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Gender differences in acute congestive heart failure

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Summary

Background: Little is known about sex differences in baseline characteristics and outcomes in patients with acute congestive heart failure (CHF).

Methods and results: This prospective observational study evaluated gender differences among 217 consecutive patients (124 men and 93 women) presenting with acute CHF to the emergency department. The primary endpoint was all-cause mortality. Women were older, and had less pulmonary comorbidity, but more noticeable jugular venous distension, as well as higher diastolic blood pressure and troponin level at presentation. Among contributing causes of acute CHF, myocardial ischaemia and anaemia were more frequent in women. Adequate medical CHF therapy was initiated more rapidly in women. Initial resource utilisation, time to discharge, and mortality were similar. Important differences to the disadvantage of women were noted during long-term follow-up. Mean cumulative survival was 619 (95% CI, 533–705) days in women as compared with 669 (95% CI, 601–737; p = 0.0663) in men. However, after multivariate adjustment female sex was not an independent predictor of long-term mortality (hazard ratio 1.14, 95% CI, 0.68–1.90; p = 0.619). Total spending for treatment cost was $ 11,858 (95% CI, 8921–14794) in women compared to $ 15,965 (95% CI, 12 328–18 003; p = 0.115) in men after 1 year. Functional status was similar in women and men at 6 and 12 months.

Conclusions: The trend towards lower survival in women seems primarily related to higher age and other factors rather than gender itself. Female sex is not an independent predictor of long-term mortality in acute CHF.

Key words: gender; congestive heart failure; mortality

Introduction

The epidemic of cardiovascular disease in women has attained increasing recognition [1–3]. Congestive heart failure (CHF) is the most frequent cause of hospitalisation in women above 65 years of age and these hospitalisations contribute significantly to the enormous cost of the disease.

Previous work revealed important differences between men and women with chronic CHF [1–8]. Importantly, women with chronic CHF have been shown to have an overall better survival than men. In contrast, gender differences in acute CHF are poorly defined. A recent study has reported that women with acute CHF have less improvement in physical health status and perceived their quality of care to be lower [9]. Together with the 2001 Institute of Medicine report *Exploring the Biological Contributions to Human Health: Does Sex Matter?* [10] and our previous findings of different outcomes in women with coronary artery disease (CAD) [11, 12] and acute dyspnea [13], these findings mandate to scrutiny.

This study determined the influence of gender on baseline characteristics, treatment, use of cardiac procedures, mortality and total treatment cost in patients with acute CHF.

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Methods

Setting and study population

This study specifically evaluated gender differences in acute CHF in the B-type natriuretic peptide for Acute Shortness of Breath Evaluation (BASEL) study [14]. The BASEL study was a prospective, randomised, single-blind study conducted in the emergency department of the Uni-

versity hospital of Basel, Switzerland, from May 2001 to April 2002. The study was carried out according to the principles of the Declaration of Helsinki and approved by our local ethical committee. Written informed consent was obtained from all participating patients.

To be eligible for the study, a patient had to present with acute dyspnea as the primary complaint and no obvious traumatic cause of dyspnea. Patients with severe renal disease (serum creatinine >250 µmol/L), patients with cardiogenic shock and patients who requested an early transfer to another hospital were excluded. A total of 452 patients were enrolled. Among these, 217 patients had acute CHF. There were no other exclusions in the BASEL trial that may have excluded women or biased the enrolment of women into that trial.

Routine clinical assessment

All patients underwent an initial clinical assessment that in general included clinical history, physical examination, electrocardiography, pulse oximetry, blood tests including arterial blood gas analysis (when indicated) and chest x-ray. Echocardiography and pulmonary function tests were strongly recommended in the emergency department on an outpatient basis or in the hospital if the patient was admitted. The final discharge diagnosis of acute CHF was based on all available information available after discharge of the patient including response to therapy and autopsy data in those patients who died in the hospital. B-type natriuretic peptide (BNP) levels were available for the diagnosis in half of the patients [15].

Endpoints

All-cause mortality was the primary endpoint of this analysis. Time to therapy was defined as the time interval from presentation to the emergency department to the initiation of therapy specific for acute congestive heart failure. This included the administration of diuretics, morphine, nitroglycerin, or ACE-inhibitors. Total days in the hospital, total treatment cost, and all-cause mortality were prospectively assessed during follow-up. The calculation of total days in the hospital and total cost of hospitalisations comprised all hospitalisations after the initial presentation to the emergency department. Since ratios of costs to charges have not been defined for the majority of services and departments at our institution, nor that of other hospitals in the area, hospital charges were used as the most appropriate estimate of the true costs [16, 17]. To avoid an imbalance owing to differences in reimbursement or charges associated with different types or classes of insurance, charges were standardised according to the actual rates for patients with general insurance who were living in Basel. Total treatment cost did include total cost of hospitalisations and medication, but not regular out-patient visits to the private doctor, and was available up to 1-year follow-up.

Patients were contacted 6, 12 and 24 months after the initial presentation by telephone interview performed by a single research nurse. In addition, referring physicians were contacted in case of uncertainties regarding health status or hospitalisations. The administrative databases of the respective home towns were assessed to ascertain the vital status of those patients who could not be contacted by telephone. All information derived from contingent hospital readmission records or provided by the referring physician or by the outpatient clinic was reviewed and entered into the computer database.

Statistical analysis

This analysis concentrating on gender differences was pre-specified. The statistical analyses were performed using the SPSS/PC (version 13.0, SPSS Inc., Chicago. IL, USA) software package. Comparisons were made using the t-test, Mann-Whitney-U test, Fisher's exact test and chi-square test as appropriate. All hypothesis testing was two-tailed. Multivariate Cox regression analysis was performed to identify independent predictors of death. Together with sex, all baseline, demographic, clinical and laboratory variables potentially reflecting disease severity and comorbidity were entered in a univariate Cox regression analysis. Sex and all variables associated with long term mortality in univariate analysis ($P < 0.05$) were entered into the multivariate model. The final model included the following variables: Sex, age, CAD, COPD, arterial hypertension, systolic and diastolic blood pressure, albumin, haemoglobin, glomerular filtration rate, BNP and troponin.

Results

Baseline characteristics

Women and men differed in baseline characteristics, symptoms, signs, and laboratory tests (table 1). Women were older, whereas men more often had pulmonary comorbidity including chronic obstructive pulmonary disease. Accompanying symptoms more often included nausea in women. At presentation, diastolic blood pressure was significantly lower in women. Among signs, elevated jugular venous pressure was found more often in women, whereas cyanosis was detected more often in men. Importantly, the troponin level was higher in women as compared with men. Among contributing causes of acute CHF, myocardial ischaemia and anaemia were more frequent in women. Echocardiography revealed that left ventricular ejection fraction was significantly higher in women as compared to men.

Medication

The baseline medication was similar in women and men with the exception of a higher use of inhaled brochodilators and corticosteroids in men. Again, discharge medication was similar in women and men with appropriate use of diuretics, ACE-inhibitors, beta-blockers, and nitroglycerin. Interestingly, more men than women were prescribed amiodarone at discharge (table 2).

Initial outcome

The adequate therapy was initiated more rapidly in women. However, initial outcome including 30-day mortality, time to discharge and total treatment cost was not different between women and men (table 3). The use of cardiac procedures during the initial evaluation was identical in women and men (table 4).

Table 1
Baseline characteristics.

Variable	Women (N = 93)	Men (N = 124)
Age (years)	78 ± 13	72 ± 10
History		
Coronary artery disease	66 (71)	87 (70)
Systemic Hypertension	57 (61)	81 (65)
Diabetes mellitus	25 (27)	42 (34)
Chronic obstructive pulmonary disease	14 (15)	38 (31)
Asthma	2 (2)	2 (2)
Pulmonary embolism	5 (5)	1 (1)
Other pulmonary disease	1 (1)	14 (11)
Pneumonia	11 (12)	16 (13)
Any pulmonary disease	29 (31)	59 (48)
Depressive disorder	6 (7)	8 (7)
Stroke or peripheral vascular disease	27 (29)	33 (27)
Chronic kidney disease	37 (40)	48 (39)
Deep vein thrombosis	6 (7)	9 (7)
Symptoms		
Dyspnea*		
Slight hill	14 (15)	12 (10)
Level ground	45 (48)	77 (62)
At rest	32 (34)	35 (28)
Paroxysmal nocturnal dyspnea	42 (45)	60 (48)
Nocturia	33 (36)	53 (43)
Weight gain	16 (17)	22 (18)
Weight loss	11 (12)	10 (8)
Chest pain	41 (44)	44 (36)
Nausea	19 (20)	13 (11)
Coughing	37 (40)	56 (45)
Expectoration	21 (23)	38 (31)
Fever	10 (11)	22 (18)
Vital status		
Systolic blood pressure (mm Hg)	144 ± 28	149 ± 33
Diastolic blood pressure (mm Hg)	84 ± 20	91 ± 21
Heart rate (beats per minute)	97 ± 27	97 ± 26
Temperature (°C)	37.2 ± 1.0	37.2 ± 0.8
Signs		
Tachypnea (>20 per minute)	44 (47)	52 (42)
Elevated jugular venous pressure	27 (29)	22 (18)
Hepatojugular reflux	16 (17)	18 (15)
Rales	62 (67)	68 (55)
Wheezing	10 (11)	20 (16)
Hyper-resonant percussion	3 (3)	13 (11)
Dullness	8 (9)	16 (13)
Lower-extremity edema	49 (53)	52 (42)
Cyanosis	3 (3)	14 (11)
Laboratory tests		
Ejection fraction (%)#	44 ± 14	38 ± 17
Glomerular filtration rate (ml/min/1.73 m^2)	49 ± 29	57 ± 27
Serum albumin (g/l)	33 ± 4	33 ± 6
Troponin I (µg/l)	0.7 [0.3–4.4]	0.5 [0.3–1.3]
B-type natriuretic peptide (in pg/ml)	872 [439–1300]	786 [306–1300]
Contributing causes of acute episode		
Malcompliance with medication or diet	13 (14)	21 (17)
Infection/Inflammation†	29 (31)	35 (28)
Myocardial ischaemia/infarction‡	60 (65)	57 (46)
Atrial fibrillation	24 (26)	40 (32)
Pulmonary embolism	1 (1)	1 (1)
Anaemia?	45 (49)	34 (27)

Data are presented as mean ± SD, median [interquartile range], or number of patients (%).
* 2 women had dyspnea only walking a steep incline
\# Available in 148 patients
† Defined as history of fever and/or body temperature above 38.3 °C and/or C-reactive protein above 50 mg/l
‡ Defined as chest pain and/or elevated troponin I
? Defined as haemoglobin below 110 g/l in women and below 120 g/l in men

Table 2
Baseline and discharge medication

Variable	Women (N = 93)	Men (N = 124)
Baseline medication		
Diuretics	53 (57)	83 (67)
Beta-blocker	30 (32)	43 (35)
Nitroglycerin	23 (25)	21 (17)
ACE-inhibitor or AT-receptor-blocker	38 (41)	67 (54)
Digoxin	12 (13)	18 (15)
Amiodarone	9 (10)	17 (14)
Calcium-channel blockers	13 (14)	21 (17)
Aspirin	39 (42)	57 (46)
Anticoagulants	26 (28)	39 (32)
Inhaled bronchodilators	4 (4)	19 (15)
Inhaled corticosteroids	2 (2)	12 (10)
Oral corticosteroids	6 (7)	11 (9)
Discharge medication in survivors (n = 198)		
Diuretics	76 (87)	96 (87)
Beta-blocker	52 (60)	65 (59)
Nitroglycerin	33 (38)	37 (33)
ACE-inhibitor or AT-receptor-blocker	66 (76)	91 (82)
Digoxin	10 (12)	10 (9)
Amiodarone	9 (10)	28 (25)
Calcium-channel blockers	11 (13)	19 (17)
Aspirin	42 (48)	50 (45)
Anticoagulants	42 (48)	60 (54)
Inhaled bronchodilators	6 (7)	24 (22)
Inhaled corticosteroids	3 (4)	18 (16)
Oral corticosteroids	6 (7)	8 (7)

Data are presented as number of patients (%).

Table 3
Outcomes.

Variable	Women (N = 93)	Men (N = 124)
Initial outcome		
Time to therapy (min)	39 [16–136]	95 [24–182]
Hospital admission	85 (91)	106 (86)
Admission to intensive care	25 (27)	33 (27)
Time to discharge (days)	11 [5-19]	11 [5-19]
30-day mortality	11 (12)	11 (9)
Total treatment cost (initial)	5940 [3091–9414]	5711 [3653–8951]
Long-term outcome		
Total days in hospital		
at 90 days	14 [5–22]	14 [7–26]
at 180 days	14 [6–25]	16 [8–28]
at 360 days	15 [7–31]	20 [8–36]
Functional status at 180 days		
NYHA Class I	12 (17)	21 (22)
NYHA Class II	25 (36)	29 (30)
NYHA Class III	29 (42)	40 (41)
NYHA Class IV	3 (4)	7 (7)
Functional status at 360 days		
NYHA Class I	14 (23)	34 (39)
NYHA Class II	20 (33)	23 (26)
NYHA Class III	19 (31)	26 (30)
NYHA Class IV	8 (13)	5 (6)
Survival at 360 days	65.6 ± 4.9%	71.0 ± 4.1%
Survival at 720 days	49.0 ± 5.2%	62.7 ± 4.4%

Data are presented as median [interquartile range], number of patients (%), or cumulative survival ± standard error in %.

Table 4
Use of cardiac procedures

Variable	Women (N = 93)	Men (N = 124)
At initial presentation		
Echocardiography	56 (60)	77 (62)
Holter-ECG	4 (4)	10 (8)
Coronary angiography	12 (13)	19 (15)
Percutaneous coronary intervention	4 (4)	4 (3)
Coronary artery bypass grafting	4 (4)	6 (5)
Valvular surgery	3 (3)	2 (2)
Myocardial perfusion SPECT	5 (5)	8 (7)
Exercise ECG	3 (3)	9 (7)
Pacemaker implantation	1 (1)	0
ICD implantation	1 (1)	0
Heart transplantation	0	0
During follow-up		
Echocardiography	31 (33)	60 (48)
Holter-ECG	9 (10)	21 (17)
Coronary angiography	7 (8)	15 (12)
Percutaneous coronary intervention	9 (7)	2 (2)
Coronary artery bypass grafting	2 (2)	1 (1)
Valvular surgery	2 (2)	1 (1)
Myocardial perfusion SPECT	14 (15)	22 (18)
Exercise ECG	12 (13)	22 (18)
Pacemaker implantation	0	6 (5)
ICD implantation	1 (1)	8 (7)
Heart transplantation	1 (1)	0

Data are presented as number of patients (%).

Long-term follow-up

Clinical 360-day follow-up data were available for all 217 patients (100%). At 24 months, follow-up data were complete in 189 of 217 patients (87.1%). The median time interval to last patient contact or patient death was 603 days in women and 705 days in men. Mean length of follow-up in survivors was 783 days in women and 784 days in men. Long-term follow-up revealed a trend towards a lower survival rate in women. Mean cumulative survival was 619 (95% CI, 533–705) days in women as compared with 669 (95% CI, 601–737); p = 0.0663) in men. However, already after adjustment for age, survival was similar in men and women (figure 1). Importantly, after multivariate adjustment, female sex was not an independent predictor of long-term mortality (hazard ratio 1.14, 95% CI, 0.68–1.90; p = 0.619).

The use of cardiac procedures was different during follow-up in women than in men. Particularly, echocardiography and pacemaker implantation were performed significantly less often in women as compared to men. In addition, we observed a trend towards reduced medical spending in women. Mean treatment cost was $ 11,858 (95% CI, 8921–14794) in women as compared to $ 15,965 (95% CI, 12 328–18 003; p = 0.115) in men after 1 year. Functional status was similar in women and men at 6 and 12 months.

Discussion

This study revealed important gender differences in acute CHF. Most importantly, women showed a trend towards worse long-term survival compared to men that seemed primarily related to higher age and other factors rather than gender itself. Female sex was not an independent predictor of long-term mortality in acute CHF. Our findings require attention for two reasons. First, previous studies in patients with chronic CHF have in general reported a better survival in women compared

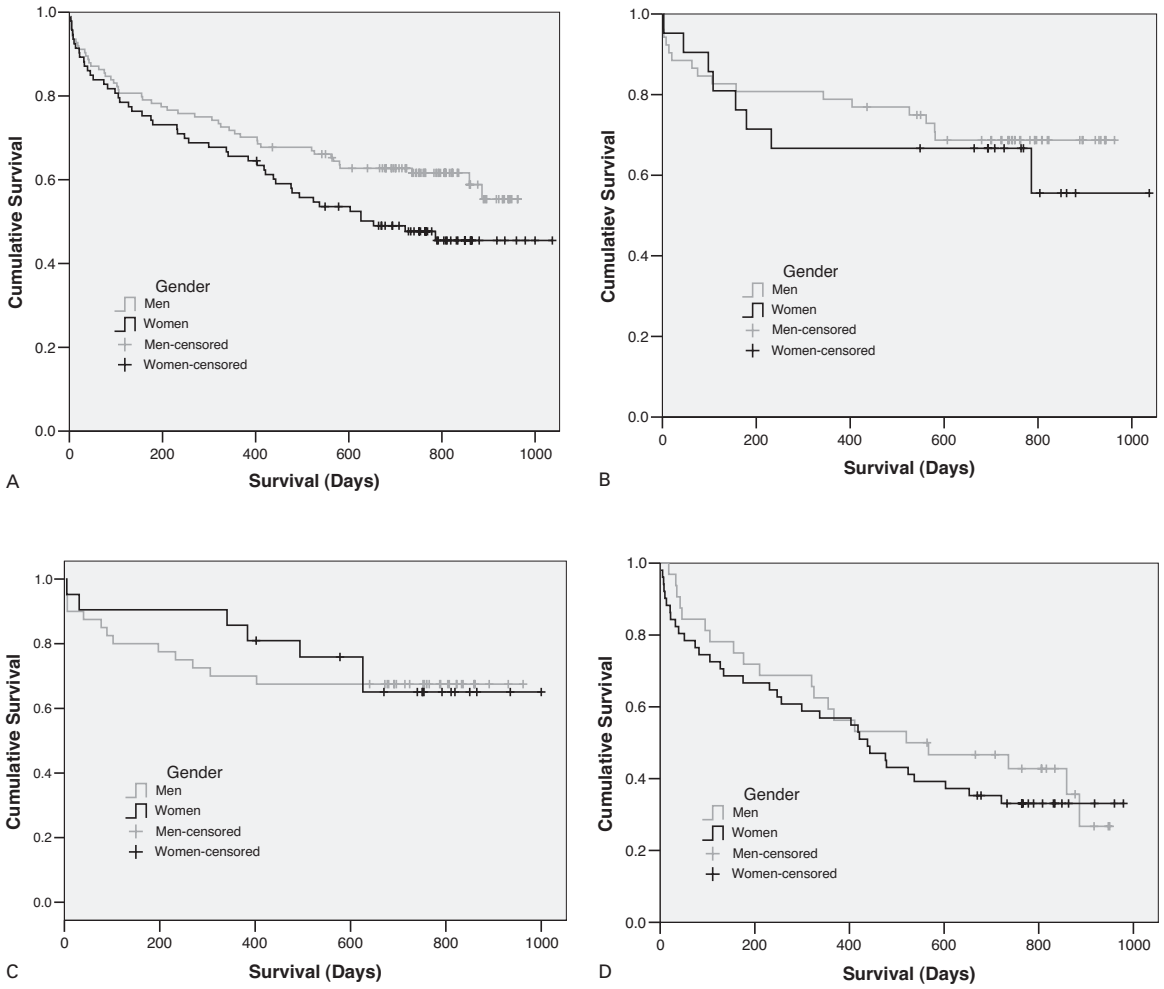

Figure 1

Cumulative survival in women and men with acute congestive heart failure:
A) unadjusted;
B–D) adjusted for age by displaying patients less than 70 years of age (B), 70–80 years of age (C), and more than 80 years of age (D) separately. After adjustment for age, survival is similar in men and women.
A) All patients
B) Age <70 years
C) Age 70–80 years
D) Age >80 years

to men [1–8]. Our finding of a worse survival in women with acute CHF exemplifies the distinct differences between chronic and acute CHF and call for further research in the setting of acute CHF. Second, the lower survival in women with acute CHF was predated by a lower use of cardiac procedures and a lower spending for total treatment cost within the months preceding death. Although female sex was not an independent predictor of long-term mortality in acute CHF, we cannot rule out that the different use of resources may have influenced outcome to the disadvantage of women.

The reasons for the lower survival rate in women with acute CHF are unknown. By its observational design, this study can only partly elucidate the causes of this finding and explain the discrepancy with the overall better survival of women enrolled in studies of chronic CHF [1–8, 18, 19]. Our data suggest six potential additive mechanisms. First, the benefit of female gender in chronic CHF seemed confined to patients with nonischaemic cardiomyopathy [1–8, 18, 19]. However, the prevalence of CAD was very high (70%!) and identical in women and men in this contemporary cohort. Second, given this predominance of CAD, the higher age of women as compared to men may well have been the critical factor responsible for the lower survival rate. Age has been the most consistent risk factor for death in studies of CAD [11, 20, 21]. In addition, age but not sex was found to be an independent predictor of death in multivariate analysis in our study. Third, elevated troponin levels reflect disease severity and have recently been shown to be powerful predictors of death also in patients with CHF [22]. Women with acute CHF had significantly higher troponin levels compared to men. Forth, elevated troponin levels in patients with non-ST-elevation acute coronary syndromes are accepted indications for coronary angiography and potential revascularisation, as invasive management significantly improves outcome in these patients [20, 21]. In patients with acute CHF, coronary angiography is generally recommended for patients in whom myocardial ischaemia is the presumed cause of acute decompensation and coronary revascularisation seems feasible in the individual patient [8, 23]. Given the predominance of CAD in this cohort and the higher troponin level in women compared to men, the low rate of coronary angiography and coronary revascularisation may well have been particularly detrimental in women. Of note, the rate of coronary angiography in this cohort of elderly patients with acute CHF was similar to that reported in comparable patients [24, 25]. Fifth, despite similar medication at presentation, significantly more men were discharged on amiodarone than women. This observation is supported by recent data from hospitalised CHF patients [26].

Amiodarone is the anti-arrhythmic agent of choice for most patients with CHF [8, 23]. Although it significantly reduces the risk of arrhythmic events including sudden cardiac death, its impact on all-cause mortality in CHF patients with contemporary co-medication including ACE-inhibitors and beta-blockers remains disputed [27]. A recent meta-analysis suggested an overall reduction of 13% in total mortality. Therefore, the lower use of amiodarone in women may contribute to their lower survival after acute CHF. Sixth, the more restrictive use of health care resources including echocardiography and pacemaker implantation in women during follow-up may have had some causal role in their lower survival rate [28].

Only some of the known sex differences in chronic CHF could be confirmed for the setting of acute CHF. This included the higher incidence of noticeable jugular venous distension. Differences in baseline characteristics including the lower incidence of pulmonary comorbidity and the higher incidence of elevated jugular venous pressure, arguably the most accurate sign for the diagnosis of congestive heart failure in the emergency department, may have been responsible for the more rapid initiation of the adequate therapy in women [8, 20]. Unfortunately, the more rapid initiation of therapy did not translate in improved medical or economic outcome. The lower use of inhaled bronchodilators and corticosteroids in women reflected their lower rate of pulmonary comorbidity.

Several limitations apply to this study. First, we prospectively decided to record all-cause mortality, since classification of death in clinical practice is inaccurate and challenging [29], and therefore may lead to questionable conclusions. Accordingly, cardiac or non-cardiac causes of death including sudden cardiac death were not specified in this study. Second, the confidence interval in the Cox model (HR 0.68–1.90) ruled out a large difference between the sexes but not a smaller but still relevant difference (eg a HR of 0.8 or 1.2). Therefore, additional larger studies are necessary to rule out smaller differences to the disadvantage of women.

In conclusion, the trend towards lower survival in women seems primarily related to higher age and other factors rather than gender itself. Female sex is not an independent predictor of long-term mortality in acute CHF.

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References

1 Adams KF, Dunlap SH, Sueta CA, et al. Relation between gender, etiology and survival in patients with symptomatic heart failure. J Am Coll Cardiol 1996;28:1781–8.
2 Adams KF, Sueta CA, Gheorghiade M, et al. Gender differences in survival in advanced heart failure: insights from the FIRST study. Circulation 1999;99:1816–21.
3 Simon T, Mary-Krause M, Funck-Brentano C. Sex differences in the prognosis of congestive heart failure: results from the cardiac insufficiency bisoprolol study (CIBIS II). Circulation 2001; 103:375–80.
4 Ghali JK, Piña IL, Gottlieb SS, Deedwania PC, Wikstrand JC. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in MERIT-HF. Circulation 2002; 105:1585–91.
5 Levy D, Kenchaiah S, Larson MG, et al. Long-term trends in the incidence of and survival with heart failure. N Engl J Med 2002;347:1397–402.
6 Rathore SS, Wang Y, Krumholz HM. Sex-based differences in the effect of digoxin for the treatment of heart failure. N Engl J Med 2002;347:1403–11.
7 DeMaria RD, Gavazzi A, Recalcati F, Baroldi G, DeVita C, Camerini F. Comparison of clinical findings in idiopathic dilated cardiomyopathy in women versus men. Am J Cardiol 1993;72:580–5.
8 Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Circulation 2001;104:2996–3007.
9 Chin MH, Goldman L. Gender differences in 1-year survival and quality of life among patients admitted with congestive heart failure. Med Care 1998;36:1033–46.
10 Wizeman TM, Pardue ML, eds for the Committee on Understanding the Biology of Sex and Gender Differences. Exploring the Biological Contributions to Human Health: Does Sex Matter? Washington DC: Board on Health Science Policy, National Acadamy Press; 2001.
11 Mueller C, Neumann FJ, Roskamm H, et al. Women do have an improved long-term outcome after Non-ST-Elevation acute coronary syndromes treated very early and predominately with percutaneous coronary intervention: a prospective study in 1450 consecutive. J Am Coll Cardiol 2002;40:245–50.
12 Mueller C, Buerkle G, Perruchoud AP, Buettner HJ. Female Sex and the Risk of Contrast Nephropathy after Percutaneous Coronary Intervention. Can J Cardiol 2004;20:505–10.
13 Mueller C, Laule-Kilian K, Scholer A, et al. Use of B-Type Natriuretic Peptide for the Management of Women with Dyspnea. Am J Cardiol 2004;94:1510–4.
14 Mueller C, Scholer A, Laule Kilian K, et al. Use of B-Type Natriuretic Peptide in the Evaluation and Management of Acute Dyspnea. N Engl J Med 2004;350:647–54.
15 Mueller C, Buser P. B-type natriuretic peptide (BNP): Can it improve our management of patients with congestive heart failure? Swiss Med Wkly 2002;132:618-22.
16 Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB, for the Panel on Cost-Effectiveness in Heath and Medicine. Recommendations of the panel on cost-effectiveness in health and medicine. JAMA 1996;276:1253–8.
17 Siegel JE, Weinstein MC, Russell LB, Gold MR, for the Panel on Cost-Effectiveness in Heath and Medicine. Recommendations for reporting cost-effectiveness analysis. JAMA 1996;276:1339–41.
18 Piña IL. A better survival for women with heart failure? It is not so simple… J Am Coll Cardiol 2003;42:2135–8.

19 Ghali JK, Krause-Steinrauf HJ, Adams KF, et al. gender differences in advances heart failure: insights from the BEST study. J Am Coll Cardiol 2003;42:2128–34.
20 Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). 2002. Available at: http://www.acc.org/clinical/guidelines/unstable/unstable.pdf.
21 The Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. Management of acute coronary syndromes in patients presenting without ST-segment elevation. Eur Heart J 2002;23:1809–40.
22 Perna ER, Macin SM, Canella JP, et al. Ongoing myocardial injury in stable severe heart failure: value of cardiac troponin T monitoring for high-risk patient identification. Circulation. 2004;110:2376–82.
23 Task Force for the Diagnosis and Treatment of Chronic heart Failure, European Society of Cardiology: W.J. Remme and K. Swedberg. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J 2001;22:1527–60.
24 Di Lenarda A, Scherillo M, Maggioni AP, et al. Current presentation and management of heart failure in cardiology and internal medicine hospital units: a tale of two worlds – the TEMISTOCLE study. Am Heart J 2003;146:E12.
25 Cleland JG, Swedberg K, Follath F, et al. Study Group on Diagnosis of the Working Group on Heart Failure of the European Society of Cardiology. The Euro Heart Failure survey programme – a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. Eur Heart J 2003;24:442–63.
26 Opasich C, De Feo S, Ambrosio GA, et al. The "real" woman with heart failure. Impact of sex on current in-hospital management of heart failure by cardiologists and internists. Eur J Heart Fail 2004;6:769–79.
27 Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomised trials. Lancet 1997;350:1417–24.
28 Indridason OS, Coffman CJ, Oddone EZ. Is specialty care associated with improved survival of patients with congestive heart failure? Am Heart J 2003;145:300–9.
29 Pratt CM, Greenway PS, Schoenfeld MH, et al. Exploration of the precision of classifying sudden cardiac death. Implications for the interpretation of clinical trials. Circulation 1996;93: 519–24.

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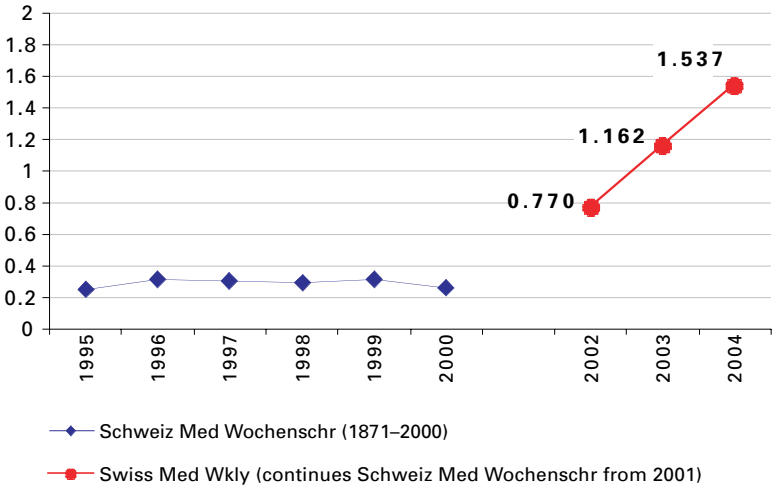

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