2,334 patients). Three patients were removed from the analysis because of missing data. This resulted in a consecutive set of 39,433 inpatients having general surgery, neurosurgery, orthopedic surgery, otolaryngology, plastic surgery, spinal surgery, and thoracic surgery for our primary analysis of the relationship between risk of mortality and sex.

Statistical analysis was performed with SPSS version 18 (IBM, Armonk, NY, USA). A multivariable model was determined to investigate the independent effect of sex on in-hospital 30-day mortality after the inclusion of established predictors of mortality. Preoperative risk factors (ASA classification, number of CC, EU status), surgical service, and patient demographics (age, sex) were entered into the model (Table 1).

Results

We analyzed 39,433 patients from higher-risk non-sex-biased surgical services to investigate the relationship between sex and the risk factors for mortality. This group of patients was evenly balanced by sex (50.65% male) with a substantially higher mortality in males, with 551 deaths (2.76%) among males and 367 deaths (1.89%) among females ($P < 0.001$). Age, ASA classification, number of CC, and EU status showed a relationship to mortality (Fig. 1). Males had higher mortality than females at all ages except the decade 31-40 (Fig. 2). Males and females are represented equally in ASA categories I, II, and III, but there are more males than females in the high-risk categories IV and V (Fig. 2). The CC show a similar pattern, with equal representation of males and females in the low-risk categories and an increasingly higher proportion of males in the higher-risk categories. More males than females had EU surgery (Fig. 2).

Each of the preoperative risk factors (age, ASA classification, number of CC, and EU status) was a significant independent predictor of mortality when considered alone. A logistic regression of the preoperative risk factors (age, ASA, number of CC, EU status, sex, and surgical service) showed good discrimination (area under the receiver operating characteristic curve of 0.90). Males had an unadjusted odds ratio for death of 1.47 (95% confidence interval [CI], 1.29 to 1.69) (Table 2). The interaction of service and sex with mortality was non-significant, indicating that this relationship was similar across all services. The risk adjusted odds ratio of mortality for males was 1.31 (95% CI, 1.14 to 1.52) indicating that some of the difference in mortality between the sexes was related to preoperative differences in the risk factors.

Discussion

In this study, we found that males and females had approximately equal rates of non-cardiovascular surgery, suggesting that the burden of illness was similar in both sexes. However, post-surgical mortality was greater among males (2.8%) compared with females (1.9%), a relative increase of almost 50%. This difference in mortality was partly explained by the finding that males present for surgery with more risk factors than females.

These findings are similar to Boersma's finding in the Netherlands, which showed an increased risk of mortality among males (2.2% mortality in males *vs* 1.3% in females) undergoing various non-cardiac procedures.[12] Wijeysundera has reported on a large cohort of non-cardiac surgical patients in Ontario,[14] and in a subsequent analysis, found virtually the same unadjusted odds ratio (OR) for male mortality (OR, 1.49; 95% CI, 1.39 to 1.61) that we report here (personal communication). Although this data included patients from our hospital, only one year of the ten-year period covered by this study overlapped with ours. This indicates the phenomenon is both robust and widely occurring.

Surgical services with a risk of mortality greater than 0.5% and without a major sex bias in their case mix showed

Table 1 Descriptive statistics

	Total sample (n = 39,433)	Males (n = 19,974)	Females (n = 19,459)	P value
Age, No. (% within sex)				
0-30 yr	3,629	1,978 (9.9)	1,651 (8.5)	<0.001
31-40 yr	3,914	2,016 (10.1)	1,898 (9.8)	
41-50 yr	6,271	3,123 (15.6)	3,148 (16.2)	
51-60 yr	8,022	4,084 (20.4)	3,938 (20.2)	
61-70 yr	8,040	4,136 (20.7)	3,904 (20.1)	
71-80 yr	6,694	3,456 (17.3)	3,238 (16.6)	
81+ yr	2,863	1,181 (5.9)	1,682 (8.6)	
Emergent Status, No. (% within sex)	12,052	6,499 (32.5)	5,553 (28.5)	<0.001
Number of Charlson Comorbidities, No. (% within sex)				<0.001
0	20,292	9,917(49.6)	10,375 (53.3)	
1	11,949	5,951(29.8)	5,998 (30.8)	
2	5,407	3,047 (15.3)	2,360 (12.1)	
3	1,389	808 (4.05)	581 (2.99)	
4+	396	251 (1.26)	145 (0.75)	
ASA Class, No. (% within sex)				<0.001
I to II	17,686	8,593 (43.0)	9,093 (46.7)	
III	16,968	8,653 (43.3)	8,315 (42.7)	
IV to V	4,507	2,560 (12.8)	1,947 (1.0)	
Service, No. (% within sex)				<0.001
General	9,893	5,125 (25.7)	4,768 (24.5)	
Neurosurgery	6,480	3,323 (16.6)	3,157 (16.2)	
Orthopedics	8,863	4,113 (20.6)	4,750 (24.4)	
Otolaryngology	5,060	2,644 (13.2)	2,416 (12.4)	
Plastics	1,430	578 (2.89)	852 (4.38)	
Spinal	3,528	1,945 (9.74)	1,583 (8.14)	
Thoracic	4,179	2,246 (11.2)	1,933 (9.93)	

ASA = American Society of Anesthesiologists physical status classification

*$P < 0.05$; **$P < 0.001$

excess mortality in males, which was reduced when adjusted for the preoperative risk factors. The analysis of the risk factors in this group provides a partial explanation for this major difference in mortality, since males present for surgery with higher ASA classification, with more comorbidities, and more often emergently. There remains a residual additional risk of male mortality which is as yet unexplained.

The finding of an association between males and an increase in postoperative mortality is consistent with the other studies examining sex and postoperative mortality in non-cardiovascular surgery, although these studies had a large sex imbalance.[6,7] Studies with a large sex bias in referral for surgery present difficulties in interpretation, because it is unclear which selection factors led to this discrepancy. Our study eliminated this problem by analyzing a subset consisting of only the surgical services without a large sex bias in presentation for surgery.

Each of these surgical services showed the same pattern of greater male mortality except orthopedic surgery, where males and females had similar mortality. However females undergoing orthopedic surgery were on average 9.6 yr older than males, while in the other services, the ages were similar or males were older. It has been reported that the odds of an orthopedic surgeon recommending total knee arthroplasty to a male was 22 times that for a female patient with similar knee osteoarthritis.[15] In females, orthopedic surgery may have been delayed until the condition was so severe that surgery was unavoidable, resulting in an age difference that increased the risk of female mortality, overcoming the typical increased risk in males. In the logistic regression, the interaction terms between sex and service were not significant, which indicated the difference in mortality between sexes was similar in all services when adjusted for risk.

There are well-documented discrepancies observed in the overall health status of males compared with females. The U.S. Department of Health and Human Services, Office on Women's Health[16] suggests the presence of a "crisis" in the state of men's health on the basis of numerous health indicators. For example, women live

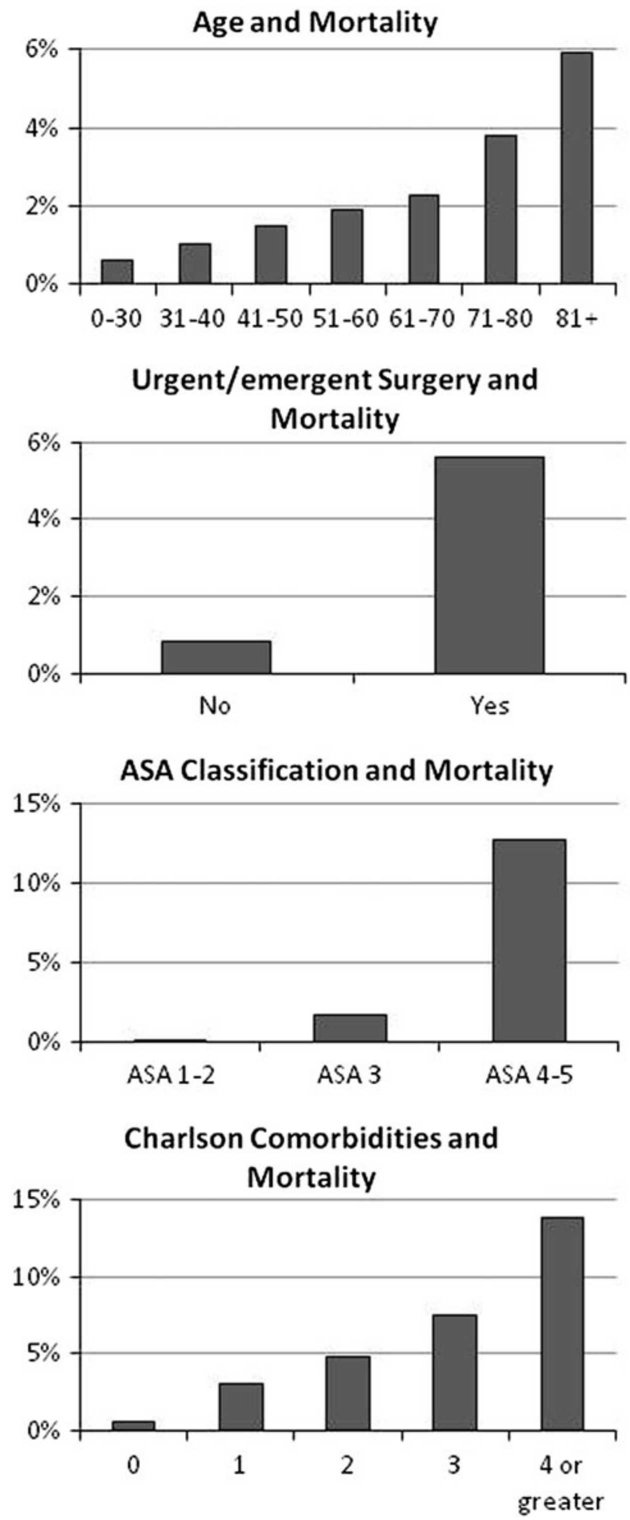

Fig. 1 Preoperative risk factors and mortality

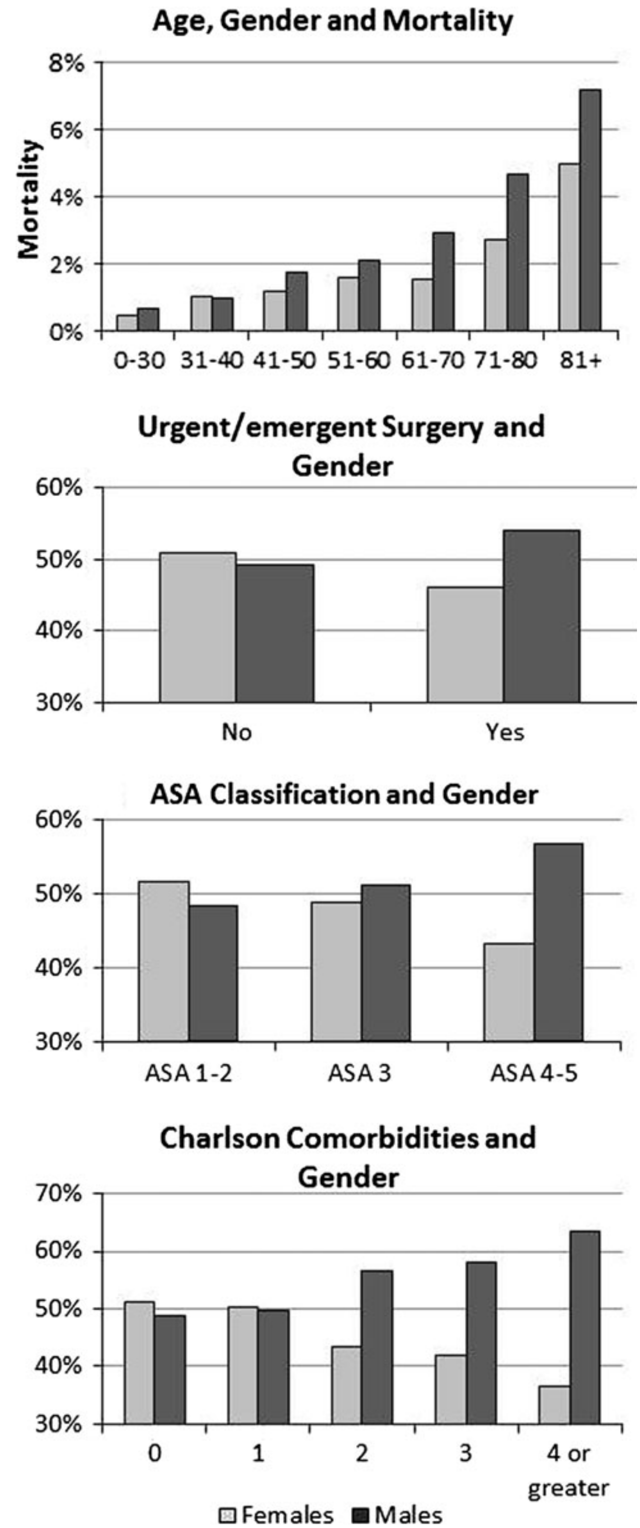

Fig. 2 Differences between sexes in preoperative risk factors

longer than men; there is greater mortality for the top ten causes of death among males *vs* females; there is greater mortality among males due to addictions; and there is an increased risk of infection following trauma in males.[16-19]

These results are consistent with our finding that males present for surgery with greater preoperative risk than females, as indicated by higher ASA scores, more comorbidities, and a higher incidence of emergent surgery.

Table 2 Unadjusted and adjusted OR for 30-day mortality (n = 39,433)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Sex		
Female	1.0	1.0
Male	1.47 (1.29 to 1.69)	1.31 (1.14 to 1.52)
Age		
0-30	1.0	1.0
31-40	1.69 (1.00 to 2.85)	1.27 (0.74 to 2.18)
41-50	2.50 (1.57 to 3.98)	1.35 (0.83 to 2.20)
51-60	3.17 (2.02 to 4.96)	1.47 (0.92 to 2.36)
61-70	3.86 (2.48 to 6.02)	1.45 (0.91 to 2.30)
71-80	6.49 (4.19 to 10.06)	2.13 (1.35 to 3.38)
81+	10.35 (6.62 to 16.18)	2.60 (1.62 to 4.19)
Emergent Status		
Non-Emergent	1.0	1.0
Emergent	7.02 (6.04 to 8.16)	3.28 (2.75 to 3.92)
ASA Class		
ASA I to II	1.0	1.0
ASA III	12.11 (8.04 to 18.24)	6.42 (4.21 to 9.81)
ASA IV to V	105.37 (70.51 to 157.48)	29.28 (19.14 to 44.79)
No. Charlson Comorbidities		
0	1.0	1.0
1	5.31 (4.32 to 6.53)	2.21 (1.78 to 2.75)
2	8.45 (6.81 to 10.50)	2.61 (2.06 to 3.29)
3	13.66 (10.47 to 17.83)	2.66 (1.99 to 3.56)
4+	26.67 (19.06 to 37.31)	4.25 (2.95 to 6.12)
Service		
General	1.0	1.0
Neurosurgery	1.59 (1.35 to 1.87)	1.04 (0.87 to 1.25)
Orthopedic	0.37 (0.29 to 0.46)	0.63 (0.49 to 0.80)
Otolaryngology	0.28 (0.21 to 0.39)	0.54 (0.39 to 0.76)
Plastics	0.22 (0.12 to 0.42)	0.40 (0.21 to 0.76)
Spinal	0.30 (0.21 to 0.43)	0.40 (0.27 to 0.58)
Thoracic	0.84 (0.67 to 1.05)	0.92 (0.72 to 1.16)

The covariates used in the model were Sex, Age, Emergent Status, ASA Class, No. Charlson Comorbidities, and Service. The unadjusted Odds Ratios are for a univariate analysis of each variable

$\chi^2 = 8.15$, df $= 8$, H-L $P = 0.385$

OR = odds ratio, CI = confidence interval, ASA = American Society of Anesthesiologists' physical status classification

Moreover, these differences in preoperative risk factors accounted for a substantial proportion of the difference in postoperative mortality we observed between sexes.

It is possible that these differences in preoperative risk factors between the sexes may be related to the tendency for males to have fewer contacts with the primary health care system, resulting in surgery at a later and more urgent stage of the disease. It is well-established that males use primary health care services less often than females in Canada, the United States (U.S.) and the United Kingdom.[20-23] This remains true even after correcting for female use of health care services related to reproductive issues.[21] Studies that have examined this issue have found that males have fewer family practitioner visits and a lower uptake of preventative health services. This trend is consistent across socioeconomic status and across various age groups, and it has also shown to be true in a study from the U.S. when services were provided for no fee.[24] Alt described the pattern of preventative health care use among men in the U.S., showing that men have a lower number of ambulatory care visits, a longer interval between visits, and they are less likely than females to have a regular family physician.[25] Several other studies have attributed the poorer health status of males to a lack of primary health care use.[23,26,27] A 2008 report from the Canadian Institute for Health Information indicated that the average cost to treat males in hospital was greater than that for females.[28] The reason for this cost differential is unknown.

We hypothesize that differences between the sexes in accessing the primary health care system may explain why males present for surgery with more preoperative risk factors. A recent study from Australia, which found a relationship between mortality and the regularity of visits to primary care physicians, supports this hypothesis.[29] Future studies will be required to determine the factors that contribute to the increased number of preoperative risk factors in males *vs* females. If differences in access to primary health care are related to the preoperative risk factors within each sex, then public health campaigns (similar to those for healthy eating and exercise) to encourage males to make greater use of primary health care may result in significant improvements in perioperative mortality.

Limitations

There are several limitations to this study that are related to the study design and measurement of variables. It is possible that the differences between the sexes may be explained by factors that are not included in our model. There is also a possibility of a selection bias in patients that present for surgery, although the fact that both sexes are almost equally represented in this consecutive sample would suggest this bias is not large. There are limitations with respect to how particular variables were measured. First, 30-day mortality could be recorded only for patients who died within hospital. Thus, patients who were discharged home or to another facility prior to death were lost to follow-up. Second, the calculation of the CC was completed using ICD-10 codes. Many studies have shown inconsistencies in the recording of ICD-10 codes, in that not all comorbidities or diagnoses are recorded. Due to these inconsistencies, the measure of patient comorbidities may be unreliable. Third, the difference in mortality between males and females could be due to well-known differences between the sexes in cardiac problems, despite the fact that these patients were having non-cardiovascular procedures. However, we found the revised cardiac risk index (RCRI) for the study patients did not change the results when it was included in the logistic regression model, suggesting that cardiac risk factors do not account for the observed differences in mortality. The RCRI was not retained in the final model as four of the variables in this index are also included in the CC index.

In conclusion, we found that males have a higher risk of mortality than females undergoing non-cardiovascular surgery. Males present for surgery with higher ASA classification, with more comorbidities, and more often emergently than females. These differences in preoperative risk factors partially explain the observed difference in mortality. We hypothesize differences between the sexes in preoperative risk factors may be related to the tendency for males to have fewer contacts with primary care, resulting in surgery at a later and more urgent stage of disease. There is a possibility of a selection bias in patients that present for surgery, although the fact that both sexes are almost equally represented in this consecutive sample would suggest this bias is not large.

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Conflicts of interests None declared.

References

1. *Guth AA*, *Hiotis K*, *Rockman C*. Influence of gender on surgical outcomes: does gender really matter? J Am Coll Surg 2005; 200: 440-55.
2. *Kim C*, *Redberg RF*, *Pavlic T*, *Eagle KA*. A systematic review of gender differences in mortality after coronary artery bypass graft surgery and percutaneous coronary interventions. Clin Cardiol 2007; 30: 491-5.
3. *Khan SS*, *Nessim S*, *Gray R*, *Czer LS*, *Chaux A*, *Matloff J*. Increased mortality of women in coronary artery bypass surgery: evidence for referral bias. Ann Intern Med 1990; 112: 561-7.
4. *Fisher LD*, *Kennedy JW*, *Davis KB*, *et al*. Association of sex, physical size, and operative mortality after coronary artery bypass in the Coronary Artery Surgery Study (CASS). J Thorac Cardiovasc Surg 1982; 84: 334-41.
5. *Loop FD*, *Golding LR*, *MacMillan JP*, *Cosgrove DM*, *Lytle BW*, *Sheldon WC*. Coronary artery surgery in women compared with men: analyses of risks and long-term results. J Am Coll Cardiol 1983; 1(2 Pt 1): 383-90.
6. *Damhuis RA*, *Schutte PR*. Resection rates and postoperative mortality in 7,899 patients with lung cancer. Eur Respir J 1996; 9: 7-10.
7. *Lie SA*, *Engesaeter LB*, *Havelin LI*, *Furnes O*, *Vollset SE*. Early postoperative mortality after 67,548 total hip replacements: causes of death and thromboprophylaxis in 68 hospitals in Norway from 1987 to 1999. Acta Orthop Scand 2002; 73: 392-9.
8. *Kannegaard PN*, *van der Mark S*, *Eiken P*, *Abrahamsen B*. Excess mortality in men compared with women following a hip fracture. National analysis of comedications, comorbidity and survival. Age Ageing 2010; 39: 203-9.
9. *Wichmann MW*, *Inthorn D*, *Andress HJ*, *Schildberg FW*. Incidence and mortality of severe sepsis in surgical intensive care patients: the influence of patient gender on disease process and outcome. Intensive Care Med 2000; 26: 167-72.
10. *Bauerle R*, *Rucker A*, *Schmandra TC*, *Holzer K*, *Encke A*, *Hanisch E*. Markov cohort simulation study reveals evidence for sex-based risk difference in intensive care unit patients. Am J Surg 2000; 179: 207-11.
11. *Schroder J*, *Kahlke V*, *Staubach KH*, *Zabel P*, *Stuber F*. Gender differences in human sepsis. Arch Surg 1998; 133: 1200-5.
12. *Boersma E*, *Kertai MD*, *Schouten O*, *et al*. Perioperative cardiovascular mortality in noncardiac surgery: validation of the Lee cardiac risk index. Am J Med 2005; 118: 1134-41.
13. *Quan H*, *Sundararajan V*, *Halfon P*, *et al*. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005; 43: 1130-9.
14. *Wijeysundera DN*, *Austin PC*, *Beattie WS*, *Hux JE*, *Laupacis A*. A population-based study of anesthesia consultation before major noncardiac surgery. Arch Intern Med 2009; 169: 595-602.
15. *Borkhoff CM*, *Hawker GA*, *Kreder HJ*, *Glazier RH*, *Mahomed NN*, *Wright JG*. The effect of patients' sex on physicians' recommendations for total knee arthroplasty. CMAJ 2008; 178: 681-7.

16. *U.S. Department of Health and Human Services, Office on Women's Health.* Literature review on effective sex- and gender-based systems/models of care. Available from URL: http://www.womenshealth.gov/owh/multidisciplinary/reports/GenderBasedMedicine/Question7.cfm. Updated 2007. (accessed October 2011).
17. *Offner PJ, Moore EE, Biffl WL.* Male gender is a risk factor for major infections after surgery. Arch Surg 1999; 134: 935-8; discussion 938-40.
18. *Solomon LM*, *Noll RC*, *Guttman R*. The weaker sex: is being male a legally cognizable defect, impairment, or disability? Gend Med 2008; 5: 200-8.
19. *Zuk M*. The sicker sex. PLoS Pathog 2009; 5: e1000267.
20. *Bertakis KD*, *Azari R*, *Helms LJ*, *Callahan EJ*, *Robbins JA*. Gender differences in the utilization of health care services. J Fam Pract 2000; 49: 147-52.
21. *Curie RJ*. Health, Health Care, and the Sexes: A new Perspective. Manitoba Centre for Health Policy. November 2005. Available from URL: http://mchp-appserv.cpe.umanitoba.ca/reference/sexdiff_summ.pdf (accessed October 2011).
22. *Mansfield AK*, *Addis ME*, *Courtenay W*. Measurement of men's help-seeking: development and evaluation of the barriers to help seeking scale. Psychology of Men & Masculinity 2005; 6: 95-108.
23. *Rafuse J*. Men's attitudes about seeking health care may put them at risk, conference told. CMAJ 1993; 149: 329-30.
24. *Stockwell DH*, *Madhavan S*, *Cohen H*, *Gibson G*, *Alderman MH*. The determinants of hypertension awareness, treatment, and control in an insured population. Am J Public Health 1994; 84: 1768-74.
25. *Alt RL*. Where the boys are not: a brief overview of male preventive health. Wisconsin Medical Journal 2002; 101: 22-7.
26. *Green CA*, *Pope CR*. Gender, psychosocial factors and the use of medical services: a longitudinal analysis. Soc Sci Med 1999; 48: 1363-72.
27. *Galdas PM*, *Cheater F*, *Marshall P*. Men and health help-seeking behaviour: literature review. J Adv Nurs 2005; 49: 616-23.
28. *Canadian Institute for Health Information.* The Cost of Acute Care Hospital Stays by Medical Condition in Canada 2004-2005-2008. Available from URL: http://secure.cihi.ca/cihiweb/products/nhex_acutecare07_e.pdf (accessed October 2011).
29. *Einarsdottir K*, *Preen DB*, *Emery JD*, *Kelman C*, *Holman CD*. Regular primary care lowers hospitalisation risk and mortality in seniors with chronic respiratory diseases. J Gen Intern Med 2010; 25: 766-73.