Research Article

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Female Sex is Associated with Higher Mortality and More Complications Following PCI

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ABSTRACT

Introduction: *Ischemic heart disease (IHD) is a leading cause of death globally. Despite clinical guidelines for treating IHD do not differentiate between sexes, females experience higher mortality compared to males. This study aimed to investigate sex disparities in mortality after standard percutaneous coronary intervention (PCI) for IHD and compare to the background expected population mortality.*

Methods: *The study included 84,335 patients treated with first entry PCI from Western Denmark Heart Registry (2000-2021). Kaplan-Meier survival curves evaluated mortality over time, and logistic regression analyses identified risk factors.*

Results: *All-cause mortality was higher in females at 30 days (4.54% vs. 3.43%), 1 year (8.24% vs. 6.42%), and 5 years (20.47% vs. 16.48%) (p<0.0001). Compared to the background population mortality, there was a considerable difference between actual and expected 1- and 5-year mortality among males and females following PCI and, despite general longer living time, a significantly higher expected mortality in females compared to males. Males had a better survival than the background population after six years, regardless of the indication for PCI, while females displayed comparable mortality to the background population at eight years. Female sex was associated with higher mortality after 30 days, 1 year, and 5 years, respectively (OR 1.65 (1.47-1.87), OR 1.43 (1.33-1.55), and OR 1.37 (1.30-1.44)).*

Conclusion: *Females experience higher mortality following first entry PCI compared to males. Additionally, they have a higher expected mortality and a delayed catch-up with the background population mortality relative to males.*

Keywords

Percutaneous Coronary Intervention, Sex disparities, Female, Risk factors.

Abbreviations

ACS: Acute Coronary Syndrome, AP: Stable Angina Pectoris, CAG: Coronary Angiography, CL: Confidence Limit, CPR-number: Civil Personal Registration Number, ICD-10: International Classification of Diseases, 10th revision, IHD: Ischaemic Heart Disease, MO: Mixed Other, n-STEMI: non-ST-Elevation Myocardial Infarction, OR: Odds Ratio, PCI: Percutaneous Coronary Intervention, STEMI: ST-Elevation Myocardial Infarction, WDHR: Western Denmark Heart Registry.

Introduction

Ischemic Heart Disease (IHD) is a leading cause of death globally in both males and females, accounting for 16% of all deaths in 2019 [1,2]. In Denmark, approximately 204,000 people live with IHD, with males compromising 61% of cases and each year, there are an estimated excess of deaths of 5.4 per 1,000 Danish citizens due to IHD [3]. There has been a global decline in age-standardized IHD prevalence, incidence, and mortality in both sexes in the period from 1990 to 2019 [4,5]. A similar decrease in age-standardized IHD-mortality has been reported in Denmark between 1970 and 2015 [6]. Uniform implementation of improved preventative strategies, enhanced surveillance, quicker and more advanced diagnostics, superior medical and interventional treatments, and more effective rehabilitation across sexes, geographical areas, economics, and social strata may explain this positive trend. One major factor is the implementation of percutaneous coronary intervention (PCI) as standard treatment for acute coronary syndrome (ACS) [6,7]. However, despite these uniform efforts and contrary to expectations, females experience higher IHD-related mortality rates than males, even though mortality among females has declined more than that of males over the past three decades [4,8,9]. This disparity is believed to be caused by factors such as older age at presentation, a higher degree of atypical symptoms, more comorbidities and risk factors, a greater incidence of complications like bleeding and heart failure, and less frequent treatment with evidence-based therapy such as PCI among females compared to males [9-12]. Furthermore, females show higher need of target lesion surgical revascularization [13], suggesting that the result of the interventional procedure may differ from those of males. The aim of this study was to investigate sex disparities in mortality after standard PCI, primarily with focus on actual and expected lifetime based on population data, with impact of age, time, and procedure factors to categorize and map relevant factors in the treatment of IHD.

Materials and Methods

Data Source

Study details were collected from the Western Denmark Heart Registry (WDHR), containing data of all adult patients undergoing cardiac diagnostic and interventional procedures in the Western part of Denmark. WDHR was established in 1999 with three public and one semi-public (since 2005) cardiac surgery centers. From the beginning of 2000, it was fully operational, offering data on coronary angiography (CAG), PCI-, and cardiac surgery procedures. The internet-based WDHR covers approximately 60% of the Danish population area with mandatory prospectively and consecutively registration of all cardiovascular procedures with detailed patient-, risk-, procedure-, and care-related data, together with in-hospital postoperative complications. All data related to the current study have been obligatory since 2006, and the registry has become an integral part of clinical practice [14]. Procedure details recorded prior to 2006 were regarded as 0 or negative if any other information was entered in the specific field, according to the procedures at that time. WDHR is known for its high accuracy and completeness ensured by regular updates, automatic validation rules at data entry, systematic validation procedures, and random spot checks [15].

WDHR is one of many Danish Health Registries. Together with the unique civil personal registration number (CPR number) assigned to all Danish citizens at birth or immigration and remaining the same throughout life, it is feasible to conduct large, population-based studies with relevant outcome follow-up on all procedures and medical treatments [16]. A more detailed description of the database and methods can be found in Bhavsar et al. [17].

Study Population

All patients submitted to PCI between 2000 and 2021 and registered in WDHR were assessed for eligibility. Exclusion criteria were patients with invalid CPR number and those who had previously undergone cardiac interventions. In patients undergoing multiple PCI procedures only the first was included.

Ethics and Permissions

The study was registered by the Danish Data Protection Agency with number 1-16-02-455-21 [17], and the agency's rules for the use and handling of data were met. Written consent is not required for registry-based studies according to Danish legislation. The study was conducted in accordance with the standards in the Declaration of Helsinki.

Factors and Outcome

The analyses were based on sex, age, primary indication, and peri-procedural complications. The indication of PCI is used to distinguish urgency and type (Supplement 1). Besides elective referrals to PCI from minor centers, most patients were referred to CAG. In the WDHR database, some factors, including indication, are inherited to the treatment level. Thus, some indications might be different from original and are correlated with registered ICD-10 codes into four major groups: ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (n-STEMI), stable angina pectoris (AP), and mixed other (MO). Complications were registered in three major groups: in-lab, and in-hospital divided in general procedure- and vessel-related complications.

The primary outcome was all-cause mortality after stipulated periods. Further analyses were based on procedure complications and new PCI within 5 years. The registered complications constituted a comprehensive list of possible outcomes (Supplement 2).

Background Population Mortality

All patients included in the study were assigned an estimated risk of death based on the official 5-year life tables from Statistics Denmark (Supplement 3) [18], considering the long study period and increase in mean living age. The allocated 1- and 5-year mortality were based on time of procedure, age, and sex, enabling analyses of the study population's actual mortality against the background (expected) population mortality in a 1:1 ratio in subgroups of sex and selected factors in question. Considering the substantial changes in life expectancy in the study period from 60 to 80 years of age, this approach seemed valid.

Statistical Analyses

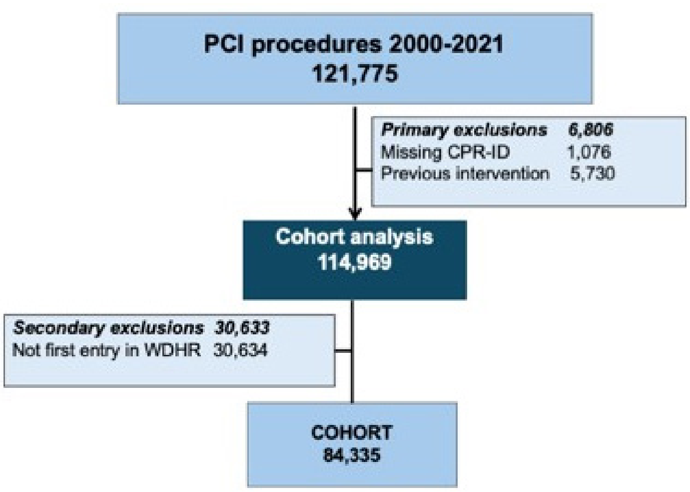
Patients were divided by age, sex, and overall indication for PCI for the detailed statistical analyses. Time-based groups of patients were used where appropriate to avoid small group sizes. Comparison of categorical variables was conducted using χ^2-test, while continuous variables were assessed with student's t-test (normally distributed data) and Mann-Whitney U-test (non-normally distributed data). Comparisons between subgroups were carried out using ANOVA or Kruskal-Wallis test. Kaplan-Meier survival curves were used to evaluate outcomes over time. Logistic regression analyses, with robust error variance to estimate adjusted odds ratios (ORs), were used to identify risk factors with an impact on outcomes, presented as OR with 95% confidence limits (CLs). The included covariates were primarily based on comorbidity factors, indication, period, and sex. All analyses were performed with MedCalc® software version 22.014 (Mariakerke, Belgium). A p-value <0.05 was considered statistically significant.

Results

Study Population

During the study period, a total of 121,775 PCI procedures were performed in Western Denmark between 2000 and 2021. One thousand seventy-six PCI procedures were performed on patients without a valid CPR number, and 5,730 procedures belonged to patients who had previously undertaken cardiac surgery or intervention before the start of WDHR and were excluded from the study. In patients undergoing multiple PCI procedures throughout the study period, only the first was considered eligible for the analyses, leaving a cohort of 84,335 first time PCI procedures (Figure 1).

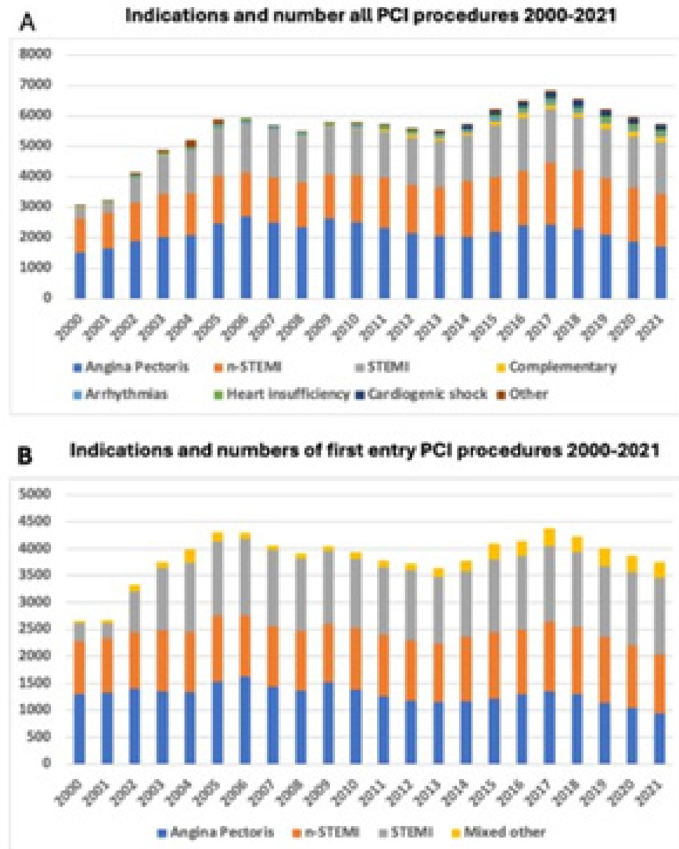
Figure 1: An error/inconsistance in the numbers (our mistake), and the design could be a little nicer. Attached as tif and jpeg.



PCI Procedures

From initiation of WDHR the number of PCI procedures increased until a peak in 2005. In the following years, the overall referral to PCI decreased slightly until 2013-14, after which especially the number of acute interventions increased with a new peak in 2017 (Figure 2A). Looking at indications of first entry procedures since 2006, the interventions due to AP declined, n-STEMI were relatively consistent, while interventions due to STEMI and MO increased. The interventions due to MO were primarily due to an increase in complementary and control PCI treatments together with more severely ill patients like cardiac arrest, cardiogenic shock and heart insufficiency (Figure 2B).

Figure 2: Number of all (A) and first entry (B) PCI procedures divided by indication and year.



Abbreviations: PCI: Percutaneous Coronary Intervention; n-STEMI: non-ST Elevation Myocardial Infarction; STEMI: ST-Elevation Myocardial Infarction; MO: Mixed Others.

Age of both males and females at the first entry PCI increased during the two decades where females were consistently 4-5 years older than males (p<0.001). The female fraction fluctuated slightly (p=0.0497) with a slight downward trend over the last years as compared to that in the beginning (p=0.0003) (Figure 3). Although within a small margin, the mean number of both treated coronary vessels (range 1.12-1.25) and lesions (range 1.22-1.43) per first entry procedure differed significantly during the period (p<0.0001). The use of balloons and stents increased constantly since 2010 and 2012, respectively (Figure 4). The number of treated vessels and lesions per PCI procedure and used equipment were significantly lower in females. Regarding the result of the procedures, significantly higher failure rate was observed among females (4.13% in females vs. 3.81% in males, p=0.021) (Table 1). Males more often received one or more additional PCIs within 5 years from first entry PCI procedure (total of 24.5% in males vs. 19.9% in females, p<0.001) (Table 2).

Figure 3: Mean age (years) and female fraction of first entry PCI procedures divided over time. Age increased significantly over time (p<0.001) and was higher in females (p<0.001). The female fraction decreased significantly over time (p=0.0497, trend p=0.0003). Abbreviations: PCI: Percutaneous Coronary Intervention.

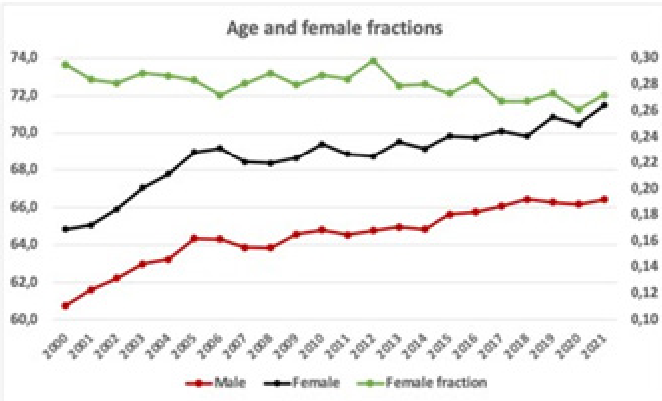


Figure 4: Mean number of treated coronary vessels and lesions, and number of used balloons and stents divided by year of first entry PCI procedures. Number of balloons and stents was not registered before 2004. All factors showed significant difference over time (p<0.001). Abbreviations: PCI: Percutaneous Coronary Intervention.

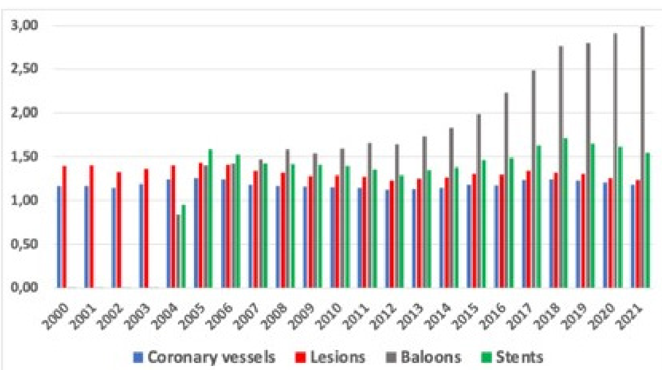


Table 1: Number of treated coronaries used balloons and stents and the validated result of first entry PCI procedure divided by sex. Statistics: $^{!)}$ One-way ANOVA; $^{*)}$ χ2-test. Abbreviations: PCI: Percutaneous Coronary Intervention.

First entry PCI procedures			
Procedure	**Male**	**Female**	***p-value***
Treated vessels	1.19	1.17	*<0.001$^{!)}$*
Treated lesions	1.33	1.29	*<0.001$^{!)}$*
Used balloons	2.01	1.90	*<0.001$^{!)}$*
Used stents	1.51	1.44	*<0.001$^{!)}$*
Result			
Successful	91.18%	90.41%	*0.021*)*
Failed	3.81%	4.13%	
Unknown	5.01%	5.45%	

PCI Complications

Complications of PCI were analyzed as in-lab and in-hospital, procedure- and vessel related (Table 2). Overall, there was a significant decline in both procedure-related (1.66% to 0.65%; P<0.0001) and vessel-bleeding related (2.37% to 1.31%; P<0.0001) complications, while in-lab fluctuated ending up with equal fraction from first to last 5-year period. Females had a substantially higher number of complications in all categories than males, being 40.3% in-lab, 31.3% in-hospital procedure-related, and 67.2% vascular-related complications.

Table 2: In-hospital complications and post procedural new PCI of first entry PCI procedures divided by sex. Statistics: $^{*)}$ χ2-test; $^{\#)}$ Independent t-test. Abbreviations: PCI: Percutaneous Coronary Intervention.

Complications after first entry PCI procedures			
Complication	**Male**	**Female**	***p-value***
In-lab all	1.77%	2.48%	*<0.0001$^{*)}$*
Procedure related discharge	0.93%	1.22%	*0.0001*
Vascular related discharge	1.83%	3.05%	*<0.0001$^{*)}$*
Mean PCI's during observation	1.35 ± 0.77	1.27 ± 0.67	<0.001$^{\#)}$
New PCI < 30-days	7.22%	5.58%	*<0.0001$^{*)}$*
New PCI < 1-year	12.12%	9.88%	*<0.0001$^{*)}$*
New PCI < 5-year	14.18%	11.80%	*<0.0001$^{*)}$*
New PCI < 10 year	19.49%	16.42%	*<0.0001$^{*)}$*

Mortality

The all-cause mortality after first entry PCI was higher in females at all time points (30 day, 1-, and 5 year) (Table 3). Related to indication there was no significant sex difference in 1-year mortality of AP and in 30-day and 5-year mortality in the MO group. Compared to the background population mortality, the data showed a considerable difference between actual and expected 1- and 5-year mortality, and a significantly higher expected mortality in females compared to males (Table 4). This is further demonstrated in Figure 5 which depicts actual, and population 10-year survival divided by sex with all indications (Figure 5A) and AP alone (Figure 5B). Overall males had better survival than the background population in all indications after six years and after three years when having AP alone. Females caught up to the background population survival at eight years in all indications and six years when having AP. These figures also demonstrated the higher female mortality in the study population as compared to males. Besides sex, the impact of other factors on all-cause mortality was also analyzed as shown in Table 5. The regression analyses identified several factors significantly associated with mortality at 30 days, 1 year, and 5 years. Pre-AMI, diabetes treatment, and elevated serum creatinine levels (>200 µmol/L) were all associated with increased mortality across all time points. On the other hand, the indications such as AP, n-STEMI, and STEMI, were each consistently associated with lower mortality. Female sex was also found to be associated with higher mortality, though with a slightly diminishing effect over time. Lastly, the period, divided into intervals, with the first interval spanning six years (2000-2006), followed by subsequent 5-year intervals, had a small, yet statistically significant association to 30 days and 1-year mortality; however, no significant effect was observed at 5 years.

Table 3: 30-day, 1-, and 5-year mortality of first entry PCI procedure divided by primary indication and sex. Statistics: 2-test.

30-day, 1-, and 5-year mortality after first entry PCI procedure									
Primary indication	**30-days**			**1-year**			**5-year**		
	Male	**Female**	***p-value***	**Male**	**Female**	***p-value***	**Male**	**Female**	***p-value***
Angina pectoris	0.59%	0.80%	*0.047*	2.97%	3.08%	*0.605*	12.97%	14.62%	*0.0007*
n-STEMI	1.92%	3.02%	*<0.0001*	5.25%	7.18%	*<0.0001*	16.15%	21.01%	*<0.0001*
STEMI	5.76%	8.66%	*<0.0001*	8.48%	12.92%	*<0.0001*	17.78%	24.91%	*<0.0001*
Mixed other	16.18%	17.93%	*0.204*	23.04%	26.22%	*0.043*	38.38%	40.95%	*0.244*
All	3.43%	4.54%	<0.0001	6.42%	8.24%	<0.0001	16.48%	20.47%	<0.0001

Abbreviations: n-STEMI: non-ST Elevation Myocardial Infarction; STEMI: ST Elevation Myocardial Infarction; PCI: Percutaneous Coronary Intervention.

Table 4: Actual and expected background population 1- and 5-year mortality. Statistics: Independent t-test.

Actual and estimated background mortality						
Sex	**1-year mortality**			**5-year mortality**		
	Actual	**Expected**	***p-value***	**Actual**	**Expected**	***p-value***
Male	6.42%	2.48%	*<0.0001*	16.48%	13.13%	<0.0001
Female	8.24%	2.59%	*<0.0001*	20.47%	13.76%	<0.0001
p-value	*<0.0001*	*<0.001*		*<0.0001*	*<0.001*	

Table 5: Logistic regression analyses of impact of available factors on 30-day, 1-, and 5-year mortality.

Impact of factors on 30-day, 1-, and 5-year mortality			
Factor	**30-days**	**1-year**	**5-years**
Pre-AMI	1.52 (1.28-1.81)	1.61 (1.44-1.79)	1.60 (1.49-1.71)
Treatment diabetes	1.56 (1.34-1.81)	1.68 (1.53-1.85)	1.72 (1.62-1.84)
s-Creatinine > 200 umol/L	5.71 (4.74-6.89)	6.07 (5.30-6.94)	6.63 (5.91-7.42)
Indication AP	0.07 (0.06-0.09)	0.16 (0.15-0.19)	0.29 0.27-0.32)
Indication n-ST	0.25 (0.21-0.30)	0.31 (0.28-0.35)	0.40 (0.37-0.44)
Indication ST	0.71 (0.59-0.84)	0.54 (0.48-0.61)	0.46 (0.42-0.51)
Period	1.03 (1.02-1.04)	1.02 (1.02-1.03)	1.00 (1.00-1.01)
Female sex	1.65 (1.47-1.87)	1.43 (1.33-1.55)	1.37 (1.30-1.44)

Abbreviations: AMI: Acute Myocardial Infarction; AP: Stable Angina Pectoris; n-STEMI: non-ST-Segment Myocardial Infarction; STEMI, ST: Elevation Myocardial Infarction.

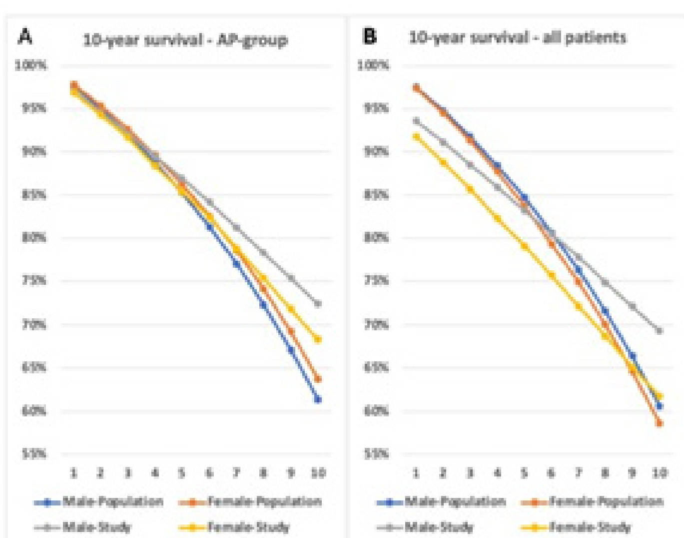


Figure 5: Actual and background population survival divided by sex in all first entry PCI with all indications (A) and all first entry with stable angina pectoris (B). Overall, male had better survival than population in all indications after 6 years and 3 years in AP. Females caught up in overall survival with all indications after 8 years and after 6 years in AP. Abbreviations: AP: Stable Angina Pectoris.

Delay to Treatment

The time from symptom onset to start of PCI treatment was significantly different between males and females presenting with STEMI, where females experienced a mean delay of 49 minutes in time symptoms debut to start of PCI treatment (433 ± 558 vs. 384 ± 512 minutes, P<0.0001, independent t-test).

Discussion

The important finding of this large, registry-based study of 84,335 patients was that females had a higher all-cause mortality at all measured time points following first entry PCI procedures for IHD. Compared to the general population, both males and females had significantly higher 1- and 5-year mortality, where mortality in females was higher than males and females caught up with the background population mortality later compared to males. Further, females had higher rates of complications in all scenarios. Numerous studies have demonstrated that females with ACS experience higher short and long-term mortality following PCI, and early interventional therapy does not provide significant benefit [10,12,19]. A review by Sambola et al. [12] concluded that females presenting with AP also had a higher rate of 30-day and 1-year mortality following PCI; however, the 5-year mortality was shown to be lower in females with AP [20]. These divergent outcomes in patients with AP were also present in the current study, as females had a significantly higher mortality following PCI for AP at 30 days and 5 years; however, there was no significant difference in mortality at 1 year following first entry PCI.

Despite clinical guidelines for ACS and AP not differentiating management and treatment based on sex, females have consistently been shown to experience delays in treatment and are less likely to receive guideline-directed therapy, including PCI [10,12,21,22]. For patients with STEMI, the delay from onset of symptoms to treatment is a known independent predictor of mortality [21], which could be a contributing factor to higher mortality in the findings of the current study, as females were found to have a significantly higher mean time from onset of symptoms to start of PCI. Apart from differences in management and treatment between males and females presenting with IHD, the higher mortality among females may further be explained by their older age and greater burden of comorbidity at the onset of IHD [8,10,12]. In the current study, females were older at time of their entry PCI throughout the whole observation period.

In the current study males received more new PCI procedures than females within 5 years following first entry PCI. In Kosmidou et al. [13], analyzing data from 21 randomized PCI trials, females had a significantly higher rate of target lesion surgical revascularization following PCI. The higher rate of target lesion revascularization in females may be explained by several factors, including anatomical differences. Females have smaller arteries, a lower success rate of coronary angiography, and a higher risk of periprocedural complications due to technical difficulties, even though they are less likely to have complex coronary artery disease [12,13,23,24]. The current study confirmed the higher incidence of complications among females. As males often constitute a larger proportion in cardiovascular research studies [10,21,24-26], the evidence-based treatment and equipment may benefit males more than females, explaining the higher rate of complications and the higher need for target lesion revascularization among females. The higher incidence of new PCI among males may be driven by disease progression in areas distant from previously treated segments, as the literature shows that males are more likely to have a prior PCI in the medical history when undergoing PCI treatment [8,11].

Females presenting with ACS are older and have higher comorbidity than males [24,25]. The mean age of females receiving first entry PCI was higher during the entire observation period in the current study. A possible protective effect of estrogen may explain the later onset of IHD in females after menopause [22,24], and the higher age is commonly linked to a clustering of concomitant risk factors and comorbidities [10]. Adjustment for age and other risk factors seems to attenuate the difference in mortality between sexes [23,25], suggesting that age and comorbidity play a crucial role in mortality perhaps more than sex itself. However, even after adjusting for age and comorbidity, females still experience disparities in treatment of ACS [12]. The delayed time from symptom onset to PCI treatment seen in females is influenced by multiple factors. Females with ACS have been found to be more likely to present with atypical symptoms, and they often attribute their symptoms to non-cardiac conditions and delay seeking medical attention, which delays the medical evaluation and may lead to misdiagnosis [10,24]. Typical troponin elevations and ECG changes are less likely to be present in females with ACS, which may also contribute to delayed diagnosis and treatment [24]. Symptoms before ACS onset among females are more likely dismissed as non-cardiac by medical staff [12], and consequently, females may develop a fear of embarrassment when they experience new or worsening symptoms. Several systematic reviews have demonstrated that after females are diagnosed with IHD, they are less likely to receive optimal medical therapy or be referred to cardiac rehabilitation [22,24], and they have lower compliance to rehabilitation programs once referred [27]. Participation in cardiac rehabilitation may be influenced by socioeconomic factors; however, this should not pose a significant issue in Denmark given the equality within the healthcare system. Thus, the sex-based disparities begin at the onset of symptoms and continue even at and after discharge, leaving several factors that could impact mortality among females following PCI for IHD.

Strengths and Limitations

A key strength of this study is its large, representative cohort from WDHR, which enhances generalizability and reliability of the findings. The long observational period of the study allows for a detailed analysis of trends in cardiovascular care over two decades, providing insights into real-world PCI practices. On the other hand, the observational and retrospective nature of the study introduces potential biases and confounding factors. The exclusion of patients with prior cardiac interventions before the initiation of WDHR may affect the mortality rates, and the lack of covariate adjustment increases the risk of confounding. The uniform treatment practices in Denmark reduce variability; however, the long study period still poses challenges due to possible changes in clinical procedures. Additionally, including the study population in the background population mortality data may slightly skew comparisons, though exclusion was not feasible in the current study.

Conclusion

Female sex is associated with higher mortality at 30 days, 1 year, and 5 years following first entry PCI for IHD compared to males. In comparison to the background population, both males and females have higher mortality at 1- and 5-years following PCI. However, both sexes catch up to the background population mortality, with females experiencing a delayed catch-up compared to males. Females consistently face treatment delays, less successful PCI-procedure results, and a higher rate of complications. These findings emphasize the need for further understanding of the diagnosis and treatment of IHD in females, particularly in identifying and addressing the factors that contribute to the persistent disparity in mortality between sexes.

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Supplement 1

CAG and PCI indications in WDHR. Primary entry is mostly CAG and indications inherited to PCI. All indications besides AP, STEMI, and n-STEMI are correlated to ICD10 codes and indications in the study changed accordingly.

CAG – PCI indications WDHR	Type	Study	All	First
STEMI – primary PCI	STEMI	STEMI	16,578	13,990
STEMI – acute PCI >12 hours	STEMI		981	895
STEMI – rescue PCI	STEMI		422	372
STEMI – facilitated primary PCI	STEMI		15	12
STEMI >12 hours – stabilised	STEMI		487	434
Primary PCI (old definition) – before 2010	STEMI		12,927	10,898
N-STEMI – not stabilised	N-STEMI/UAP	N-STEMI	2,405	1,661
N-STEMI – stabilised	N-STEMI/UAP		13,612	9,665
N-STEMI – before 2010	N-STEMI/UAP		14,656	11,390
UAP – not stabilised	N-STEMI/UAP		1,105	560
UAP – stabilised	N-STEMI/UAP		3,124	1,725
Stable Angina/documented ischemia	**AP**	**AP**	**47,763**	**26,647**
Arrythmia	Arrythmia	MO	1,780	1,068
Valve disease (incl. endocarditis)	Valve		461	344
Cardiomyopathy/undecided insufficiency	CHF		1,655	1,221
Post infarction VSD	Mixed		2	2
Undecided chest pain	Mixed		7	3
Other, before non-cardiac surgery	Mixed		5	3
Other	Mixed		813	522
Cardiac arrest	Shock		943	739
Cardiogenic shock	Shock		297	185
Control after PCI	Control	Controls – not first	176	0
Control after CABG	Control		973	0
Complementary PCI after PCI stable AP	Comtrol		117	0
Complication after CAG	Control		38	0
Complication after PCI	Control		145	0
Complication after CABG	Control		129	0
Complementary PCI after CABG	Control		159	0
Totals			**121,775**	**84,336**

Abbreveations: CAG: Coronary Angiography; PCI: Percutaneous Coronary Intervention; WDHR: Western Denmark Heart Registry; STEMI: ST-Elevation Myocardial Infarction; n-STEMI: non-ST- Elevation Myocardial Infarction; UAP: Unstable Angina Pectoris; AP: Stable Angina Pectoris; CHF: Chronic Heart Failure; VSD: Ventricular Septal Defect; MO: Mixed Others; CABG: Coronary Artery Bypass Grafting; ICD10: International Calssification Of Diseases, 10th revision.

Supplement 2

List of possible complications in WDHR.

In-lab complications
IABP
Mechanical assist
Assistance from anaesthesiologists
Arrythmias (types)
Temporary pacemaker
DC-conversion
Severe contrast reaction

In-hospital: after procedure/before discharge
Acute myocardial infarction
Dialysis-requiring renal failure
Stroke/central nerve damage
IABP
Acute PCI
Acute CABG

No flow/slow flow condition
Distal embolisation
Catheter induced dissection
Acute segment occlusion
Side-vessel occlusion
Respiratory insufficiency (ventilation needed)
Perforation/tamponade
New acute PCI
Acute CABG
Stroke during procedure
Vasopressor treatment (hypotension)
Coronary perforation
Cardiac arrest
Cardiogenic shock – procedure induced
Dead on table

In-hospital: Perioperative vessel issues
Haematoma – requiring longer in-hospital stay
Pseudoaneurism requiring treatment
Other major bleeding
Transfusion after bleeding
Vessel treatment – surgical intervention
Clossure device – surgical intervention
Arterial occlusion – surgical intervention
Other

Abbreviations: IABP: Intra-Aortic Balloon Pump; DC: Direct Cardioversion; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; PCI: Percutaneous Coronary Intervention; WDHR: Western Denmark Heart Registry.

Supplement 3

Background population survival divided by 5-year periods and sex. Survival curves based on 1-year mortality of the actual age (15-99 years); Data from Danish Statistics. https://www.dst.dk/en/