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ORIGINAL RESEARCH

Trends in Abdominal Aortic Aneurysm Repair Incidence, Comorbidity, Treatment, and Mortality: A Danish Nationwide Cohort Study, 1996–2018

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Background: Significant changes in Western populations' abdominal aortic aneurysm (AAA) epidemiology have been reported following the introduction of screening, endovascular AAA repair, and reduced tobacco consumption. We report incidence and mortality of AAA repair in Denmark from 1996 to 2018, where AAA screening was not implemented.

Methods: Nationwide cohort study of prospective data from population-based Danish registries covering 1996 to 2018. We identified 15,395 patients undergoing first-time AAA repair using the Danish Vascular Registry. Comorbidity was assessed by Charlson's Comorbidity Index (CCI). Incidence rate (IR) ratios and mortality rate ratios (MRR) were estimated by multivariable Poisson and Cox regression, respectively.

Results: Overall AAA repair IR decreased by 24% from 1996 through 2018, mainly reflecting a 53% IR reduction in ruptured AAA repairs in men. Overall, the IR decreased 52–63% in age groups below 70 years and increased 81% among octogenarians. The proportion of intact AAAs repaired endovascularly increased from 2% in 1996–1999 to 42% in 2015–2018. For both ruptured and intact AAAs the CCI score increased by 0.9% annually independently of age and sex. The adjusted five-year MRR in 2016–2018 vs.1996–2000 was 0.46 (95% confidence interval (CI): 0.39–0.54) following ruptured and 0.51 (95% CI: 0.44–0.59) following intact AAA repair.

Conclusion: In Denmark, overall AAA repair incidence decreased between 1996 and 2018, primarily reflecting a reduction among males and a shift to an older population requiring intervention. These trends mirror changes in tobacco consumption in Denmark. Regardless of age and comorbidity, AAA repair mortality decreased markedly during the study period.

Keywords: vascular surgery, open surgery, endoluminal repair, Danish Vascular Registry, Danish National Patient Registry, registries

Introduction

Abdominal aortic aneurysm (AAA) is a frequent and potentially fatal condition that predominately affects males with a prevalence of 1.3–5% in men aged 65–75 years.[1–4] Recent studies report decreasing prevalence in UK and Sweden,[1,2,5] in contrast to stable or even increasing prevalence in Denmark.[3,4,6] AAA rupture is fatal in more than 80% of cases.[7] Only a minority of ruptured AAA patients reaches the hospital alive, and those who undergo emergency repair have a 30–50% mortality within 30 days.[8–10] Preemptive measures such as open- or endovascular AAA repair are effective.

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Number needed to treat with elective AAA repair to avoid one death is three.[11,12] However, open AAA repair is associated with significant risks of death and ischemic events.[13,14] Historically, the threshold for elective open AAA repair was set at AAA diameters above 5.5 cm in men and 5.0 cm in women, balancing the risk of rupture with the risks of open surgery. Since the introduction of endovascular AAA repair (EVAR) in 1990, the technology has undergone significant advancements while the AAA diameter threshold for repair has been maintained.[7,15,16] Initially, EVAR was primarily reserved for high-risk patients, but it has become increasingly utilized as a first-line treatment option due to improvements in techniques and patient and surgeon preferences.[8,10] Meta-analyses have shown that there is a state of equipoise of long-term mortality between endovascular and open repair for patients with anatomical suitability for both options.[17] The optimal surgical approach is thus unsettled.[18]

Considering the shifting prevalence of AAA, changing treatment strategies, and the associated risks,[19,20] this study aimed to provide novel Danish nationwide data to inform the design of future screening programs, trials, and observational studies. This included data of AAA repair incidence and mortality for sample size calculations and determination of inclusion criteria. In addition, the study also examined the impact of sex, age, and Charlson's comorbidity index (CCI) on these outcomes, as these factors play a significant role in both the incidence and mortality of AAA. The findings of this study will contribute to a better understanding of the epidemiology of AAA and inform future research in this field. In a related manuscript, we have also documented the epidemiology of occlusive lower extremity artery disease repair in Denmark from 1996 to 2018.[21]

Methods

Study Design and Setting

This is a nationwide, longitudinal cohort study on prospectively collected data from the Danish Vascular Registry (DVR) and population-based medical and administrative registries.[22] The Danish National Health Service ensures tax-supported health-care to all Danish citizens. The Danish Civil Registration System (CPR) assigns each citizen a unique ten-digit personal identifier that enables individual-level linkage across registries.[23] The Danish population was 5,781,190 persons in 2018.

Study Population

We used the DVR to identify Danish patients undergoing first-time "index" aortoiliac aneurysm repair from January 1st, 1996 to December 31st, 2019. The DVR is the first nationwide Danish surgical database. It was established for quality improvement and research purposes and contains prospective data on all vascular procedures since January 1st, 1996.[24] Patient data are registered prospectively by the vascular surgeon with either direct data entry into the DVR, or into a paper chart which is later transferred to the DVR. Validation of the DVR has shown an external validity of 98.4% for AAAs and a high data quality superior to local administrative data.[25,26] The CPR was used to add information on sex, age, vital status, and migration, and was last updated on October 31st, 2019. From the Danish National Patient registry (DNPR), we gathered information on all somatic inpatient hospitalizations since 1977 and all hospital outpatient and emergency visits since 1995, including discharge diagnoses according to the International Classification of Diseases [Eighth Revision (ICD-8) until 1993 and Tenth Revision (ICD-10) hereafter].[27] The DNPR data set was updated December 31st, 2018. We also present smoking prevalence data extracted from a Danish Cancer Society review on smoking surveys in Denmark since 1953.[28]

Inclusion was based on the DVR, which exclusively registers operations/procedures, and the criteria were i) operation code for aortoiliac reconstruction (Scandinavian coding system: PDG10-99, PDH10-35, PDQ10-30), ii) indication being either ruptured AAA or intact AAA (symptomatic or elective), iii) age above 40 and below 100 years. The age cut off has been used as inclusion criteria in randomized trials and was chosen to fit the general vascular surgery target population.[29] To ensure all patients were AAA repair naive at our study base, we excluded patients with AAA surgery before 1996 using the DNPR. Patients were also categorized into two groups based the technique, open (ie, surgical) vs endovascular AAA repair. Patients who received conservative management for AAA were not included in this study.

We used the same methods in this study as in a accompanying manuscript on occlusive lower extremity artery disease repair, with the exception that patients could only be included once in the current AAA study.[21]

Comorbidity

At baseline, patients were described by CCI score using both in- and outpatient records in the DNPR since 1977.[30] We exclusively used DNPR records concluded before the date of repair, which means that AAA diagnosed on the day of the procedure or in ongoing outpatient records could not contribute to the CCI score. We grouped patients with a CCI score of 0, 1, 2, or 3 and above, as having normal, moderate, severe, or very severe comorbidity, respectively. We chose moderate CCI as the reference group because an AAA diagnosis accounts for one CCI point.

Mortality

We obtained vital status from the CPR and report 5-year survival following AAA repair. Five-year survival was the primary analysis, as endovascular and open repair have a different short-term risk of death, but similar long-term.

Statistical Analyses

Ruptured and intact AAA patients were analyzed separately, and only aggregated for the incidence reporting. We described the population by sex, age group (of six decades from 41 to 99 years), CCI group, and calendar period (5 intervals from 1996 to 2018). We exclusively included year 2019 in the age-and sex-standardized incidence plots. Mortality was not compared between open and endovascular repair.

Based on the CPR, we identified residents aged above 40 and below 100 years as of January 1st from 1996 to 2019. Using the DNPR, we computed each resident's annual accrued CCI score. We then calculated i) person-years at risk for AAA operation in the population as follow-up time resident in Denmark by age, sex, calendar year and CCI group; ii) crude incidence rates (IRs) by calendar-period, age, sex and CCI, iii) annual IRs standardized to the year 2000 age and sex composition of the Danish population by means of direct standardization; iv) and finally, incidence rate ratios (IRRs) using a log-linear Poisson regression model including the covariates: calendar-period, age-category, sex, and CCI group, offset by the logarithm of person-years at risk.

To compare the CCI of AAA patients to the Danish population, we calculated a mean observed CCI by each sex-, age-, and calendar year-strata and standardized this to the Danish population's corresponding strata of year 2000, as reference. We then used Poisson regression to estimate CCI ratios with 95% confidence intervals. The same method was applied to compare CCI ratios across age groups with persons aged 71–75 years as reference.

We used the Kaplan–Meier estimator to compute mortality risks for each calendar-period. Patients were censored five years following the repair, on migration, or on October 31st, 2019, at the latest. Using Cox regression, we compared the five-year mortality rate ratio (MRR, via hazard ratios for death) of each calendar-period. We present the crude MRR, and MRRs adjusted for age, sex, CCI group, health care region, and stratified for repair technique (open vs endovascular repair). Visual inspection of Schoenfeld residuals indicated no gross violation of the proportional-hazards assumption for any of the analyses. In our secondary analysis, we also adjusted for smoking history, alcohol abuse, and care dependency and case priority. There were only missing data in the secondary analysis's discrete variables, and missingness was included as separate levels in these covariates. We additionally computed 90-day sex specific MRR to aid the discussion of the results from other studies.

The adequacy of the models for estimating incidence and mortality were examined by tentatively adding an interaction term between calendar year, as a linear predictor, and each of the remaining covariates. The effect of adding an interaction term was assessed by the likelihood ratio test.

Ethics

The study was submitted to Region Zealand's research-related processing activities record (record nr. REG-144-2017) and approved by Statens Serum Institute compliance (journal no: 21/00805). No permission from the Danish Ethical Committee was required as the study did not involve contact with study participants. The accessed data complied with relevant data protection and privacy regulations.

Results

Incidence

We identified 15,395 first-time incident AAA repairs, see study flow chart in eFigure 1 of the supplemental material. Figure 1A shows the trend in sex- and age-standardized IR of AAA by repair type. Overall, the IR declined by 24% from 25.1 (95% CI, 23.2–27.1) per 100,000 person-years in 1996 to 19.1 (95% CI, 17.4–20.9) per 100,000 person-years in 2018. This decrease was primarily attributable to a reduction of ruptured AAA repair from 8.1 to 4.0 per 100,000 person-years (IRR, 0.48; 95% CI, 0.39–0.60), whereas the intact AAA repair IR was reduced from 17.0 to 15.1 per 100,000 person-years (IRR, 0.89; 95% CI, 0.78–1.01). Intact AAA repair demonstrated a transient increase in IR from 2002 to 2011 which coincided with the introduction of endovascular AAA repair and an IR increase in persons aged 71–90, eFigures 2 and 3.

Figure 2 shows the adjusted IRR by sex, age group, and CCI group along with the crude IR for each parameter. When adjusting the IR for sex, age and CCI group, a 20% IR reduction was demonstrated for intact AAAs from 1996–1999 to 2015–2018 (IRR, 0.80; 95% CI, 0.75–0.85). For both intact and ruptured AAA repair, the IR peaked in age group 71–80 years. Females had 81% lower incidence of intact and 88% lower incidence of ruptured AAA repair compared with males. Intact AAA repair was rare among persons registered with normal CCI (IRR, 0.04; 95% CI, 0.04–0.05), and most frequent in the population with very severe CCI (IRR, 1.29; 95% CI, 1.22–1.34), compared to moderate CCI. The IR of ruptured AAA repair was most frequent in the population with moderate CCI.

Incidence Trend by Age

Figure 1B shows the trend in age-specific IRs of all AAA repairs in five-year age intervals. From 1996 to 2018, the sex adjusted IR for all AAA repairs was more than halved for persons aged 51–70 years, remained largely stable for persons aged 71–80 years, and increased by 81% persons aged 81–90 years ([$IRR_{51\text{-}60}$, 0.37; 95% CI, 0.23 − 0.58]; [$IRR_{61\text{-}70}$, 0.48; 95% CI, 0.40 − 0.58]; [$IRR_{71\text{-}80}$, 0.95; 95% CI, 0.81 − 1.12]; [$IRR_{81\text{-}90}$, 1.81, 95% CI, 1.27 − 2.59]). This age heterogeneity was significant for both intact and ruptured AAA repairs (p interaction < 0.001, eTable 1).

Incidence Trend by Sex

Figure 3 shows the sex-specific trends in AAA repair IR, adjusted for age. For all AAA repairs, the average annual IR reduction throughout the study period was most pronounced in men ([annual IRR_{males}, 0.98; 95% CI, 0.98–0.98]; [annual $IRR_{females}$, 1.00; 95% CI, 1.00–1.01]; p interaction = 0.001). While this sex disparity was marked in ruptured AAA repair ([annual IRR_{males}, 0.96; 95% CI, 0.96–0.97]; [annual $IRR_{females}$, 0.98; 95% CI, 0.97–1.00]; p interaction < 0.001), we could not discern any sex heterogeneity in the IR trend for intact AAA repair (p interaction = 0.45).

Patient Characteristics

Table 1 shows the baseline characteristics of patients operated for ruptured (n = 4508) and intact (n = 10,887) AAA. Notably, more ruptured AAA patients had a normal CCI-score 38% vs 5.4% of intact AAA patients. History of cardio- or cerebro-vascular (50%) and chronic pulmonary (23%) disease was common among AAA patients. Endovascular repair was a rare technique for ruptured (2%) compared to intact (25%) AAAs. Baseline characteristics disaggregated by calendar period are available in eTable 2 of the supplementary data.

From 1996 to 2018 the mean age increased by 3.9 years in intact and 2.5 years in ruptured AAA patients.

Figure 4 panel a shows the trend in CCI score by repair type and the Danish population, while panel b shows the relative change in CCI per five-year age interval. The CCI score peaked in the octogenarians, for both AAA patients and the Danish population, followed by a declining trend in persons aged above 90 years. The CCI varied less across age groups in AAA-patients compared to the Danish population. The annual CCI increased by 0.9% among intact (95% CI, 0.7–1.1%) and by 0.9% in ruptured (95% CI, 0.5–1.3%) AAAs, set against 2.4% in the Danish population (CI 95%, 2.4–2.4%).

Mortality

Table 2 shows the 5-year mortality risk and 5-year the crude and adjusted MRR. Comparing 2015–2018 with 1996–1999, the adjusted 5-year MRR was 0.51 for intact (95% CI, 0.44–0.59) and 0.46 for ruptured (95% CI, 0.39–0.54) AAA repair. Increasing

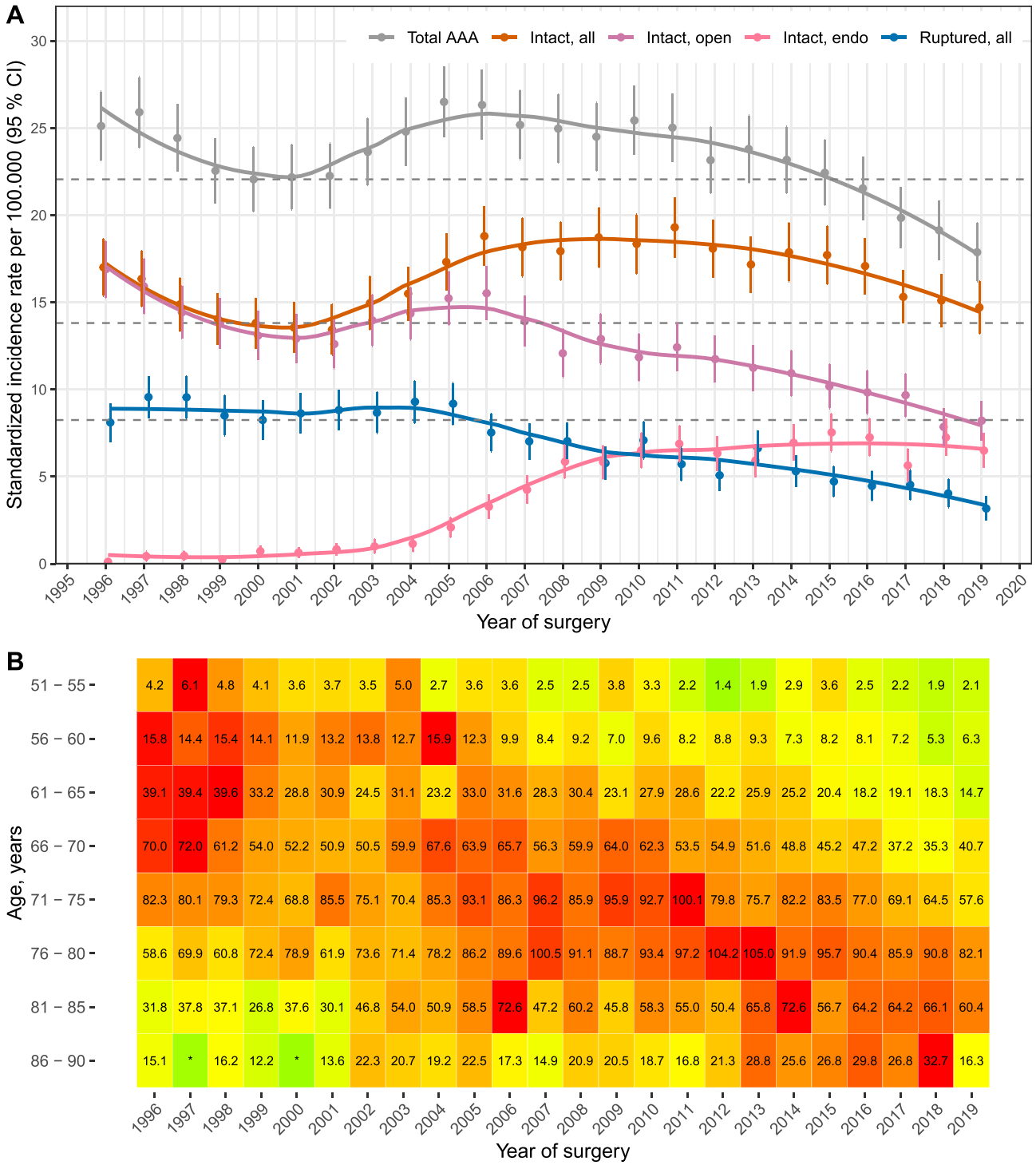

Figure 1 Standardized incidence rate (**A**) and age specific incidence (**B**) for AAA repair in Denmark 1996–2019.
Notes: (**A**) Incidence rate standardized to the age and sex distribution of the Danish population aged above 40 and below 100 years in 2000. Dashed lines indicate the incidence rate in the reference year 2000. Note, the 2019 data are exclusively used graphically in this plot and not in any tables or the result section, as we did not have Danish National Patient Registry (DNPR) data for 2019. (**B**) age-specific incidence rates of total AAA repair by calendar year. The crude incidence rates per 100.000 person-years are presented in each tile. Tiles are colored by each row (age band) in a red-yellow-green gradient from the highest value, red, to incidence rates of 50% of the highest value, yellow, to incidence rate of 0% percent of the highest value, green.

age and CCI explained the difference between crude and adjusted MRR for both ruptured and intact AAA. Adjusting for smoking, alcohol abuse, care dependency or priority at time of repair did not explain the mortality reduction, see eTable 3, and even when we replaced missing parameters of these covariates with best- or worst-case scenarios (eg, non-smoker or smoker) the

Intact AAA	Cases	Person–Years	Crude IR per 100,000	IRR (95% CI)
Calendar year				
1996 – 1999	1,529	9,800,052	15.6 (14.8–16.4)	Reference
2000 – 2004	1,824	12,697,911	14.4 (13.7–15.0)	0.85 (0.79–0.91)
2005 – 2009	2,499	13,392,843	18.7 (17.9–19.4)	0.99 (0.93–1.06)
2010 – 2014	2,792	14,075,863	19.8 (19.1–20.6)	0.93 (0.88–0.99)
2015 – 2018	2,243	11,712,246	19.2 (18.4–19.9)	0.80 (0.75–0.85)
Age, years				
41 – 50	75	18,192,142	0.4 (0.3–0.5)	0.03 (0.03–0.04)
51 – 60	849	16,844,751	5.0 (4.7–5.4)	0.26 (0.25–0.28)
61 – 70	3,961	13,398,250	29.6 (28.6–30.5)	Reference
71 – 80	5,076	8,678,501	58.5 (56.9–60.1)	1.49 (1.43–1.55)
81 – 90	918	3,947,749	23.3 (21.7–24.8)	0.56 (0.52–0.60)
91 – 99	8	617,522	1.3 (0.4–2.2)	0.04 (0.02–0.08)
Sex				
Male	9,072	29,731,151	30.5 (29.9–31.1)	Reference
Female	1,815	31,947,764	5.7 (5.4–5.9)	0.19 (0.18–0.20)
CCI group				
Normal	589	43,644,149	1.3 (1.2–1.5)	0.04 (0.04–0.05)
Moderate	3,972	8,162,109	48.7 (47.2–50.2)	Reference
Severe	2,687	5,332,614	50.4 (48.5–52.3)	0.97 (0.92–1.02)
Very Severe	3,639	4,540,043	80.2 (77.5–82.8)	1.29 (1.23–1.35)
Ruptured AAA	**Cases**	**Person–Years**	**Crude IR per 100,000**	**IRR (95% CI)**
Calendar year				
1996 – 1999	880	9,800,052	9.0 (8.4–9.6)	Reference
2000 – 2004	1,114	12,697,911	8.8 (8.3–9.3)	0.96 (0.88–1.05)
2005 – 2009	1,000	13,392,843	7.5 (7.0–7.9)	0.78 (0.71–0.85)
2010 – 2014	907	14,075,863	6.4 (6.0–6.9)	0.63 (0.57–0.69)
2015 – 2018	607	11,712,246	5.2 (4.8–5.6)	0.46 (0.42–0.51)
Age, years				
41 – 50	26	18,192,142	0.1 (0.1–0.2)	0.02 (0.01–0.02)
51 – 60	293	16,844,751	1.7 (1.5–1.9)	0.17 (0.15–0.20)
61 – 70	1,395	13,398,250	10.4 (9.9–11.0)	Reference
71 – 80	2,088	8,678,501	24.1 (23.0–25.1)	2.24 (2.09–2.40)
81 – 90	692	3,947,749	17.5 (16.2–18.8)	1.80 (1.64–1.97)
91 – 99	14	617,522	2.3 (1.1–3.5)	0.31 (0.18–0.52)
Sex				
Male	3,923	29,731,151	13.2 (12.8–13.6)	Reference
Female	585	31,947,764	1.8 (1.7–2.0)	0.12 (0.11–0.13)
CCI group				
Normal	1,727	43,644,149	4.0 (3.8–4.1)	0.46 (0.43–0.49)
Moderate	1,278	8,162,109	15.7 (14.8–16.5)	Reference
Severe	746	5,332,614	14.0 (13.0–15.0)	0.81 (0.74–0.89)
Very Severe	757	4,540,043	16.7 (15.5–17.9)	0.77 (0.71–0.85)

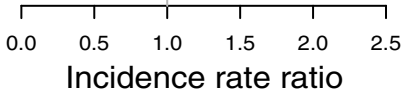

Figure 2 Incidence rate of Intact (top) and Ruptured (bottom) AAA repair.

Notes: Figure 2 shows the crude incidence rate (IR) and adjusted incidence rate ratio (IRR) with Forest plot of abdominal aortic aneurysm (AAA) repair. The IRRs were computed by a multivariable Poisson regression model adjusted for calendar year, age group, sex, and Charlson's comorbidity index (CCI) score. The CCI score was based on records concluded before the date of the procedure, which meant that AAA diagnosed on the day of the repair, or in ongoing outpatient records, could not contribute to the CCI score. Thus, some patients were characterized with normal CCI. The time trend in CCI-specific IR is plotted in eFigure 5.

Abbreviations: AAA, abdominal aortic aneurysm. CCI, Charlson's comorbidity index. IR, incidence rate. IRR, incidence rate ratio. CI, confidence interval.

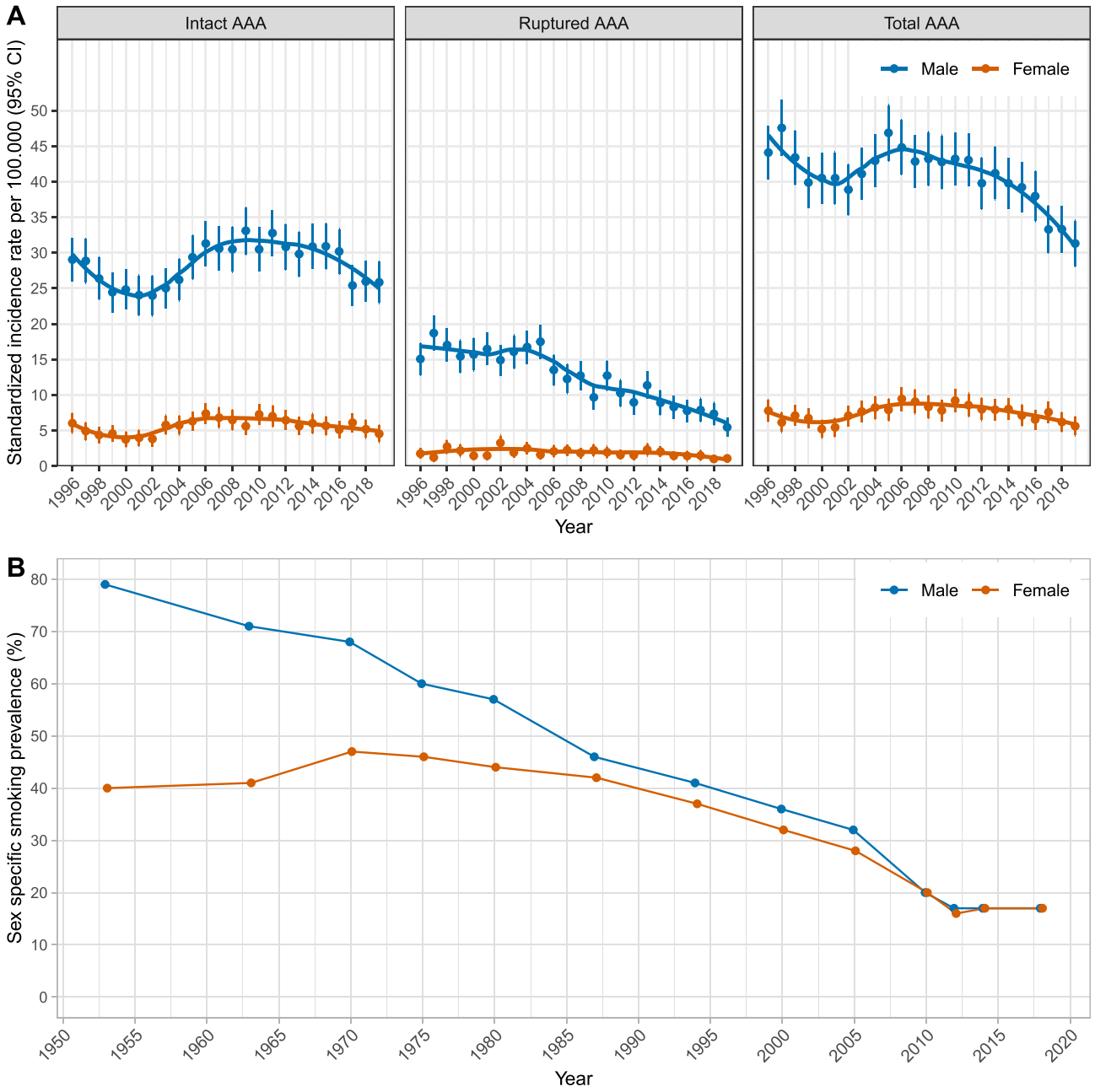

Figure 3 Sex-specific trends in age-standardized incidence rate of AAA repair in Denmark 1996–2017 (**A**) and smoking prevalence in Denmark 1953–2018 (**B**).
Notes: (**A**) Sex-specific trends in incident AAA repair, standardized to the age distribution of the Danish population in 2000. (**B**) displays the sex-specific trends in smoking prevalence. Data were extracted from a Danish Cancer Society review on smoking surveys in Denmark since 1953.[28]

MRR changed by 0.01 or less. Due to frequent missing data in the beginning of the study period we did not include these covariates in the primary analysis.

The 5-year mortality rate was also reduced in the Danish population aged 41–99 during the same period ([sex, age and CCI adjusted MRR, 0.56; 95% CI, 0.56–0.56]; [sex and age adjusted MRR 0.72; 95% CI, 0.72–0.72], eFigure 4).

Mortality by Age and Sex

We found age heterogeneity in the improved survival during the study period following ruptured AAA repair, Figure 5 ([$MRR_{81\text{-}90\ years}$, 0.72; 95% CI, 0.51–1.00)]; [$MRR_{71\text{-}80\ years}$, 0.44; 95% CI, 0.35–0.55]; [$MRR_{61\text{-}70\ years}$, 0.40; 95% CI,

Table 1 Baseline Characteristics of Patients Undergoing Repair for Ruptured and Intact AAA in Denmark 1996–2018

	Intact AAA (n=10,887)	Ruptured AAA (n=4508)	Total (n=15,395)
Age – mean (sd)	71.0 (7.3)	72.5 (7.9)	71.4 (7.5)
Male sex – no. (%)	9072 (83)	3923 (87)	12,995 (84)
Charlson's comorbidity index group – no. (%)			
Normal	589 (5)	1727 (38)	2316 (15)
Moderate	3972 (36)	1278 (28)	5250 (34)
Severe	2687 (25)	746 (17)	3433 (22)
Very Severe	3639 (33)	757 (17)	4396 (29)
Chronic pulmonary disease – no. (%)	2445 (22)	1053 (23)	3498 (23)
Diabetes – no. (%)	1225 (11)	425 (9)	1650 (11)
Renal disease – no. (%)	368 (3)	108 (2)	476 (3)
Cardiovascular disease – no. (%)			
Any	5554 (51)	2109 (47)	7663 (50)
Angina history	2680 (25)	823 (18)	3503 (23)
Stroke or TCI	1718 (16)	731 (16)	2449 (16)
CABG or PCI	1954 (18)	531 (12)	2485 (16)
Congestive heart failure	870 (8)	355 (8)	1225 (8)
Heart valve disease	548 (5)	170 (4)	718 (5)
Acute myocardial infarction	2139 (20)	782 (17)	2921 (19)
Pacemaker or ICD	446 (4)	119 (3)	565 (4)
Other	840 (8)	387 (9)	1227 (8)
Cancer history – no. (%)	1841 (17)	499 (11)	2340 (15)
Care dependency – no. (%)			
Independent	10,131 (93)	3572 (79)	13,703 (89)
Home care	547 (5)	317 (7)	864 (6)
Nursing home	28 (0)	88 (2)	116 (1)
Missing	181 (2)	531 (12)	712 (5)
Tobacco use – no. (%)			
None	1790 (16)	705 (16)	2495 (16)
Previous (>6 weeks)	4225 (39)	907 (20)	5132 (33)
Current smoker	4527 (42)	1514 (34)	6041 (39)
Missing	345 (3)	1382 (31)	1727 (11)
Alcohol abuse – no. (%)			
None	10,022 (92)	3628 (80)	13,650 (89)
More than > 5 units/day	216 (2)	131 (3)	347 (2)
Missing	649 (6)	749 (17)	1398 (9)
Endovascular repair – no. (%)	2669 (25)	106 (2)	2775 (18)

Notes: Dependency, tobacco and alcohol history was based on the DVR. Other cardiac disease included: cardiomyopathy (DNPR); unspecified cardiac surgery history with no current symptoms (DVR); AMI< 6 weeks, unstable angina or congestive heart failure (DVR); AMI> 6 weeks or asymptomatic arrythmia (DVR), stable angina or heart medication (DVR). Full list of International Classification of Diseases-codes uses from the DNPR is available in the Supplementary Data. When excluding non-melanoma skin cancer, the prevalence of patients with a history of any cancer was 14% in intact and 8% in ruptured AAA repair. 2020 (18%) of intact AAA patients had symptomatic aneurisms. Less than 2% were iliac repair without aortic involvement in both groups.

Abbreviations: TCI, transient cerebral ischemia. CABG, Coronary artery bypass. PCI, Percutaneous coronary intervention. ICD, implantable cardioverter-defibrillator. Data source for Charlson's comorbidity index was the Danish National Patient Registry, DNPR. Other disease items were the union set of data in the DNPR and the Danish Vascular Registry, DVR.

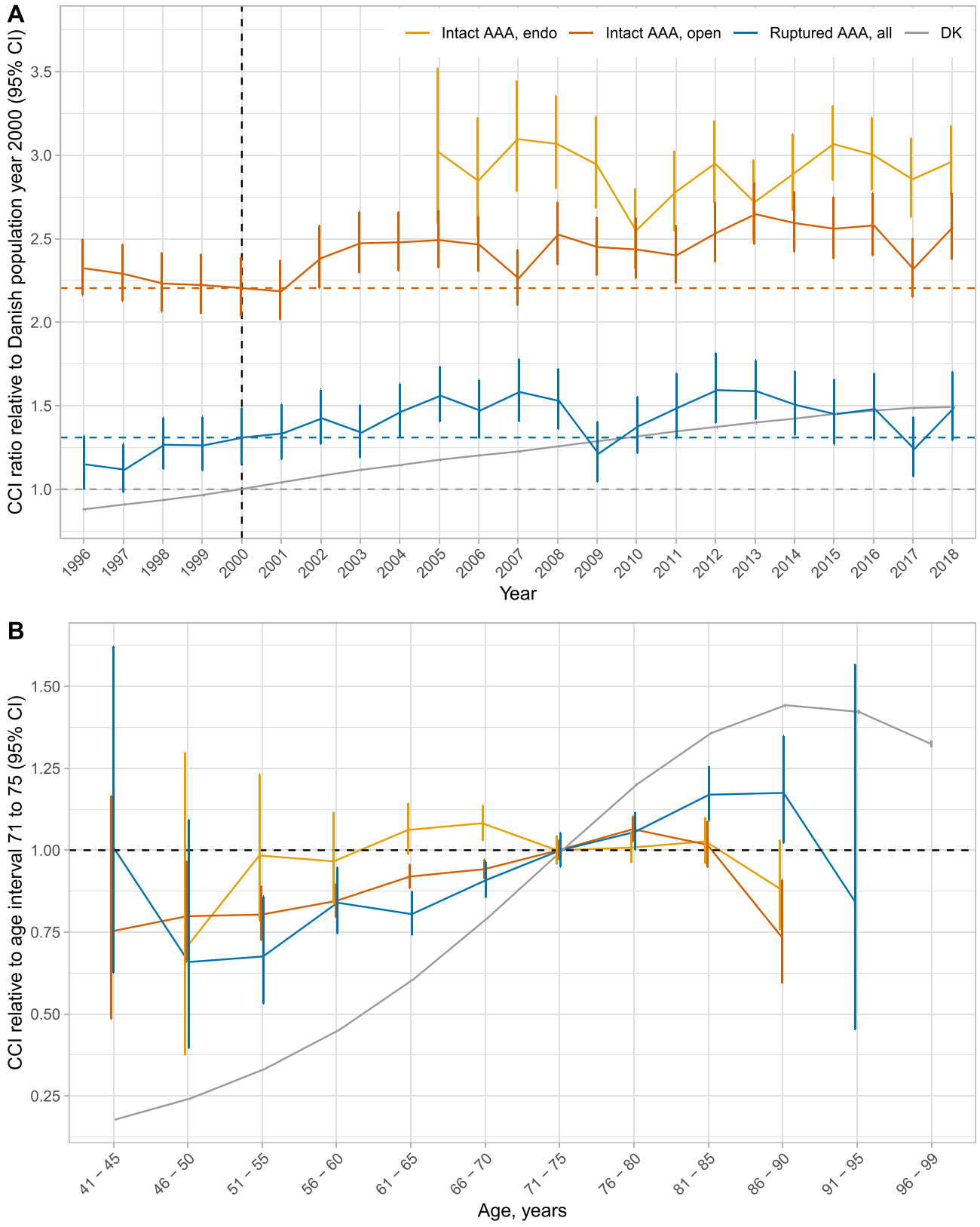

Figure 4 Trend in Charlson's comorbidity index score of AAA repair relative to the Danish population in calendar year 2000 (**A**) and relative to age group 71–75 (**B**).
Notes: (**A**) Trends in Charlson's comorbidity index (CCI) presented as ratios standardized to the age- and sex distribution of the Danish (DK) population's CCI in year 2000. (**B**) CCI presented as ratios standardized to calendar year and sex distribution of persons aged 71–75 years within each population (intact and ruptured abdominal aortic repair, and the Danish population). For both panels, the bars indicate the 95% confidence intervals and were computed by Poisson regression including the covariates calendar year, age, sex and CCI score. Compared to the Danish population over the study period, the age- and sex-adjusted CCI-score was 2.10-fold higher in intact (95% CI, 2.08–2.13) and 1.21-fold higher in ruptured (95% CI, 1.18–1.25) AAA patients.

Table 2 Five-Year Mortality Following AAA Repair in Denmark 1996–2018

Calendar Period of Repair	No. of Deaths	No. of Patients	Risk of Death % (95% CI)	Mortality Rate Ratio (95% CI)	
				Crude	Adjusted[a]
Intact AAA					
1996–1999	539	1529	35.3 (32.8–37.6)	Reference	Reference
2000–2004	584	1824	32.0 (29.8–34.1)	0.88 (0.79–0.99)	0.84 (0.74–0.94)
2005–2009	741	2499	29.7 (27.8–31.4)	0.80 (0.72–0.90)	0.67 (0.60–0.75)
2010–2014	678	2792	24.3 (22.7–25.9)	0.63 (0.56–0.71)	0.51 (0.46–0.58)
2015–2018	337	2243	24.7 (22.4–27.0)[b]	0.65 (0.56–0.74)	0.51 (0.44–0.59)
Ruptured AAA					
1996–1999	555	880	63.1 (59.7–66.1)	Reference	Reference
2000–2004	716	1114	64.3 (61.3–67.0)	1.04 (0.93–1.16)	1.00 (0.90–1.12)
2005–2009	550	1000	55.0 (51.8–58.0)	0.81 (0.72–0.91)	0.76 (0.67–0.86)
2010–2014	474	907	52.3 (48.9–55.4)	0.71 (0.63–0.81)	0.64 (0.57–0.73)
2015–2018	207	607	39.7 (35.4–43.8)[b]	0.50 (0.43–0.59)	0.46 (0.39–0.54)

Notes: [a]Adjusted for age, sex, Charlson's comorbidity index, health care region in a Cox regression stratified for open versus endovascular repair. In 2010–2014, 84 and 19 were censored, and in 2016–2018, 1906 and 400 were censored for intact and ruptured AAA, resp. [b]For Calendar period 2015–2018 the 5-yr risk of death was predicted using a univariable Cox model with calendar year 1996–1999 as the baseline hazard.
Abbreviations: CCI, Charlson's comorbidity index. LEAD, lower extremity artery disease. PCI, percutaneous transluminal angioplasty.

0.28–0.57]; p interaction = 0.006). The decrease in mortality rate over calendar time was consistent across age groups for intact AAA repair (p interaction = 0.43).

The adjusted five-year MRR in women vs men was 1.06 in intact (95% CI, 0.96–1.16) and 1.03 in ruptured (95% CI, 0.92–1.15) AAA repair, eTable 4. The crude five-year MRR indicated higher mortality in women ([MRR_{intact}: 1.11; 95%

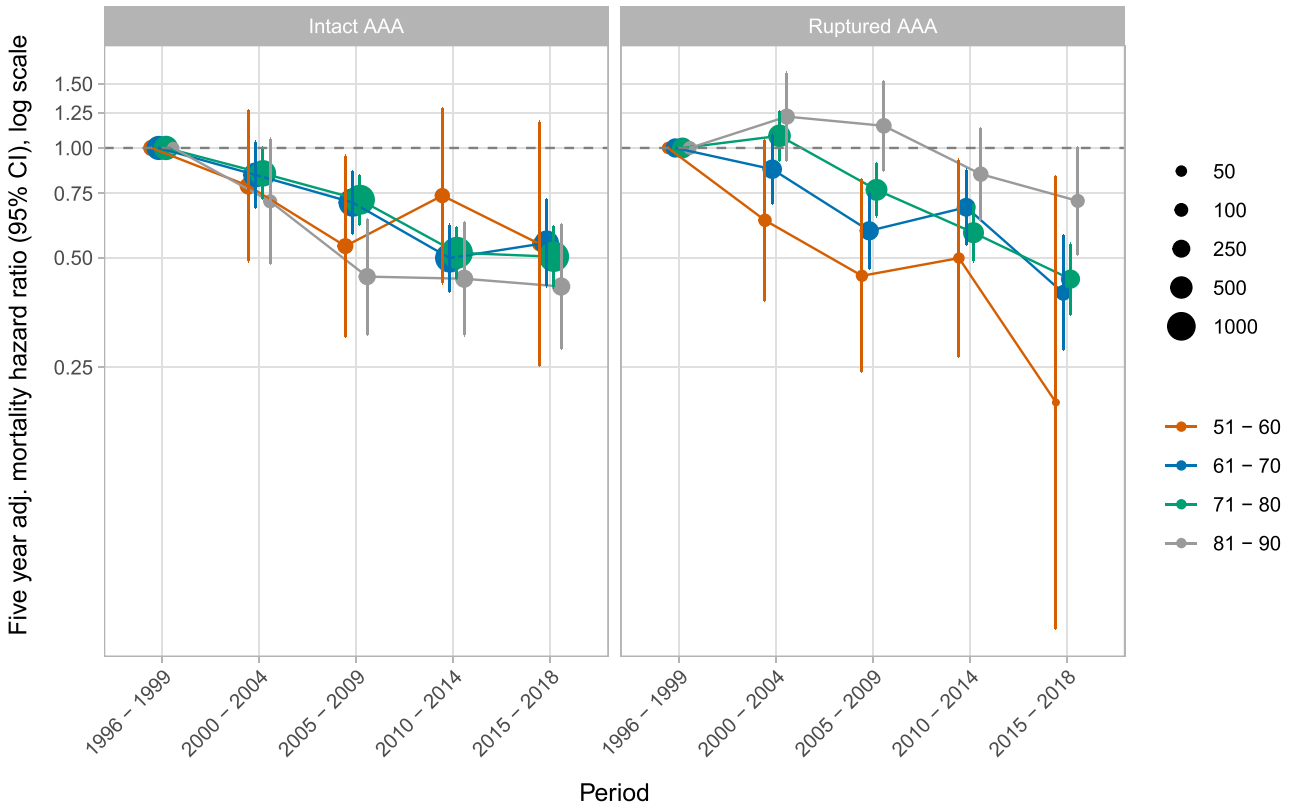

Figure 5 Trends in five-year mortality rate ratio following AAA repair stratified by age.

CI, 1.01–1.22], [$MRR_{ruptured}$: 1.17; 95% CI, 1.05–1.31]), but adjusting for age alone explained the sex difference. Ninety days following repair, the adjusted MRR was higher in women following intact, but not for ruptured AAA repair ([MRR_{intact}, 1.29; 95% CI, 1.06–1.57], [$MRR_{ruptured}$, 1.03; 95% CI, 0.90–1.18]).

Mortality by Comorbidity

Compared with moderate comorbidity, severe comorbidity associated to an adjusted five-year MRR of 1.28 (95% CI, 1.16–1.42) following intact and 1.24 (95% CI, 1.10–1.39) following ruptured AAA repair; and very severe comorbidity associated to an adjusted MRR of 1.90 (95% CI, 1.73–2.08) in intact and 1.51 (95% CI, 1.35–1.69) in ruptured AAA repair, eTable 4.

Epidemiology of Endovascular Repair

The age- and sex-standardized IR of endovascular repair for intact AAA was less than 1.1 per 100.000 person-year before year 2005 (Figure 1). It steadily increased from 2005 to 2011 and then stabilized at approximately 6.7 procedures per 100.000 person-years from 2011 to 2018. The proportion of intact AAAs managed with endovascular repair increased from 2% in 1996–1999 to 42% in 2015–2018.

Between 2005 and 2018, the mean age for endovascular repair patients was 73.8 years, compared to 70.6 years for open AAA repair patients. The age, sex, and calendar year adjusted CCI for intact AAA patients was 2.21 (95% CI, 2.16–2.26)-fold higher in endovascular repair and 2.05 (95% CI, 2.02–2.09)-fold higher in open repair compared to the Danish population during the study period.

Discussion

In this registry-based investigation of AAA repair epidemiology, we found a 24% decline in the overall AAA repair IR in Denmark from 1996 to 2018, mostly attributable to a marked IR reduction of ruptured AAA repair in men. We observed considerable age heterogeneity in the incidence change over calendar time with a decrease among persons aged below 75 years and an increase in those aged above 75 years. Comorbidity, defined according to CCI, increased independently of age and sex during the study period. The adjusted five-year mortality rate was halved following intact and ruptured AAA repair. In ruptured AAAs, the most significant mortality reduction was seen in the youngest age groups and was less pronounced in the octogenarians. Age and CCI, but not sex, were strongly associated to 5-year mortality.

Incidence Findings in Relation to Other Studies

United Kingdom (UK) and Swedish registry data have also demonstrated a stable IR in intact AAA- and decreasing IR of ruptured AAA – repair or hospital admission.[10,31] Since the UK and Sweden have implemented AAA screening, it is unclear how much of the IR reduction in AAA rupture is attributable to screening vs a reduction in patients risk factors for AAA rupture. Since Denmark has not implemented screening yet, our data suggest that changes in patient risk factors are contributing to the observed trends.

Additionally, our study highlights significant age and sex-heterogeneities in the IR trend, consistent with previous research. In the UK, hospital admission incidence for AAA has decreased among patients below 75 years old and increased among those above 75 years.[31,32] Swedish registry data on ruptured AAA repair revealed a declining IR in men but a stable IR among women.[10] We propose that these findings can be explained by changes in smoking patterns, which we will discuss it in detail below, although this is a theoretical notion and not directly supported by the study results.

During the 20th century, AAA was a disease rising in the US, UK, and Denmark, as evidenced by a surge in AAA-related deaths.[33–35] A later report covering 1994 to 2010 suggested a decline in the AAA-specific mortality in Western countries, except for Denmark.[32,35] One possible explanation for the reduced AAA-related mortality is the reduction in tobacco use, as smoking is strongly associated with the development and expansion rate of AAA.[36–38] The prevalence of smoking among Danish men has been steadily decreasing since 1953, while it initially increased among women before declining after 1970.[28,39] We interpret, similar to what has been observed for lung cancer,[40] that a cohort effect of smoking contributes to the age and sex heterogeneity in the trends of the AAA repair incidence observed in this study. Specifically, a large proportion of persons born in the interwar period (1920–1940) were exposed to tobacco in the 1950s

and 1960s at the age of 20–40 years. This explains the high incidence among the youngest age groups in the 1990s, and as individuals from that birth cohort age over time, the highest incidence follows along, as reflected by the red colored tiles in Figure 1B. Towards the end of our study period, the incidence was halved in the youngest age groups and doubled in those aged >80 years. The latter may also reflect that surgeons accept increasing age for repair following advances in repair technique and perioperative care. However, we believe that change in indications for repair only explain little of the 52–63% IR reduction in persons aged 50–70 years because an expanding AAA cannot be treated conservatively.

Few risk factors specific for AAA expansion and rupture have been identified, with smoking and female sex being the most significant.[15,37] The considerable reduction in tobacco use among Danish men since 1950 likely explains the sex heterogeneity in the change of ruptured AAA repair IR observed in this study. Alternatively, increased exposure to stress and hypertension among of women entering the labor marked during the 20th century could also contribute.[8,35] Previously proposed environmental explanations for AAA development, such as carbon monoxide emission[31] seems less plausible, as this would likely affect both sexes equally. Increased utilization of abdominal radiography over the study period may have detected AAAs coincidentally before rupture, causing a shift from ruptured to elective AAA repair. However, this is unlikely to explain the sex heterogeneity, as this was seen for both ruptured and total AAA repairs.

The Use of Endovascular Repair in Relation to Other Studies

Endovascular repair was introduced during the study period and in 2018 around half of all intact AAA were treated with endovascular repair. This differs from the US and Swedish practice where endovascular repair became the most frequently used repair type in 2005 and 2009, respectively.[8,10] Compared with open intact AAA repair in our cohort, patients undergoing endovascular repair were, on average, 3 years older and had a higher CCI score, independently of age, sex, and calendar year. The use of endovascular repair for ruptured AAA was very rare in this cohort and is not further discussed. The total AAA repair IR increased transiently from 2005 to 2010, which could be interpreted as either more patients being invited for AAA repair due to the availability of the less invasive endovascular treatment, or due to the occurrence of AAAs among birth cohorts from the interwar period with high smoking prevalence; like the observed trend in first-time hospitalization for myocardial infarction in Denmark.[41]

Mortality Findings in Relation to Other Studies

UK mortality statistics have also shown a 50% reduction in AAA- and aortic dissection-related deaths in persons aged below 75 years and a 25% reduction in those aged 75 years or above.[31] That mortality reduction was observed between 1997 and 2009, which coincides with the age-group separation we observed for ruptured AAAs. The reasons for the age heterogeneity are unclear.[31] The introduction of endovascular repair does not seem to explain our findings because this was an exceedingly rare technique in ruptured AAAs. It appears that all age bands approach a 50% mortality rate reduction but occurs with a delay in the oldest patients undergoing ruptured AAA repair, which could be a cohort effect, eg, of smoking or unknown patient risk factors, such as social status. Another possible explanation is that AAA rupture is a surgical emergency where the patient often encounters recurrent episodes of hypovolemic shock that puts high demand on cardiovascular compensatory mechanisms to maintain tissue oxygenation. The physiological reserve decreases with age, which makes it harder to achieve a 50% mortality reduction given the higher absolute mortality in the octogenarians.[42]

A WHO mortality database study 1994–2010 showed a global reduction in age-standardized AAA mortality, with a few exceptions, including Danish women.[28] Our study shows that the mortality trend has now reversed in females too. EU countries, including the UK, have reported higher in-hospital mortality rates for women than men after elective AAA repair.[43,44] We also found a higher 90-day mortality rate in females undergoing intact AAA repair, but five years following repair the evidence was less firm, although the point-estimate indicated a 4–5% higher five-year mortality rate in females for both types of repair. Higher female survival in the general population, may explain the difference in 90-day- and five-year MRR. As the repair-specific hazards abate from 90-days to 5 years following repair, the female survival following AAA repair approaches that of men. It is worth considering that the data from the UK and Sweden may be biased, as these countries introduced male AAA screening between 2006 and 2009. As a result, men scheduled for elective repair of a screening-detected AAA may be otherwise healthy, whereas females are often referred for elective AAA repair due to co-existing disease, eg, cancer, that prompts the radiography disclosing

the AAA. Notably, previous findings lack adjustment for comorbidity or have high missingness of comorbidity data.[43,44] The impact of female gender warrants further study and follow-up to inform the decision of when to pursue AAA repair, and whether to screen for AAA in women.[11,20,45,46]

We performed a survival analysis of the general Danish population aged 41–99 years, demonstrating a marked mortality rate reduction during the study period. So, generally improved health and health care in the Danish population may explain some, but not all, of the improved survival following AAA repair. Thus, there seems to be an excess improved survival unique to the AAA population that needs further exploration.

Strengths and Limitations

Strengths of our study include the longitudinal design covering 23 years of data from well-validated registries that enable individual-level linkage and estimation of comorbidity-specific incidences. AAA coding rules and classifications were unaltered during the study period. Our estimates are comparable to other studies. Furthermore, because screening is not implemented in Denmark, as opposed to the US, UK, and Sweden, our data provide unique information on the trends in incident AAAs requiring repair in a country with a historically high smoking prevalence where the incidence is not affected by screening programs.[39] However, our results may have limited the generalizability to countries that have implemented AAA screening.

Around 2010, the female AAA diameter threshold for repair was lowered from 5.5 to 5.0 cm, which likely affected the incidence. However, a rather stable female incidence in both intact and ruptured AAA repairs suggests that it may have had limited significance. The temporal CCI increase among AAA patients could partly be attributed to a greater tendency to register diagnoses at discharge, even though the Danish healthcare system has included reimbursement for registration throughout the study period.

The CCI score will not capture all patient comorbidity, as this may be influenced by the patient's inclination to seek medical help. Chronic lung disease and diabetes managed exclusively in primary healthcare are not recorded in the Danish registries. The higher CCI in intact vs ruptured AAA patients may reflect that intact AAA patients have undergone abdominal radiography for other health-related reasons, potentially revealing the AAA before rupture and contributing to CCI points.

Clinical Implications and Conclusion

AAAs also occur in non-smokers,[37] but smoking shortens time to AAA development in genetically predisposed.[32] Combined with increased life expectancy, AAAs requiring repair will continue to occur but will probably present at a higher age and a reduced rate, especially in males. This may have important implications for the future hospital caseload, planning hospital capacity, and the design and cost-effectiveness of screening programs. Given the marked mortality reduction, we observed, continuous reevaluation of the threshold for AAA repair seems prudent.[47] However, a proposed randomized trial assigning men with AAAs 5.5 to 6.5 cm to treatment or watchful waiting lacked equipoise among surgeons.[48]

Our results should not discourage repair of ruptured AAA in the octogenarians. Survival of ruptured AAA has improved in the elderly, but apparently with a delay/time-shift, indicating that mortality has decreased due to altered patients risk factors more than due to changes in surgical technique or proficiency.

In conclusion, Danish AAA repair incidence is decreasing due to a reduction in males undergoing repair and a shift toward treatment of an older population, which may be explained by a cohort effect. Both crude and adjusted mortality was markedly reduced over the study period. Thus, reasons for the improved survival are unclear but likely include generally increased longevity in the population.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Svensjo S, Bjorck M, Gurtelschmid M, Djavani Gidlund K, Hellberg A, Wanhainen A. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. *Circulation*. 2011;124(10):1118–1123. doi:10.1161/CIRCULATIONAHA.111.030379
2. Oliver-Williams C, Sweeting MJ, Turton G, et al. Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. *Br J Surg*. 2018;105(1):68–74. doi:10.1002/bjs.10715
3. Lindholt JS, Juul S, Fasting H, Henneberg EW. Hospital costs and benefits of screening for abdominal aortic aneurysms. Results from a randomised population screening trial. *Eur J Vasc Endovasc Surg*. 2002;23(1):55–60. doi:10.1053/ejvs.2001.1534
4. Lindholt JS, Rasmussen LM, Sogaard R, et al. Baseline findings of the population-based, randomized, multifaceted Danish cardiovascular screening trial (DANCAVAS) of men aged 65-74 years. *Br J Surg*. 2019;106(7):862–871. doi:10.1002/bjs.11135
5. Heather BP, Poskitt KR, Earnshaw JJ, Whyman M, Shaw E. Population screening reduces mortality rate from aortic aneurysm in men. *Br J Surg*. 2000;87(6):750–753. doi:10.1046/j.1365-2168.2000.01476.x
6. Lindholt JS, Sogaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet*. 2017;390(10109):2256–2265. doi:10.1016/S0140-6736(17)32250-X
7. Wanhainen A, Verzini F, Van Herzeele I, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57(1):8–93. doi:10.1016/j.ejvs.2018.09.020
8. Kent KC. Clinical practice. Abdominal aortic aneurysms. *N Engl J Med*. 2014;371(22):2101–2108. doi:10.1056/NEJMcp1401430
9. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK Small Aneurysm Trial Participants. *Ann Surg*. 1999;230(3):289–296. doi:10.1097/00000658-199909000-00002
10. Lilja F, Mani K, Wanhainen A. Editor's Choice - Trend-break in Abdominal Aortic Aneurysm Repair With Decreasing Surgical Workload. *Eur J Vasc Endovasc Surg*. 2017;53(6):811–819. doi:10.1016/j.ejvs.2017.02.031
11. Bergqvist D, Bjorck M, Wanhainen A. Abdominal aortic aneurysm--to screen or not to screen. *Eur J Vasc Endovasc Surg*. 2008;35(1):13–18. doi:10.1016/j.ejvs.2007.06.012
12. Wilmink AB, Quick CR, Hubbard CS, Day NE. Effectiveness and cost of screening for abdominal aortic aneurysm: results of a population screening program. *J Vasc Surg*. 2003;38(1):72–77. doi:10.1016/S0741-5214(03)00135-6
13. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery. *Can J Cardiol*. 2017;33(1):17–32. doi:10.1016/j.cjca.2016.09.008
14. Schwarze ML, Barnato AE, Rathouz PJ, et al. Development of a list of high-risk operations for patients 65 years and older. *JAMA Surg*. 2015;150(4):325–331. doi:10.1001/jamasurg.2014.1819
15. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2–77 e72. doi:10.1016/j.jvs.2017.10.044
16. Friedman SG. *A History of Vascular Surgery*. 2nd ed. Malden, Mass: Blackwell Futura; 2005.
17. Powell JT, Sweeting MJ, Ulug P, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *Br J Surg*. 2017;104(3):166–178. doi:10.1002/bjs.10430
18. Lederle FA, Kyriakides TC, Stroupe KT, et al. Open versus Endovascular Repair of Abdominal Aortic Aneurysm. *N Engl J Med*. 2019;380(22):2126–2135. doi:10.1056/NEJMoa1715955
19. Bahia SS, Holt PJ, Jackson D, et al. Systematic Review and Meta-analysis of Long-term survival After Elective Infrarenal Abdominal Aortic Aneurysm Repair 1969-2011: 5 Year Survival Remains Poor Despite Advances in Medical Care and Treatment Strategies. *Eur J Vasc Endovasc Surg*. 2015;50(3):320–330. doi:10.1016/j.ejvs.2015.05.004
20. O'Donnell TFX, Landon BE, Schermerhorn ML. AAA Screening Should Be Expanded. *Circulation*. 2019;140(11):889–890. doi:10.1161/CIRCULATIONAHA.119.041116
21. Møller A, Eldrup N, Wetterslev J, et al. Trends in lower extremity artery disease repair incidence, comorbidity, and mortality: a Danish nationwide cohort study, 1996–2018. *Vasc Health Risk Manag*. In Press 2024
22. Sorensen HT. Regional administrative health registries as a resource in clinical epidemiology: a study of options, strengths, limitations and data quality provided with examples of use. *Int J Risk Saf Med*. 1997;10(1):1–22. doi:10.3233/JRS-1997-10101
23. Schmidt M, Pedersen L, Sorensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29(8):541–549. doi:10.1007/s10654-014-9930-3
24. Eldrup N, Cerqueira C, de la Motte L, Rathenborg LK, Hansen AK. The Danish Vascular Registry, Karbase. *Clin Epidemiol*. 2016;8:713–718. doi:10.2147/CLEP.S99506
25. Altreuther M, Menyhei G. International Validation of the Danish Vascular Registry Karbase: a Vascunet Report. *Eur J Vasc Endovasc Surg*. 2019;58(4):609–613. doi:10.1016/j.ejvs.2019.04.008
26. Laustsen J, Jensen LP, Hansen AK. Danish National Vascular R. Accuracy of clinical data in a population based vascular registry. *Eur J Vasc Endovasc Surg*. 2004;27(2):216–219. doi:10.1016/j.ejvs.2003.11.011

27. Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sorensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449–490. doi:10.2147/CLEP.S91125
28. Clemmensen KK, Lynge E, Clemmensen IH. Nationwide tobacco surveys and sales data in Denmark from 1920 to 2010. *Dan Med J*. 2012;59(6):657.
29. Moller A, Nielsen HB, Wetterslev J, et al. Low vs high hemoglobin trigger for transfusion in vascular surgery: a randomized clinical feasibility trial. *Blood*. 2019;133(25):2639–2650. doi:10.1182/blood-2018-10-877530
30. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383. doi:10.1016/0021-9681(87)90171-8
31. Anjum A, Powell JT. Is the incidence of abdominal aortic aneurysm declining in the 21st century? Mortality and hospital admissions for England & Wales and Scotland. *Eur J Vasc Endovasc Surg*. 2012;43(2):161–166. doi:10.1016/j.ejvs.2011.11.014
32. Choke E, Vijaynagar B, Thompson J, Nasim A, Bown MJ, Sayers RD. Changing epidemiology of abdominal aortic aneurysms in England and Wales: older and more benign? *Circulation*. 2012;125(13):1617–1625. doi:10.1161/CIRCULATIONAHA.111.077503
33. Eickhoff JH. Incidence of diagnosis, operation and death from abdominal aortic aneurysms in Danish hospitals: results from a nation-wide survey, 1977-1990. *Eur J Surg*. 1993;159(11–12).
34. Fowkes FG, Macintyre CC, Ruckley CV. Increasing incidence of aortic aneurysms in England and Wales. *BMJ*. 1989;298(6665):33–35. doi:10.1136/bmj.298.6665.33
35. Sidloff D, Stather P, Dattani N, et al. Aneurysm global epidemiology study: public health measures can further reduce abdominal aortic aneurysm mortality. *Circulation*. 2014;129(7):747–753. doi:10.1161/CIRCULATIONAHA.113.005457
36. Lederle FA, Nelson DB, Joseph AM. Smokers' relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg*. 2003;38(2):329–334. doi:10.1016/S0741-5214(03)00136-8
37. Norman PE, Curci JA. Understanding the effects of tobacco smoke on the pathogenesis of aortic aneurysm. *Arterioscler Thromb Vasc Biol*. 2013;33(7):1473–1477. doi:10.1161/ATVBAHA.112.300158
38. Jahangir E, Lipworth L, Edwards TL, et al. Smoking, sex, risk factors and abdominal aortic aneurysms: a prospective study of 18 782 persons aged above 65 years in the Southern Community Cohort Study. *J Epidemiol Community Health*. 2015;69(5):481–488. doi:10.1136/jech-2014-204920
39. Pisinger C, Jorgensen T, Toft U. A multifactorial approach to explaining the stagnation in national smoking rates. *Dan Med J*. 2018;65(2).
40. Skuladottir H, Olsen JH, Hirsch FR. Incidence of lung cancer in Denmark: historical and actual status. *Lung Cancer*. 2000;27(2):107–118. doi:10.1016/S0169-5002(99)00104-X
41. Schmidt M, Jacobsen JB, Lash TL, Botker HE, Sorensen HT. 25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. *BMJ*. 2012;344:e356. doi:10.1136/bmj.e356
42. Alvis BD, Hughes CG. Physiology Considerations in Geriatric Patients. *Anesthesiol Clin*. 2015;33(3):447–456. doi:10.1016/j.anclin.2015.05.003
43. Budtz-Lilly J, Venermo M, Debus S, et al. Editor's Choice - Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *Eur J Vasc Endovasc Surg*. 2017;54(1):13–20. doi:10.1016/j.ejvs.2017.03.003
44. Sidloff DA, Saratzis A, Sweeting MJ, et al. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *Br J Surg*. 2017;104(12):1656–1664. doi:10.1002/bjs.10600
45. LeFevre ML, Force USPST. Screening for abdominal aortic aneurysm: u.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161(4):281–290. doi:10.7326/M14-1204
46. Sweeting MJ, Masconi KL, Jones E, et al. Analysis of clinical benefit, harms, and cost-effectiveness of screening women for abdominal aortic aneurysm. *Lancet*. 2018;392(10146):487–495. doi:10.1016/S0140-6736(18)31222-4
47. Earnshaw JJ. The Indication for Elective Repair of Abdominal Aortic Aneurysm Should Be Reviewed. *Eur J Vasc Endovasc Surg*. 2021;61(1):7–8. doi:10.1016/j.ejvs.2020.09.001
48. Oliver-Williams C, Sweeting MJ, Jacomelli J, et al. Safety of Men With Small and Medium Abdominal Aortic Aneurysms Under Surveillance in the NAAASP. *Circulation*. 2019;139(11):1371–1380. doi:10.1161/CIRCULATIONAHA.118.036966