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Original Article

Sex Differences in Trends in Incidence of Thoracic Aortic Aneurysm Repair and Aortic Dissection: 2005-2015

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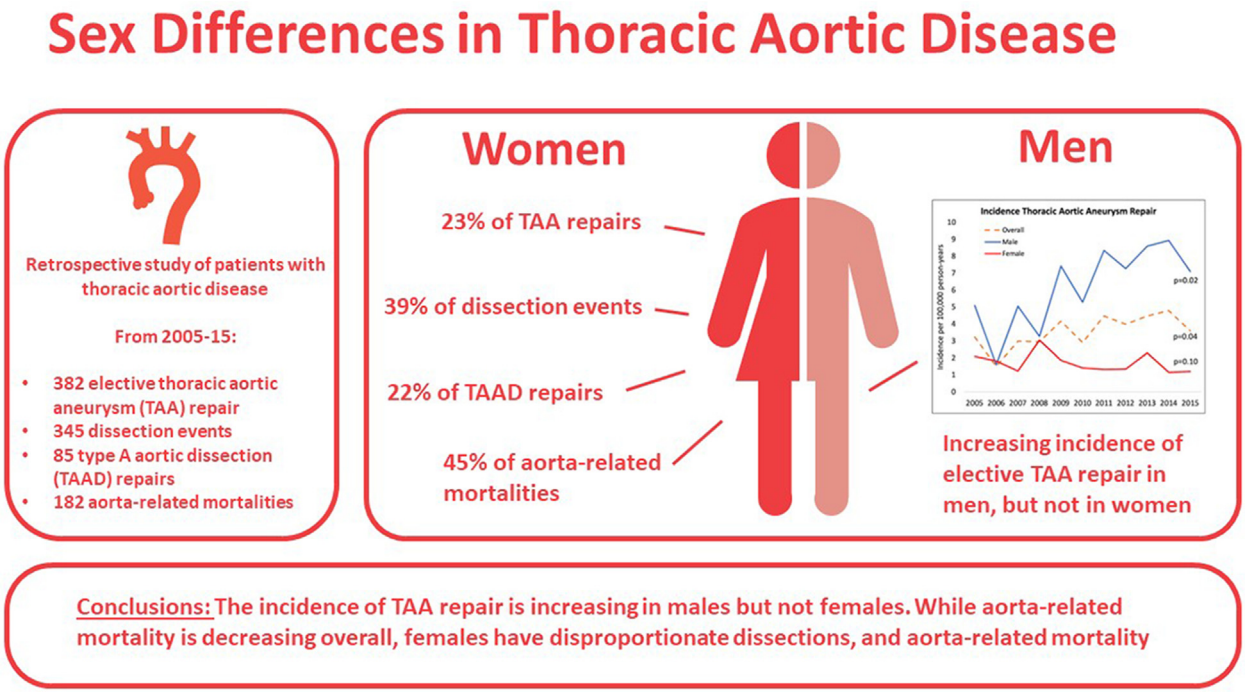

ABSTRACT

Background: The purpose of this study was to examine trends in the incidence of thoracic aortic aneurysm (TAA) repair and aortic dissection.

Methods: A retrospective study was conducted of patients from the period 2005-2015 with thoracic aortic disease. Unadjusted mortality was compared in women vs men. Rates of scheduled TAA repair,

RÉSUMÉ

Introduction : L'objectif de cette étude était d'examiner les tendances relatives à l'incidence des réparations d'anévrisme de l'aorte thoracique (AAT) et de dissection aortique.

Méthodes : Nous avons mené une étude rétrospective de patients atteints d'une maladie de l'aorte thoracique de la période 2005-2015.

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dissection events, acute type A aortic dissection (TAAD) repair, and aorta-related mortality were obtained from our institution's clinical registry and administrative data sources and used to calculate the age-adjusted incidence for each sex, adjusted to the Canadian standard population. Weighted linear regression was performed to analyze trends over time.

Results: A total of 382 scheduled TAA repair operations, 345 dissection events, 85 TAAD repairs, and 182 aorta-related mortalities were identified. Women accounted for 23% of TAA repairs, 39% of dissection events, 22% of TAAD repairs, and 45% of aorta-related mortalities. The incidence of TAA repair was 3.5 per 100,000 person-years (95% confidence interval [CI]: 3.2-3.9), and increased in men ($P = 0.02$) but not women ($P = 0.10$) over time. The incidence of aortic dissection was 3.4 per 100,000 (95% CI: 3.1-3.8) and was stable over time ($P = 0.43$). The average annual age-adjusted incidence of TAAD repair was 0.8 per 100,000 (95% CI: 0.6-1.0) and increased over time ($P = 0.001$). The overall incidence of aorta-related mortality was 1.8 per 100,000 (95% CI: 1.5-2.0) and decreased over time ($P = 0.02$).

Conclusion: The incidence of TAA repair is increasing in men but not women. Although aorta-related mortality is decreasing overall, disparities exist between the male and female population.

Nous avons comparé la mortalité non ajustée entre les femmes et les hommes. Nous avons obtenu les taux de réparations planifiées d'AAT, de dissections, de dissections aortiques de type A (DATA) à la phase aiguë et de mortalité d'origine aortique du registre clinique de notre établissement et des sources de données administratives, et les avons utilisés pour calculer l'incidence ajustée selon l'âge pour chacun des sexes, ajustée à la population canadienne type. Nous avons effectué une régression linéaire pondérée pour analyser les tendances temporelles.

Résultats : Nous avons recensé un total de 382 réparations planifiées d'AAT, 345 dissections, 85 réparations de DATA et 182 cas de mortalité d'origine aortique. Les femmes représentaient 23 % des cas de réparation d'AAT, 39 % des cas de dissection, 22 % des cas de réparations de DATA et 45 % des cas de mortalité d'origine aortique. L'incidence des réparations d'AAT était de 3,5 par 100 000 années-personnes (intervalle de confiance [IC] à 95 % : 3,2-3,9) et augmentait chez les hommes ($P = 0,02$), mais non chez les femmes ($P = 0,10$) avec le temps. L'incidence des dissections aortiques était de 3,4 par 100 000 (IC à 95 % : 3,1-3,8) et était stable au fil du temps ($P = 0,43$). L'incidence moyenne annuelle selon l'âge de réparations de DATA était de 0,8 par 100 000 (IC à 95 % : 0,6-1,0) et augmentait avec le temps ($P = 0,001$). L'incidence globale de mortalité d'origine aortique était de 1,8 par 100 000 (IC à 95 % : 1,5-2,0) et diminuait avec le temps ($P = 0,02$).

Conclusion : L'incidence des réparations d'AAT augmente chez les hommes, mais non chez les femmes. Bien que la mortalité d'origine aortique tende dans l'ensemble à diminuer, il existe des disparités entre la population masculine et la population féminine.

Acute aortic dissection (AAD) is a costly event with high morbidity risk.[1] Estimates of the incidence of AAD vary widely, due to the inclusion or exclusion of prehospital deaths, and range from 2.5 to 15.3 per 100,000.[2,3] Contemporary estimates of hospitalization for AAD have shown an increasing incidence, from 0.9 to 1.6 per 100,000 in the US,[4] with studies in Canada reporting stable but higher rates of AAD ranging from 1.9 to 3.0 per 100,000, with no change over time.[5,6]

The epidemiology of thoracic aortic aneurysm (TAA) is challenging to study due to the indolent nature of the disease, as TAAs typically remain silent until they are detected incidentally or present as an acute aortic syndrome. The goal of screening and scheduled repair of TAA is to prevent acute aortic events. Guideline recommendations have evolved over time to include screening of relatives of patients with aortopathy and aneurysm repair based on prespecified size criteria.[7-9] Rates of screening for TAA and volume of proximal aortic repair are rising.[4,5,10] Whether the evolution of treatment approaches for thoracic aortic disease translates to increased scheduled TAA repair and decreased aorta-related mortality is unclear.

Women are often underrepresented in cardiovascular research, including the study of thoracic aortic disease.[11] Women typically represent 30%-40% of patients presenting with thoracic aortic disease, and the detection of thoracic aortic disease is increasing at a faster rate in women than in men.[5] Despite this level of need, women account for fewer scheduled proximal aortic aneurysm repairs,[4] and a disproportionately increasing incidences of aortic dissection and aortic-related mortality occur among women.[12] Analysis of sex-based trends in the incidence of thoracic aortic disease can help inform screening and intervention and address sex-based disparities within the population.

The province of Nova Scotia, Canada has one tertiary centre that provides cardiac surgery for the entire province, allowing for population-based analysis of rates of aortic surgery. This concentration of care, combined with administrative data regarding cause of death, allows for analysis of trends of scheduled operations, rates of aortic dissection, aortic dissection operations, and aorta-related mortality. The purpose of this study was to examine sex-based trends in the incidence of proximal TAA repair and aortic dissection over time.

Material and Methods

Study design

A retrospective cohort study of patients from 2005-2015 with thoracic aortic disease in Nova Scotia was conducted. All

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Ethics Statement: Approval for this study was granted on November 22, 2016 by the Nova Scotia Health Authority Research Ethics Board (No. 1021911), and a waiver of informed consent was granted.

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See page 1088 for disclosure information.

Table 1. Incidence of scheduled TAA repair, AAD, TAAD repair, and aorta-related mortality

	Scheduled TAA repair n = 382	AAD n = 345	TAAD repair n = 85	Aorta-related mortality n = 182
Age, y, mean ± SD	58.4 ± 13.5	67.6 ± 15.8	61.7 ± 12.5	72.3 ± 15.2
Female sex, n (%)	88 (23)	133 (39)	19 (22)	82 (45)
Incidence				
Overall	3.55 (3.18−3.92)	3.40 (2.21−4.53)	0.78 (0.61−0.96)	1.76 (1.51−2.02)
2005	3.23 (2.08−4.37)	3.37 (3.05−3.76)	0.56 (0.09−1.02)	1.76 (0.93−2.60)
2006	1.50 (0.72−2.28)	3.55 (2.35−4.75)	0.43 (0.01−0.85)	2.15 (1.21−3.08)
2007	2.98 (1.87−4.09)	3.38 (2.20−4.57)	0.42 (0.00−0.84)	1.99 (1.08−2.91)
2008	2.95 (1.84−4.06)	3.14 (1.99−4.28)	0.52 (0.06−0.99)	1.88 (0.99−2.76)
2009	4.16 (2.84−5.49)	3.38 (2.17−4.58)	1.33 (0.58−2.08)	1.64 (0.80−2.47)
2010	2.90 (1.80−4.00)	2.71 (1.62−3.79)	0.51 (0.04−0.97)	1.40 (0.62−2.18)
2011	4.47 (3.09−5.85)	4.05 (2.74−5.36)	0.92 (0.30−1.54)	2.09 (1.14−3.04)
2012	3.98 (2.67−5.30)	4.18 (2.83−5.53)	0.71 (0.15−1.26)	2.56 (1.50−3.62)
2013	4.48 (3.10−5.86)	3.69 (2.41−4.98)	1.17 (0.44−1.89)	1.93 (1.00−2.86)
2014	4.78 (3.32−6.25)	3.19 (2.01−4.37)	0.90 (0.28−1.53)	0.87 (0.25−1.50)
2015	3.59 (2.32−4.87)	2.80 (2.25−3.36)	1.14 (0.42−1.87)	1.11 (0.74−1.47)
Trend coefficient (95% CI)	0.22 (0.01 to 0.42)	−0.03 (−0.11 to 0.05)	0.06 (0.04 to 0.09)	−0.08 (−0.15 to −0.01)
	$P = 0.04$	$P = 0.43$	$P = 0.001$	$P = 0.02$

Incidence is presented as incidence per 100,000 person-years, age-adjusted to the 2012 Canadian standard population.
AAD, acute aortic dissection; CI, confidence interval; SD, standard deviation, TAA, thoracic aortic aneurysm; TAAD, type A aortic dissection.

patients presenting for TAA repair and aortic dissection were identified, to calculate trends in incidence over time. Approval for this study was granted on November 22, 2016 by the Nova Scotia Health Authority Research Ethics Board (No. 1021911), and a waiver of informed consent was granted.

Patient selection

Patients presenting for scheduled TAA repair and acute type A aortic dissection (TAAD) repair were identified from our institution's clinical registry. Patients admitted to the hospital with aortic dissection who did not undergo surgery, and those who died of an aortic dissection, were identified through administrative data using the International Classification of Diseases, version 10 (ICD-10) code for thoracic aortic dissection (I71.0). Patients identified through either the institution's clinical registry or administrative data were linked through provincial medical services insurance program numbers to exclude duplicate entries. Chart review was conducted to confirm diagnosis in cases identified using administrative data.

Rates of scheduled TAA repair were calculated based on the number of patients who underwent surgery for any ascending aortic aneurysm, either in isolation or in combination with other cardiac surgical procedures. Patients presenting with TAA who were managed medically and/or declined surgery were not included in the estimation of the rate of TAA repair. Patients undergoing root enlargement or root repair for infective endocarditis were excluded. The overall rate of combined TAAD and type B aortic dissection (TBAD) was calculated based on the combined rate of TAAD repair, admission for diagnosis of aortic dissection obtained through the discharge abstract database using the ICD-10 code I71.0, and any death with aortic dissection listed as an underlying cause of death, obtained through vital statistics (I71.0). The rate of TAAD repair was obtained based on patients who underwent surgery specifically for TAAD, identified through the institution's registry. Aorta-related mortality was calculated based on patients who died with the underlying cause of death listed as aortic dissection (I71.0), TAA with rupture (I71.1), or TAA without rupture (I71.2), as identified through vital statistics. The age-adjusted incidence of TAA repair, the overall rates of combined TAAD and TBAD, surgery for TAAD, and aorta-related mortality were calculated for each sex and each year of study, based on Canadian census estimates, and then were adjusted to the 2012 Canadian standard population to allow for trend analysis accounting for changes in population age distribution over time.[13]

Statistical analysis

Baseline characteristics of patients presenting with scheduled TAA repair, combined TAAD and TBAD, TAAD repair, and aorta-related mortality were presented using numbers and proportions, as well as mean ± standard deviation (SD), as appropriate. Unadjusted mortality at home, 30-day mortality, and operative mortality were calculated for patients in both scheduled TAA repair and in emergent TAAD repair and were compared in men vs women using χ^2 or Fisher's exact test, as appropriate. Operative mortality during the first half of the study (2005-2009) vs the second half (2010-2015) of the study was compared using the χ^2 test. Weighted linear regression was performed to analyze trends in the incidence of TAA repair, the rate of combined TAAD and TBAD, TAAD repair, and aorta-related mortality, overall and among men and women individually per year, with inverse weighting used for the standard error estimates for the population. Statistical analysis was performed using Stata, version 14 (StataCorp, College Station, TX).

Results

A total of 382 scheduled TAA repair operations and 345 dissection events were identified from the period 2005-2015. Of the dissection events, 85 underwent surgical TAAD repair, and 182 aorta-related mortalities occurred.

Of the 382 patients presenting for scheduled TAA repair, the mean age was 58.4 ±13.5 years, and 88 (23%) were female (Table 1). Unadjusted operative mortality occurred significantly more often in women, vs men (5.7% vs 1.4%, $P = 0.03$). No difference occurred in unadjusted operative mortality in the first half (2005-2009) vs second half (2010-2015) of the study (2.9% vs 2.1%, $P = 0.73$). The average annual age-adjusted

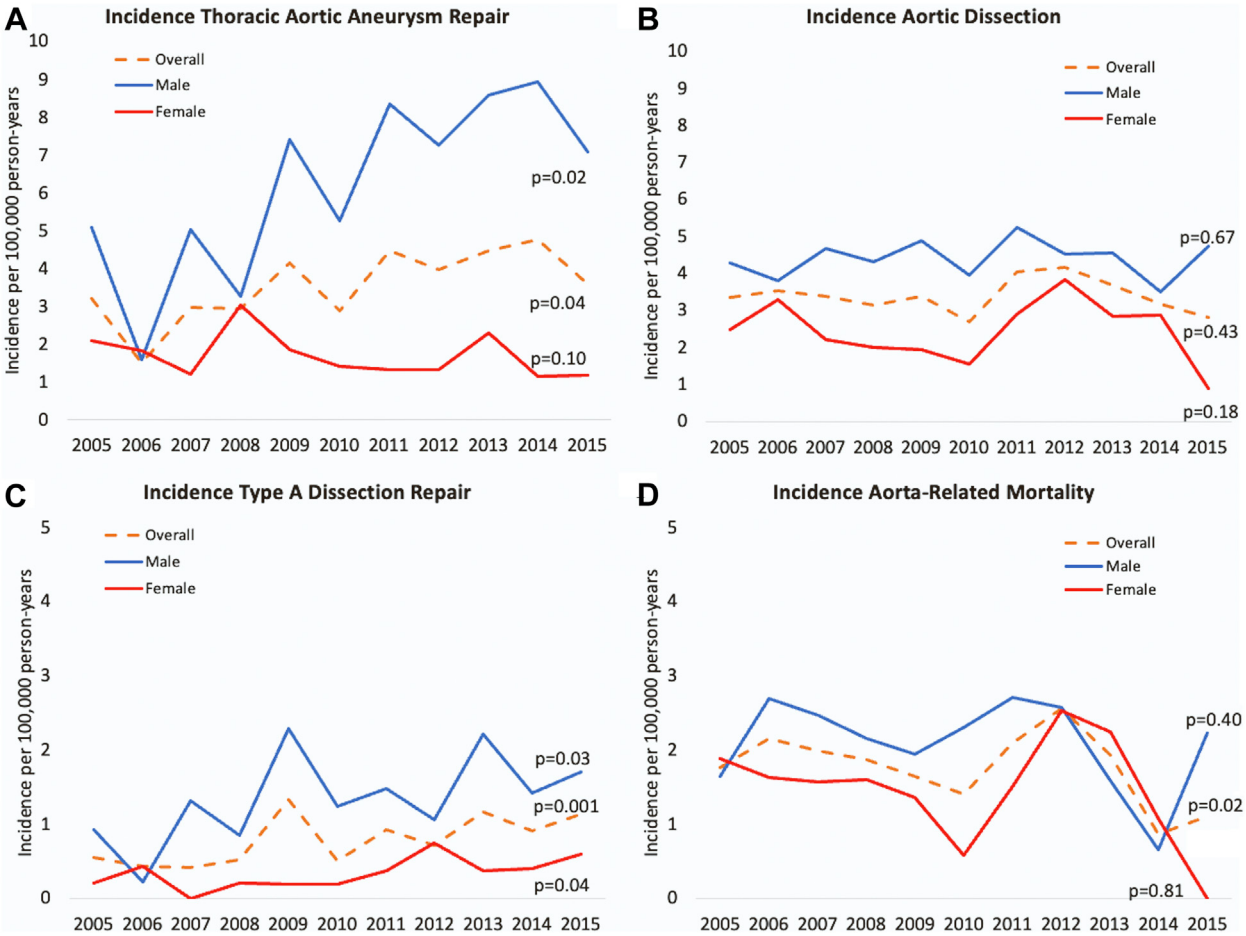

Figure 1. Age-adjusted incidence of thoracic aortic aneurysm repair and acute aortic dissection: 2005-2015. Age-adjusted incidence of thoracic aortic aneurysm repair, aortic dissection, type A aortic dissection repair, and aorta-related mortality over time. *P* values are for trend coefficients.

incidence of TAA repair was 3.5 per 100,000 person-years (95% confidence interval [CI]: 3.2-3.9), with an increasing trend over time ($P = 0.04$; Table 1). The average incidence in men was 5.6 per 100,000 (95% CI: 4.9-6.2), whereas the average incidence in women was only 1.6 per 100,000 (95% CI: 1.3-1.9). The age-adjusted incidence in men increased over time ($P = 0.02$), whereas no statistically significant trend over time ($P = 0.10$) occurred in women (Fig. 1A).

Of the 345 patients presenting with TAAD and TBAD, the mean age was 67.6 years (SD ±15.8), and 133 (39%) were female. Unadjusted 30-day mortality occurred in 74 women (56%) vs 94 men (44%; $P = 0.045$). Mortality at home occurred in 36 women (27%) and 59 men (28%; $P = 0.19$). Unadjusted 30-day mortality among patients undergoing nonoperative management was 50% for female patients vs 33% for male patients, $P = 0.01$ (Fig. 2). The average annual age-adjusted incidence of AAD was 3.4 per 100,000 (95% CI: 3.1-3.8) and did not increase or decrease over time ($P = 0.43$; Table 1). The average incidence of combined TAAD and TBAD in men was 4.4 per 100,000 (95% CI: 3.8-5.0) and remained stable over time ($P = 0.67$). The average incidence in women was 2.4 per 100,000 (95% CI: 2.0-2.9) and also remained stable over time ($P = 0.18$; Fig. 1B).

Of the 85 patients who underwent TAAD repair, the mean age was 61.7 years (SD ±12.5), and 19 (22%) were female (Table 1). Operative mortality occurred in 13 patients (15.3%) with no significant trend over time ($P = 0.37$). No statistically significant difference occurred in unadjusted operative mortality in women vs men (10.5% vs 16.7%, $P = 0.72$) or in the first era (2005-2009) vs the second era of the study (2010-2015) (22.6% vs 11.1%, $P = 0.21$; Table 2). The average annual age-adjusted incidence of surgery for TAAD was 0.8 per 100,000 (95% CI: 0.6-1.0), with an increasing trend over time ($P = 0.001$; Table 1). The average incidence of surgery for TAAD in men was 1.2 per 100,000 (95% CI: 0.9-1.6) and increased over time ($P = 0.03$). The average incidence of surgery for TAAD in women was 0.3 per 100,000 (95% CI: 0.2-0.5) and also increased over time ($P = 0.04$; Fig. 1C).

Of the 182 patients experiencing aorta-related mortality, the mean age was 72.3 years (SD ±15.2), and 82 (45%) were female. The overall incidence of aorta-related mortality was 1.8 per 100,000 (95% CI: 1.5-2.0), with a decreasing trend over time ($P = 0.02$; Table 1). The incidence of aorta-related mortality was 2.1 per 100,000 (95% CI: 1.7-2.5) in men, with no statistically significant trend over time ($P = 0.40$). The incidence of aorta-related mortality was 1.5 per 100,000

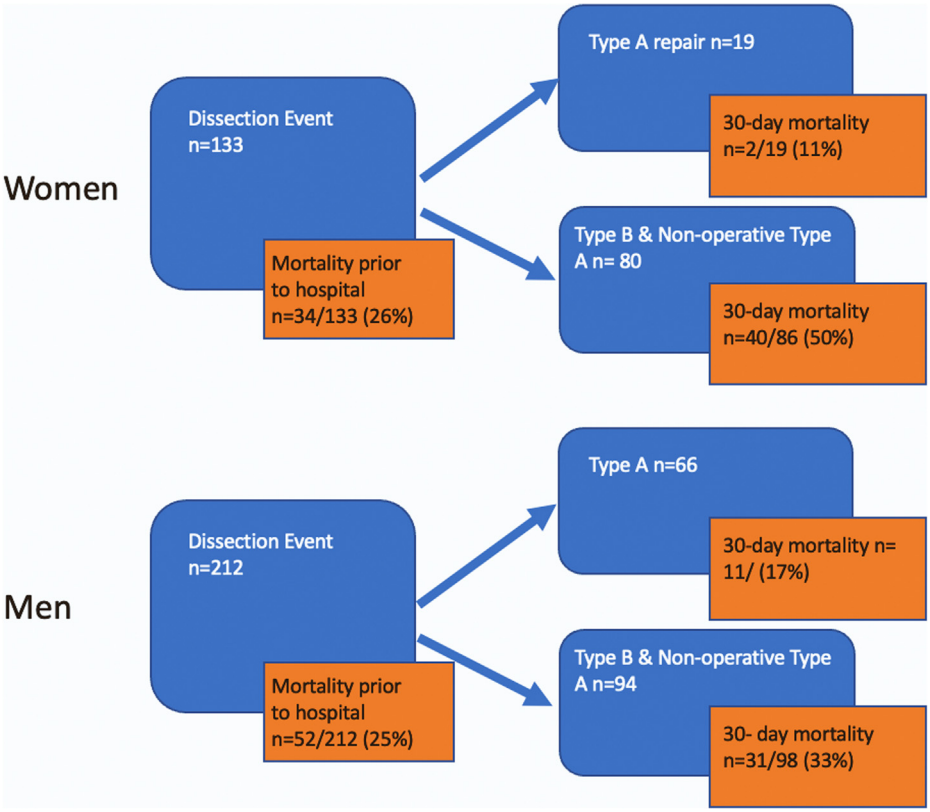

Figure 2. Mortality and operative management of of women and men with aortic dissection. Flow chart depicts the numbers and proportions of women and men presenting with combined type A and type B aortic dissection, unadjusted mortality prior to hospital, operative type A aortic dissection repair, nonoperative management, and 30-day mortality.

(95% CI: 1.1-1.8) in women, with no statistically significant trend over time ($P = 0.81$; Fig. 1D).

Discussion

The age-adjusted incidence of TAA repair is increasing in men but not in women, and women account for only 20% of patients undergoing TAA repair and experience 4 times the unadjusted operative mortality. The overall rate of combined TAAD and TBAD events is stable in both men and women. Of those with TAAD or TBAD who undergo medical management, unadjusted mortality is over 50% higher in women vs men. The incidence of TAAD repair is increasing in both men and women. Aorta-related mortality overall shows a decreasing trend. These trends highlight favourable advances in the management of proximal thoracic aortic disease, resulting in decreased aorta-related mortality, but they also suggest areas for improvement, particularly in the female population.

Rates of proximal TAA repair

In an analysis of the US National Inpatient Sample from 2005-2014, the incidence of proximal TAA repair was found to have increased from 1.8 to 3.2 per 100,000. The authors also found that women represented 30.5% of those undergoing scheduled proximal TAA repairs in 2005, but only 28.4% in 2014, a statistically significant trend.[4] In Ontario from 2002-2014, the rates of TAA increased from 3.5 to 7.6 per 100,000, and revealed an increasing incidence in both men and women, but this included both nonoperative hospitalizations and ambulatory care visits.[6] In our study, the incidence of proximal TAA repair increased over the decade of interest, but only in men and not in women. This finding suggests that women may be found to have TAA by screening, as indicated by the greater incidence in women in studies that include outpatient visits. But a lag is present in subsequent referral to surgical evaluation, or a hesitancy to offer intervention in women, as demonstrated by a decreasing rate of scheduled TAA repair in the US[4] and a stable rate of scheduled TAA repair in women in our study.

Unlike Mullan et al., who observed a significant decrease in TAA repair operative mortality, from 4% in 2005 to 2.5% in 2014,[4] we did not observe a statistically significant change in unadjusted operative mortality over time; however, our cohort's small sample size limits the ability to make statistical inferences for this outcome. Our overall unadjusted operative mortality of 2.4% is already similar to the rate at the latter era of the study by Mullan et al.[4] and lower than the observed mortality rate of 3.4% from 2004 to 2009 cited in a report from the Society of Thoracic Surgeons,.[10] In our study, the unadjusted operative mortality was 4 times higher in women vs men. Women tend to be older, with more comorbidities at the time of presentation with aortic disease, and they have

Table 2. Trend of scheduled TAA repair and TAAD repair unadjusted operative mortality over time

	Scheduled TAA repair n = 382	TAAD repair n = 85
Operative mortality	9 (2.4)	13 (15.3)
Operative mortality in men	4 (1.4)	11 (16.7)
Operative mortality in women	5 (5.7)	2 (10.5)
Year		
2005	1 (3.3)	1 (20.0)
2006	1 (7.1)	0 (0)
2007	0 (0)	2 (50.0)
2008	1 (3.6)	1 (20.0)
2009	1 (2.5)	3 (23.1)
2010	1 (3.6)	1 (20)
2011	0 (0)	0 (0)
2012	1 (2.5)	0 (0)
2013	1 (2.3)	3 (25)
2014	2 (4.1)	0 (0)
2015	0 (0)	2 (16.7)
Trend coefficient (95% CI)	−0.00 (-0.01 to 0.00) $P = 0.59$	−0.01 (−0.04 to 0.01) $P = 0.37$

Values are n (%), unless otherwise indicated.

CI, confidence interval; TAA, thoracic aortic aneurysm; TAAD, type A aortic dissection.

been shown to have higher mortality when undergoing complex TAA repair,[10] with one study showing no difference after accounting for multiple comorbidities in a propensity-score analysis.[14] In this study, because operative mortality was not the main outcome of interest, extensive analysis of the independent effect of female sex on that outcome was not performed.

The prevalence of TAA was not calculated in this study. The prevalence of TAA is difficult to estimate due to the asymptomatic nature of the disease. Prior studies have estimated the prevalence of TAA to be increasing, but they have a large range of estimates, from 11.3 per 100,000 using hospitalization data,[4] to as high as 243 per 100,000 using a more liberal estimate that accounts for outpatient computed tomography surveillance and nonoperative management of TAA.[5] A recent review of a single year of computed tomography scans revealed the prevalence of TAA to be as high as 2.1%, but this figure included patients who did not meet size criteria for intervention.[15] This study also did not include the incidence of medically managed TAA, due to similar difficulties in detecting incident TAA that meets or does not meet size criteria for intervention but patient age or comorbidities preclude offering an operative intervention.

Rates of aortic dissection

In the US, overall admissions for acute aortic syndrome were increasing, in the period 2005-2014.[4] However, that study did not account for prehospital events. In a similar study of hospital admission of Medicare beneficiaries during 2000-2011, hospital admission for acute aortic dissections was stable.[16] In the province of Ontario, the incidence of TAAD and TBAD increased from 2.7 to 4.6 per 100,000 person-years from 2002 to 2014,[6] whereas in the province of Manitoba, the combined incidence of TAAD and TBAD was found to be 3.0 per 100,000 person-years and stable over time.[5] Our study found the overall rate of aortic dissection to be stable from 2005 to 2015. Conflicting results can be explained by prior studies accounting for only aortic dissection hospitalizations and omitting prehospital mortalities. Studies including prehospital deaths have estimated prehospital mortality to range from 18% to 38%.[3,17-19] Two separate studies over a similar time period in Germany estimated the incidence of aortic dissection to be 2.7 per 100,000 person-years when accounting for only those who underwent intervention,[20] and as high as 11.9 per 100,000 with the inclusion of autopsy reports in the same population.[18] Our study includes patients with the diagnosis of aortic dissection as the underlying cause of death and found a stable rate of combined TAAD and TBAD at around 3.4 per 100,000. This stable rate occurred concurrently with an increase in TAAD repair from 0.6 per 100,000 to 1.1 per 100,000. Our findings also suggest that the paradoxical increase in aortic dissections observed in other studies, despite increases in scheduled proximal aortic repair,[4,6] may be due to increased numbers of patients presenting with aortic dissection surviving to specialized care and receiving an operation, and a decrease in prehospital deaths that are not accounted for in other trend analyses. Although our study showed stable overall rates of aortic dissection and a decrease in aorta-related mortality, an increase was found in incidence of TAAD repair, further supporting this observation.

The incidence of dissection events and aorta-related mortality does not differentiate between TAAD and TBAD in this study. The ICD-10 code for aortic dissection (I71.0: "dissection of aorta, any part") does not allow for differentiation of TAAD and TBAD. Other studies have attempted to differentiate these 2 entities by linking with the Canadian Classification of Health Interventions coding system for surgical intervention and assuming that those who are admitted and discharged are medically treated TBADs.[6] This approach, however, might misclassify chronic TAAD patients or even the subset of acute TAAD patients who are too comorbid for surgical management and offered medical therapy.[21,22] In this study, we made no attempt to distinguish these 2 entities, to allow for broad estimates of dissection events and aorta-related mortality to evaluate trends in dissection events over time. Linkage with our institutional registry allowed for evaluation of trends in TAAD operative management over time. This study is novel in that it demonstrates that increasing TAAD

operations does not necessarily mean dissection events are increasing. We demonstrate stable dissection events during the time period, indicating greater success in getting patients to the operating room and being more aggressive in offering intervention when a TAAD occurs.

Mortality

Our study found a decrease in aorta-related mortality. In the US and Ontario, in-hospital mortality for both AAD and proximal aortic surgery decreased over time.[4,6,16] Our study did not demonstrate a significant decrease in operative mortality in either scheduled or emergent repairs, possibly due to a low sample size limiting such trend analysis, or to our already low scheduled operative mortality incidence of 2.4% and similarly, a relatively low mortality incidence of 15.3% for TAAD repair, which are both comparable to contemporary outcomes.[10,21,23] Increasing rates of scheduled TAA and emergent TAAD repair suggest that we are being more liberal in offering operative management to patients who may have been declined intervention or did not survive to intervention in the past. This approach, coupled with improvements in overall perioperative care that is observed in other studies,[4] results in a decrease in aorta-related mortality within the population. This observation was also made in the province of Manitoba, where an increase in TAA diagnoses and a similar unchanged rate of aortic dissection, suggesting that combined medical and surgical management has improved for patients with TAA, blunting a corresponding increase in acute aortic complications.[5]

Sex differences

Women account for only 23% of TAA repair and 22% of TAAD repairs, but they account for 39% of dissection events and 45% of aorta-related mortalities. Of those undergoing nonoperative management of acute aortic dissection, women experienced a higher unadjusted 30-day mortality. These findings echo previous research showing an inequity in thoracic aortic disease management in women, compared with men.[11,24] Current guidelines are unclear on distinct cutoffs for surgical intervention in women,[7] despite women having lower body surface area than male patients, and a higher risk of rupture and dissection at lower aneurysm sizes.[25] Previous studies have shown a decreasing proportion of women presenting for proximal aortic surgery,[4] and in this study, we found a similar increase in the incidence of proximal TAA repair in men, with no increase in women. This finding, along with a parallel increase in incidence of TAAD repair in both men and women, suggests the presence of a screening gap, delay in referral, or inappropriate deferral of intervention in women with TAA in our population. In Manitoba, a unique study using outpatient diagnosis of aortic aneurysm and follow-up commuted tomography (CT) imaging found that the diagnosis of TAA was increasing at a faster rate in women compared to that in men, with no proportionate decrease in aortic dissection, also suggesting that the delay is at referral or offer of intervention rather than screening.[5] In our study, the proportion of women among those being offered TAAD repair increased over the course of the study, suggesting that operative management is being performed once the dissection occurs. In our population, the lag in uptake of scheduled TAA in women results in a high number of dissection events and aorta-related mortality. Education surrounding appropriate screening protocols, diameters for referral, and intervention should be conducted among both primary care providers and surgeons offering scheduled repair.

Limitations

This study has several limitations. First, this study utilizes administrative data for the calculation of aortic dissection events and aorta-related mortality and was therefore subject to errors of coding. The impact of such errors would have been partially mitigated by chart review of patients' imaging and admission information as available. Nonetheless, a diagnosis of aortic dissection as underlying cause of death when death occurred at home may have been presumptive based on prior diagnosis of TAA when death could have been caused by another cardiac event. Although this approach might inflate the number of patients counted as aortic-related mortality, prior studies performing systematic autopsies demonstrate that prehospital mortality occurs in almost 50% of patients,[26] and that the incidence of aortic dissection is much higher in studies that include prehospital mortality than relying on hospital admission data.[18,20] If we relied on only definite confirmed cases, we would likely underestimate the burden of aortic dissection and aorta-related mortality. Also, overlap is likely present in TAA rupture and dissection among patients who experience aorta-related mortality, which could affect the calculated incidence. However, we expect no change in the rate of error throughout the time period of the study, meaning that trends are in fact reflective of the true pattern of disease.

Second, this study sample size was small in comparison to nationwide studies,[4] and our findings may not be applicable to other jurisdictions. Additionally, our study included only the time period 2005-2015, due to limitations in data access through administrative data sources; however, in a system in which care is delivered provincially, this study was representative of the entirety of thoracic aortic disease within the province. This study can help guide province-specific improvements and resource planning for the future.

Third, we did not examine comorbidities or complexity of operation in this study, in part due to the epidemiologic basis of this study, to describe population-based incidence. One possibility is that women present with more comorbidities with more advanced aneurysmal disease than men, resulting in higher unadjusted mortality. However, examination of the comorbid presentation of women was not the purpose of this study, but rather the incidence trends of disease at the population level. Should women have higher comorbidities, they still have an excessive risk of mortality after adjusting for comorbidities,[11] and the impetus remains to offer earlier intervention and improve care for the female population.

Fourth, as this study did not calculate the prevalence of TAA or the incidence of medically treated TAA, we do not know if the incidence of TAA overall is increasing in women in Nova Scotia. A possibility is that the increase in proximal TAA repair in men is due to a true increase in TAA disease in men in our population. However, the incidence of TAA has been shown to be increasing in women at a faster rate than in

men in other jurisdictions.[5] Additionally, Nova Scotia is a predominantly rural population, and prior studies have shown adverse outcomes in patients with thoracic aortic disease who reside remotely in our province.[27] Detection of TAA and aortic dissections could be lower in some areas of the province, but we expect this to affect men and women similarly, and to not affect the findings of our study. Thus, our findings are still actionable, requiring education surrounding all elements of care, including screening, referral, and offers of intervention.

Finally, although we identified women as a potentially undertreated population, this study did not capture race, ethnicity, Indigenous status, or socioeconomic status of patients presenting for TAA repair or aortic dissection. Race is associated with poor self-reported health,[28] and a high burden of cardiovascular risk factors,[29] and Indigenous populations face a rapidly growing incidence of cardiovascular morbidity and mortality.[30,31] Understanding of the effect of racial and social inequalities on outcomes in thoracic aortic disease, to identify further underserved populations, should be an area of further research.

Conclusions

Improvements in management of thoracic aortic disease have resulted in an overall decrease in aorta-related mortality. A lag is present in scheduled proximal thoracic aortic repairs in women, contributing to a high proportion of adverse outcomes in female patients with thoracic aortic disease. Ongoing efforts to increase screening, referrals, and interventions should continue the downward trend in aorta-related mortality, with additional research evaluating size at detection, referral, and offer of intervention to close the gap in the female population.

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Disclosures

The authors have no conflicts of interests to disclose.

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