Does Gender Bias Compromise the Treatment of Women with Coronary Artery Disease?

Nina Butwell Radford, M.D.
University Of Texas Southwestern Medical Center
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Introduction

In 1991, the *New England Journal of Medicine* published two studies which suggested that there is gender bias in the management of coronary heart disease. Steingart and the Survival and Ventricular Enlargement Study (SAVE) investigators examined gender differences in the management of coronary artery disease in men and women enrolled in the Survival and Ventricular Enlargement Study from January 1987 to January 1990; they concluded that

> "physicians pursue a less aggressive management approach to coronary disease in women than in men, despite greater cardiac disability in women (1)."

Ayanian and Epstein examined over 80,000 discharge summaries of men and women admitted to hospitals in Maryland and Massachusetts during 1987 for treatment of coronary heart disease; they concluded that

> "...women who are hospitalized for coronary heart disease undergo few major diagnostic and therapeutic procedures than men (2)."

In her introduction to the accompanying editorial, Bernadine Healy wrote:

> "Being different from men has meant being second-class and less than equal for most of recorded time and throughout most of the world. It may therefore be sad, but not surprising, that women have all too often been treated less than equally in social relations, political endeavors, business, education, research, and health care (3)."

These dramatic studies are part of a rapidly growing literature which examines gender-related differences in the management of suspected or known coronary artery disease. By no means however, have these studies reached a consensus; in fact, many recent studies have reached contrary conclusions. The goal of this work is to carefully review this literature in an effort to answer the question: Does gender bias compromise the treatment of women with coronary artery disease?

This answer to this question is complex and requires three issues to be addressed:

- Are there, in fact, gender-related differences in the management of patients with coronary artery disease? Tangible differences in management of coronary artery disease can be measured by differences in utilization rates of procedures or therapies such as thrombolytic therapy, percutaneous transluminal angioplasty (PTCA) or coronary artery bypass grafting (CABG).

- If there are differences between men and women in utilization rates of cardiovascular procedures, do they arise because procedures are underutilized in one group or overutilized in the other? Although this issue is often difficult to sort out, the utilization rate of a procedure in either group can be compared to regional or national standards.
- Finally, if in fact, cardiovascular procedures are underutilized in one group, does that result in an adverse clinical outcome? This can be measured in terms of total mortality or subsequent non-fatal and fatal cardiovascular events.

Utilization of Thrombolytic Therapy

For the eligible patient who presents with acute myocardial infarction, treatment with thrombolytic therapy is the clearly the standard of care (4). Large, randomized, placebo controlled studies of thrombolysis in myocardial infarction demonstrate a significant reduction in early mortality in both men and women (5). In selected patients undergoing thrombolytic therapy and cardiac catheterization for acute myocardial infarction, there is also comparable benefit with regard to infarct-related artery patency and recovery of global and regional left ventricular function (6). Only recently, however, have investigators examined potential differences in utilization of thrombolytic therapy in women compared with men.

In order to fully explore gender-related differences in access to thrombolytic therapy, two important issues should be addressed. First, in eligible patients, are there gender differences in the use of thrombolytic therapy? Second, in ineligible patients, do exclusion criteria exclude one gender more than another?

<u>Gender Differences in the Use of Thrombolytic Therapy in Eligible Patients.</u> There is one study in the literature which directly examines this issue. Maynard and colleagues medical examined medical records from all patients with documented acute myocardial infarction who were admitted to 8 Seattle area hospitals (7). These 1078 patients were potential participants in the Western Washington Emergency Department tPA trial in which exclusion criteria included age >75 years, time from symptom onset >6 hours, non-diagnostic ekg changes and medical contraindications to thrombolysis. Sixteen percent of women were eligible to receive thrombolytic therapy compared with 25% of men. Of those 55 women who were eligible, only 35 (55%) received thrombolytic therapy compared to 78% of 166 eligible men. Information on why therapy was not given to these patients could not be determined from the records in 41% of these patients. The remaining records indicated that similar proportions of men and women either refused or were not offered tPA and that the mean age of these men and women were the same (62 years).

Indirectly, this issue can be examined by determining the percentage of women and men with comparable baseline characteristics who are eligible and actually receive thrombolytic therapy and comparing those numbers to the incidence of myocardial infarction in those men and women. So for example, if within a given age group and clinical status, the male to female ratio of thrombolytic therapy use is 10:1 and yet the male to female ratio of incidence of myocardial infarction is 3:1, eligible female patients have less access to thrombolytic therapy.

The Fibrinolytic Therapy Trialists' (FTT) Collaborative Group recently published a systematic overview of the effects of treatment on mortality and morbidity in various patient categories in those trials which randomized more than 1000 patients with suspected acute myocardial infarction between thrombolytic therapy and control (5). There were nine such trials:

GISSI-1: Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (8);
ISAM: Intravenous Streptokinase in Acute Myocardial Infarction (9);
AIMS: APSAC Intervention Mortality Study (10)
ISIS-2: Second International Study of Infarct Survival (11)
ASSET: Anglo-Scandinavian Study of Early Thrombolysis (12)
USIM: Urochinasi per via Sistemica nell'Infarto Miocardico (13)
ISIS-3: Third International Study of Infarct Survival (14)
EMERAS: Estudio Multicentrico Estreptoquinasa Republicas de America del Sur (15)
LATE: Late Assessment of Thrombolytic Efficacy (16).

Table 1. Design Characteristics of Trials that Randomized More than 1000 Patients to Thrombolysis or Control

Design feature	**Trial**								
	GISSI-1	ISAM	AIMS	ISIS-2	ASSET	USIM	ISIS-3*	EMERAS	LATE
Fibrinolytic regimen									
Dose	SK, 1 5 MU	SK, 1 5 MU	APSAC, 30 U	SK, 1 5 MU	tPA 100 mg	UK, 1 MU × 2	SK, 1 5 MU; tPA, 0 6 MU/kg; or APSAC, 30 U	SK, 1 5 MU	tPA, 100 mg
Duration	1 h	1 h	5 min	1 h	3 h	Bolus repeated at 60 min	1 h; 4 h; 3 min	1 h	3 h
Control	Open	Placebo	Placebo	Placebo	Placebo	Open	Open	Placebo	Placebo
Routine antiplatelet	No	Aspirin (single iv bolus)	No	Aspirin (50%)	No	No	Aspirin	Aspirin	Aspirin
Routine heparin	No	Yes, iv	Yes, iv at 6 h	No	Yes, iv	Yes, iv	50%, sc	No	64%, iv
Dose		5000 U + 800–1000 U/h	1000–1500 U/h		5000 U + 1000 U/h	10 000 U + 1000 U/h	12 500 U bd		5000 U (× 1 or 2) + 1000 U/h
Duration		72–96 h, then oral anticoagulant	Until effective oral anticoagulation		24 h	48 h	7 days		48 h
Recruitment period	Jan 1984–Jul 1985	Mar 1982–Mar 1985	Sept 1985–Oct 1987	Mar 1985–Dec 1987	Nov 1986–Feb 1988	Apr 1986–Sep 1988	Sept 1989–Jan 1991	Jan 1988–Jan 1991	Apr 1989–Feb 1992

*In ISIS-3, 37 000 patients considered to have a "certain" indication for fibrinolytic therapy were randomised between SK, tPA, and APSAC, and are not part of present report, which is restricted to those in whom indication was "uncertain". The latter were allocated half to fibrinolytic (1/3 SK, 1/3 tPA, 1/3 APSAC; all taken together in this report) and half to open control.

Table 1 describes the design characteristics of these nine trials. Thrombolytic agents studied included streptokinase (SK), anistreplase or anisoylated plasminogen streptokinase activator complex (APSAC), tissue plasminogen activator (tPA) and urokinase (UK) with a variety of antiplatelet and anticoagulant regimens (5). The recruitment period of these trials spans a decade from 1982 to 1992. Table 2 describes the percentage of patients who had specific characteristics in these trials including EKG features, time to presentation, age, gender and presence of previous myocardial infarction, hypertension or diabetes (5). In all the trials, 24% of the participants were female. Does this ratio suggest an under-representation of women or is this appropriate given the difference in incidence of coronary heart disease in men and women?

Table 2. Patient Characteristics of Trials that Randomized More than 1000 Patients to Thrombolysis or Control

Presentation features	Trial (and number randomised)									All trials (n = 58 600)	
	GISSI-1 (n = 11 802)	ISAM (n = 1741)	AIMS (n = 1254)	ISIS-2 (n = 17 187)	ASSET (n = 5012)	USIM (n = 2201)	ISIS-3 (n = 9158)	EMERAS (n = 4534)	LATE (n = 5711)	No	%
Entry ECG											
BBB	1	5	—	4		—	8	6	2	2146	4
ST elev, anterior	37	44	35	22		42	16	33		13 229	23
ST elev, inferior	34	48	47	25	82	47	11	27	55	16 203	28
ST elev, other	20	2	18	14		-	3	16		10 187	17
ST depression	4	—	1	7		—	19	4	12	4237	7
Other abnormality	5	1	—	25		10	25	12	30	9691	17
Normal	0	—	—	2	18	—	17	2	0	2907	5
Hours from onset											
0–1	11	9	3	4	6	24	3	1	—	3348	6
2–3	41	51	43	26	49	65	22	2	—	16 632	28
4–6	31	40	54	33	44	12	29	12	2	16 493	28
7–12	17	—	—	23	—	—	28	46	38	12 788	22
13–24	—	—	—	14	—	—	18	40	60	9339	16
Age (yr)											
< 55	29	35	39	29	27	30	22	32	22	16 238	28
55–64	35	34	43	35	36	36	29	32	30	19 608	33
65–74	24	30	18	28	37	24	32	26	35	17 000	29
75 +	11	1	—	8	—	10	17	11	13	5754	10
Sex											
Male	80	82	82	77	77	82	69	77	72	44 745	76
Female	20	18	18	23	23	18	31	23	28	13 855	24
SBP (mm Hg)											
< 100	5	5	5	4	4	5	3	6	3	2466	4
100–149	60	60	66	63	56	62	60	70	62	36 052	62
150–174	29	27	24	27	29	26	28	20	28	15 907	27
175 +	6	8	5	7	11	7	9	4	8	4175	7
Heart rate (/min)											
< 80		52	55	69	58		50	46	50	25 865	58
80–99		34	35	19	30		33	35	35	12 518	28
100 +		14	10	12	12		16	19	15	6214	14
Prior MI											
Yes	16	12	17	17	27		32	12	22	11 329	20
No	84	88	83	83	73		68	88	78	45 070	80
Diabetes											
Yes		12		7	7		13	17	13	4529	10
No		88		93	93		87	83	87	38 814	90

— = none; blank = not recorded in trial.

Arriving at an answer to this question requires several generous assumptions. First, these patients were randomized in many countries where rates of death from ischemic heart disease in men and women vary (17). However, in representative countries such as the United Kingdom, the United States, Italy, Spain and the Scandinavian countries the female to male ratio of death rates is fairly similar ranging from 0.40 to 0.51 (17). This ratio also varies a great deal with age because of the increased prevalence of coronary disease in women after menopause.

Figure 1 shows the 2 year rate per 1000 incidence of myocardial infarction in a 26-year follow-up of the Framingham population (18). In the age ranges of 45-54, 55-64, 65-74 and 75-84, the incidence of MI in women and men was 1.4 and 10.7 , 5.0 and 18.2, 10.2 and 23.8, and 17.9 and 33.7 respectively (18). So that over a 2 year period in a population of 1000, the percentage of patients with MI in each age group who were female would be 12%, 22%, 30% and 33% respectively. Let's assume that is also true in other countries.

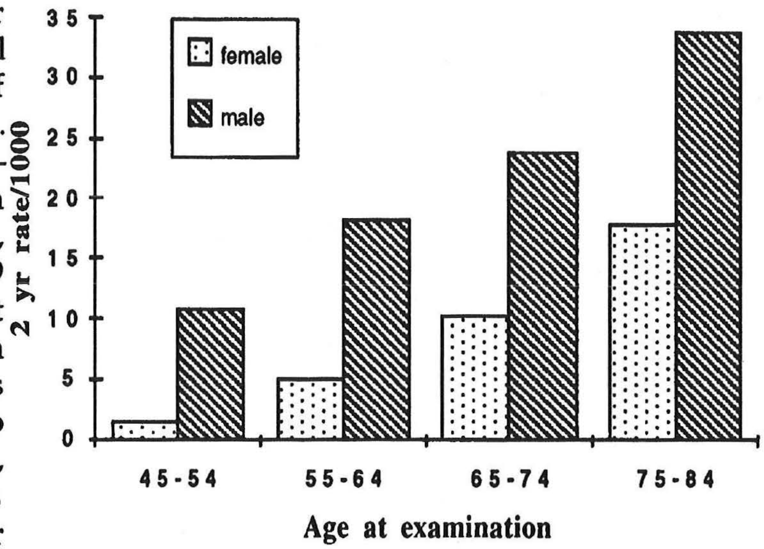

Figure 1. Incidence of Myocardial Infarction by Age and Gender

This effect of age on the incidence of myocardial infarction in men and women is reflected in these summary data from the nine thrombolysis trials where 44% of patients aged 75 or over were women compared with only 12% of those under 55 (5). So then, in studies with the majority of patients under the age of 64, such as AIMS, we might expect 12-22% of the population to be women (10). Whereas, in studies such as ISIS-3 and LATE where almost half of their patients are age 65 or older, the number of women represented would be greater (14,16). If the Framingham incidence rates are applied to each age range in this summary data (although this application is fraught with potential confounders), the projected number of women participants would be 13,377 out of 58,600 trial participants or 23%. These values are not markedly different from the actual rate of 24% in these trials.

In summary then, in patients who met inclusion criteria in these thrombolytic trials, the percentage of female patients within each age group appears to reasonably reflect the gender specific incidence of myocardial infarction (having made several very broad assumptions). So, in contrast to the findings of Maynard et al. (7), in these trials, there does not appear to be gender bias in the selecting patients for thrombolytic therapy in randomized trials who meet inclusion criteria.

What might account for these contrary findings? The assumptions made to analyze the pooled data may be spurious and I have underestimated the incidence of myocardial infarction in women in different countries. The data from Maynard et al. reflects the experience of a single county in 1987 and 1988. Results had been published from GISSI-1 and ISAM which showed that increased mortality from stroke offset gains in survival from myocardial reperfusion in older patients. These results, in addition to personal experience, may have biased physicians to withhold treatment from certain patients who were technically eligible but perhaps thought to be high risk.

Recent studies of pooled data have reported that thrombolytic therapy is used in only a minority of patients with acute myocardial infarction who are eligible (19,20). Clearly more information is needed to specifically address gender differences in the use of thrombolytic therapy in eligible patients. If in fact, women who are eligible for thrombolytic therapy are less likely to receive it compared to eligible men, then gender bias does compromise their treatment.

Influence of Gender on Exclusion from Thrombolytic Therapy. What is known about the characteristics of the patients who are excluded from thrombolytic treatment protocols. Is there gender bias in the exclusion criteria? For the nine trials in the meta-analysis, there is little published information on the relationship between gender and exclusion from randomization. In GISSI-1 which had no age limitations, 20% of patients randomized were women and 28% of patients excluded from randomization were women (8). In the USIM trial which also had no age limitations, those percentages were 18% and 15% respectively (13).

Since there is little direct data, is there an indirect means of addressing this issue of gender and exclusion from thrombolytic therapy? Yes, if we examine other distinguishing features of women with infarction. Women with acute myocardial infarction are much more likely to be older, are more likely to present later after onset of symptoms and are more likely to have co-morbidities such as recent stroke or uncontrolled hypertension (21-25). These are precisely the reasons for which patients are excluded from treatment with thrombolytic therapy.

The relations among age, gender and exclusion form thrombolysis are illustrated by results published by Weaver and colleagues who examined the effect of age on use of thrombolytic therapy and mortality in 3,256 patients who and had a discharge diagnosis of acute myocardial infarction (and were enrolled in the Myocardial Infarction, Triage and Intervention (MITI) Project) (25). Figure 2 shows the age and gender distribution of these 3256 patients. Thirty-nine percent of the patients under the age of 55 received thrombolysis in contrast to only 5% in patients over the age of 75.

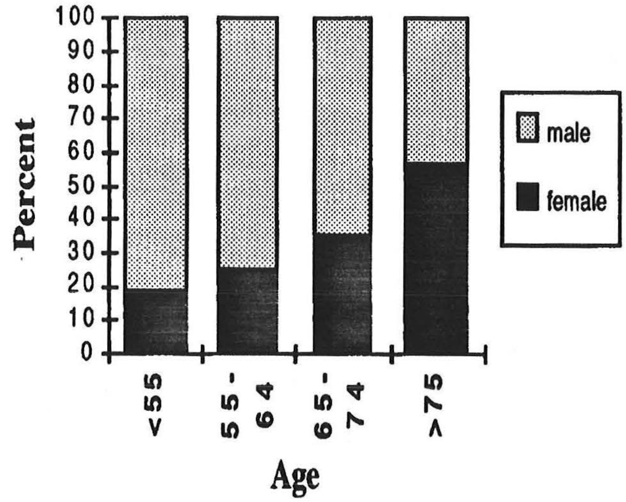

Figure 2. Age and gender distribution in 3256 patients with AMI from the MITI Registry.

Advancing age is a significant cause of exclusion from thrombolytic therapy. In the nine trials in the meta-analysis, two studies (AIMS and ASSET) excluded patients over the age of 75 while in the remainder, patients over the age of 75 made up only 10% of the study population (10,12). In GISSI-1, for example, twice as many patients over the age of 75 were excluded as included for randomization (8). Table 3 summarizes eligibility for and exclusions from a variety of trials of thrombolysis from which these data are readily available (9,7,12,26-28). Less than one-third of screened patients were eligible to receive thrombolysis. One third of patients were excluded because of older age.

Only one study listed in Table 3 examined the relative proportions of men and women excluded on the basis of any indication. Maynard et al., using the Seattle area database of almost 1100 patients described earlier, reported that the women were more often excluded from eligibility on the basis of age (39% vs 19%, women vs men, respectively) (7).

Table 3. Delay in Presentation and Age as Exclusion Criteria for Thrombolytic Therapy

Study(ref)	Screened	%Eligible	%Too Late	%Too Old
ASSET(12)	13318	33	32	17
ISAM(9)	7715	23	37	20
Cragg(26)	1471	16	41	27
Maynard(7)	1078	22	18	26
Murray (28)	403	14	39	10
Jagger(27)	131	51	13	7
#weighted mean	**24116**	**28#**	**34#**	**19#**

For a variety of reasons, most commonly advancing age, women are more likely to be considered ineligible for thrombolytic therapy. Does ineligibility from thrombolysis in the setting of an acute myocardial infarction portend a poor prognosis and more importantly, would inclusion of ineligible patients enhance survival?

Ineligibility for Thrombolysis and Outcome. Cragg et al. evaluated the outcome of patients with acute myocardial infarction who were ineligible for thrombolytic therapy (26). Of 1471 patients with acute myocardial infarction, 230 (16%) received standard protocol thrombolytic therapy and 114 (78%) did not receive reperfusion therapy (the remaining 6% received nonprotocol thrombolytic therapy or primary PTCA or both).

Figure 3 shows the percentage of study sample (1471 patients) in the treated group and in subgroups of the excluded patients. Of the protocol treated patients, 20% were women. Of the excluded patients, 40% were women. Interestingly, if enrollment criteria were further expanded to include all patients irrespective of age and within 12 hours of chest pain onset, a maximum of 27% of all patients would be eligible for thrombolytic therapy.

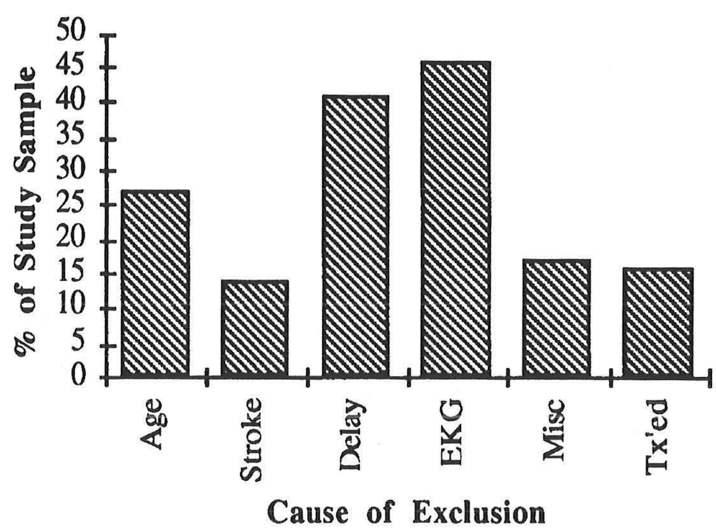

Figure 3. Exclusion Subgroups

Figure 4 shows the in-hospital mortality rates for the study group and each of the exclusion subgroups. It is not surprising that the mortality of the excluded subgroups is higher than the treated group given that they were denied a mortality enhancing treatment and they have unfavorable clinical characteristics.

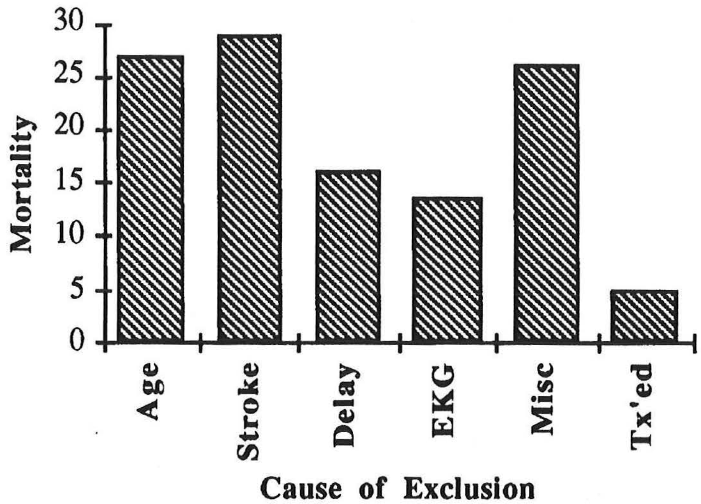

Figure 4. Mortality and Causes of Exclusion from Thrombolysis

The important question is whether reperfusion therapy in these excluded subgroups would improve mortality. Because the age exclusion is particularly relevant to women, it will be the focus of this discussion. Do we compromise the survival of the elderly patient with myocardial infarction by excluding them from treatment with thrombolysis? Older patients are excluded from thrombolytic therapy trials primarily because of the potential for increased hemorrhage. The decreased mortality from myocardial infarction may be offset by increased mortality from intracerebral hemorrhage. In the pooled data from the Fibrinolytic Therapy Trialists' Collaborative Group (5), patients over the age of 75 made up only 10% of the study population but in absolute numbers this represents 5754 patients. Table 4 and Table 5 list the absolute differences in mortality and stroke respectively during days 0-35 subdivided by presentation features (5).

The early excess of death on days 0-1 that is associated with thrombolytic therapy increased with age, but so too did the benefits during days 2-35. The early excess of death is related to a significant excess of strokes associated with thrombolytic therapy which tended to increase with age. These opposing effects offset each other in patients over the age of 75 so that the benefit/1000 was not statistically significant.

Table 4. Absolute Differences in Mortality during Days 0-35 Subdivided by Presentation Features (from ref 5)

Presentation features	Patients		Deaths during days 0–1			Deaths during days 2–35			Deaths during days 0–35		
	Fibrinolytic	Control	Fibrinolytic	Control	Benefit per 1000 (SD)	Fibrinolytic	Control	Benefit per 1000 (SD)	Fibrinolytic	Control	Benefit per 1000 (SD)
Entry ECG											
BBB	1007	1025	82	96	12 (13)	106	146	43 (16)	188 (18·7%)	242 (23·6%)	49 (18)
ST elev, anterior	6587	6642	413	446	4 (4)	455	674	35 (5)	868 (13·2%)	1120 (16·9%)	37 (6)
ST elev, inferior	6556	6484	173	126	−7 (3)	320	416	15 (4)	493 (7·5%)	542 (8·4%)	8 (5)
ST elev, other	3053	3024	138	120	−6 (6)	186	284	34 (7)	324 (10·6%)	404 (13·4%)	27 (8)
ST depression	1779	1784	108	69	−11 (7)	163	158	−4 (9)	271 (15·2%)	247 (13·8%)	−14 (11)
Other abnormality	3988	3963	67	67	−5 (3)	122	163	11 (5)	209 (5·2%)	230 (5·8%)	6 (6)
Normal	995	990	12	[illegible]	−7 (4)	18	18	[illegible] (2)	30 (3·0%)	23 (2·3%)	−7 (7)
Hours from onset											
0–1	1678	1670	78	53	3 (8)	81	134	34 (9)	159 (9·5%)	217 (13·0%)	35 (11)
2–3	8297	8315	302	339	4 (3)	381	550	21 (4)	683 (8·2%)	889 (10·7%)	25 (5)
4–6	8294	8195	325	307	−2 (3)	477	638	21 (4)	802 (9·7%)	945 (11·5%)	19 (5)
7–12	6478	6404	298	257	−6 (4)	421	556	22 (5)	719 (11·1%)	813 (12·7%)	16 (6)
13–24	4568	4701	167	117	−12 (4)	290	376	16 (6)	457 (10·0%)	493 (10·5%)	5 (6)
Age (yr)											
<55	8082	8158	113	137	3 (2)	165	236	9 (2)	278 (3·4%)	373 (4·6%)	11 (3)
55–64	9911	9678	291	288	0 (3)	418	576	18 (3)	709 (7·2%)	864 (8·9%)	18 (4)
65–74	8487	8496	459	434	−3 (3)	685	938	31 (5)	1144 (13·5%)	1372 (16·1%)	27 (5)
75+	2835	2953	307	244	−26 (8)	382	504	35 (11)	689 (24·3%)	748 (25·3%)	10 (13)
Sex											
Male	22 353	22 412	732	721	−1 (2)	1103	1537	20 (2)	1835 (8·2%)	2258 (10·1%)	19 (3)
Female	6962	6873	438	382	−7 (4)	547	717	27 (5)	985 (14·1%)	1099 (16·0%)	18 (6)
SBP (mm Hg)											
<100	1263	1182	237	261	33 (16)	128	154	42 (16)	365 (28·9%)	415 (35·1%)	62 (18)
100–149	17 979	18 063	699	648	−3 (2)	1032	1433	23 (3)	1731 (9·6%)	2081 (11·5%)	19 (3)
150–174	7907	8005	171	163	−1 (2)	398	531	16 (4)	569 (7·2%)	694 (8·7%)	15 (4)
175+	2166	2035	63	31	−14 (5)	92	136	24 (7)	155 (7·2%)	167 (8·2%)	11 (8)
Heart rate (/min)											
<80	12 922	12 965	358	311	−4 (2)	568	786	17 (3)	926 (7·2%)	1097 (8·5%)	13 (3)
80–99	6268	6221	235	204	−5 (3)	344	502	26 (5)	579 (9·2%)	706 (11·3%)	21 (5)
100+	3095	3126	228	238	2 (6)	309	408	33 (9)	537 (17·4%)	646 (20·7%)	33 (10)
Prior MI											
Yes	5719	5577	287	263	−3 (4)	430	521	19 (5)	717 (12·5%)	784 (14·1%)	15 (6)
No	22 468	22 635	842	794	−2 (2)	1151	1673	23 (2)	1993 (8·9%)	2467 (10·9%)	20 (3)
Diabetes											
Yes	2236	2260	117	121	1 (6)	186	270	38 (10)	303 (13·6%)	391 (17·3%)	37 (11)
No	19 423	19 424	693	607	−4 (2)	1004	1374	19 (3)	1697 (8·7%)	1981 (10·2%)	15 (3)
All patients	29 315	29 285	1170 (4·0%)	1103 (3·8%)	−2 (2)	1650 (5·9%)	2254 (8·0%)	21 (2)	2820 (9·6%)	3357 (11·5%)	18 (3)

Results for "uncertain" indication arm of ISIS-3 (see footnote to table 1), which have not been published separately, were included in all subdivisions: in summary, for patients with ST elevation or BBB in ISIS-3, the results were 84/782 fibrinolytic vs 97/760 control for delay 0–6 h, 69/586 vs 86/597 for 7–12 h, and 68/445 vs 59/431 for 13–24 h; and for patients with other ECG changes they were 104/1713 vs 65/1682 for 0–6 h, 47/694 vs 42/674 for 7–12 h, and 28/381 vs 26/413 for 13–24 h.

Certain of the presentation features were not recorded in GISSI-1 (heart rate and diabetes), AIMS (diabetes), USIM (heart rate, prior MI, diabetes), and ASSET and LATE (these particular ECG categories), so data from these trials could not be included in subdivisions by these features. Where the value of some presentation feature was missing for a particular patient then that patient was excluded from subdivision of that feature.

Table 5. Stokes during Days 0-35 Subdivided by Presentation Features (from ref 5)

Presentation features	Patients		Strokes during days 0–1			Strokes during days 2–35			Strokes during days 0–35		
	Fibrinolytic	Control	Fibrinolytic	Control	Excess per 1000 (SD)	Fibrinolytic	Control	Excess per 1000 (SD)	Fibrinolytic	Control	Excess per 1000 (SD)
Entry ECG											
BBB	1007	1025	13	3	10·0 (3·9)	8	8	0·1 (2·0)	21 (2·1%)	11 (1·1%)	10·1 (5·5)
ST elev, anterior	6091	6203	29	7	3·6 (1·0)	34	52	-2·8 (1·5)	63 (1·0%)	59 (1·0%)	0·8 (1·8)
ST elev, inferior	6015	5984	29	8	3·5 (1·0)	32	29	0·5 (1·3)	61 (1·0%)	37 (0·6%)	4·0 (1·7)
ST elev, other	3053	3024	17	6	3·6 (1·6)	14	24	-3·4 (2·0)	31 (1·0%)	30 (1·0%)	0·2 (3·4)
ST depression	1779	1784	14	3	6·2 (2·3)	4	6	-1·1 (1·7)	18 (1·0%)	9 (0·5%)	5·1 (2·9)
Other abnormality	3897	3829	19	8	2·8 (1·3)	14	9	1·2 (1·3)	33 (0·8%)	17 (0·4%)	4·0 (1·8)
Normal	995	990	10	0	10·1 (3·2)	2	0	2·0 (1·4)	12 (1·2%)	0 (0·0%)	12·1 (3·5)
Hours from onset											
0–1	1252	1265	2	2	0·0 (3·5)	3	7	-3·1 (2·5)	5 (0·4%)	9 (0·7%)	-3·1 (2·9)
2–3	6354	6378	32	[illegible]	3·9 (1·0)	25	34	-1·4 (1·2)	57 (0·9%)	41 (0·6%)	2·5 (1·5)
4–6	6973	6924	45	10	5·0 (1·1)	37	48	-1·6 (1·3)	82 (1·2%)	58 (0·8%)	3·4 (1·7)
7–12	5333	5285	32	12	3·7 (1·2)	28	25	0·5 (1·4)	60 (1·1%)	37 (0·7%)	4·2 (1·8)
13–24	2925	2987	20	4	5·5 (1·6)	15	14	0·4 (1·8)	35 (1·2%)	18 (0·6%)	5·9 (2·4)
Age (yr)											
< 55	6441	6517	8	4	0·6 (0·5)	10	25	-2·3 (0·9)	18 (0·3%)	29 (0·4%)	-1·7 (1·1)
55–64	7727	7582	50	8	5·4 (1·0)	33	35	-0·3 (1·0)	83 (1·1%)	43 (0·6%)	5·1 (1·5)
65–74	6310	6313	46	20	4·1 (1·3)	45	41	0·6 (1·4)	91 (1·4%)	61 (1·0%)	4·8 (1·9)
75 +	2359	2427	27	3	10·2 (2·3)	20	27	-2·6 (2·9)	47 (2·0%)	30 (1·2%)	7·6 (3·7)
Sex											
Male	17 434	17 514	92	24	3·9 (0·6)	73	91	-1·0 (0·7)	165 (0·9%)	115 (0·7%)	2·9 (1·0)
Female	5403	5325	39	11	5·2 (1·3)	35	37	-0·5 (1·8)	74 (1·4%)	48 (0·9%)	4·7 (2·0)
SBP (mm Hg)											
< 100	1036	950	10	1	8·6 (3·4)	3	8	-5·5 (3·3)	13 (1·3%)	9 (0·9%)	3·1 (5·0)
100–149	14 107	14 257	74	27	3·4 (0·7)	64	72	-0·5 (0·8)	138 (1·0%)	99 (0·7%)	2·8 (1·1)
150–174	6132	6162	31	6	4·1 (1·0)	35	38	-0·5 (1·4)	66 (1·1%)	44 (0·7%)	3·6 (1·7)
175 +	1562	1470	16	1	9·6 (2·7)	6	10	-3·0 (2·7)	22 (1·4%)	11 (0·7%)	6·6 (3·7)
Heart rate (/min)											
<80	10 045	10 056	61	12	4·9 (0·8)	42	49	-0·7 (1·0)	103 (1·0%)	61 (0·6%)	4·2 (1·3)
80–99	4515	4501	31	11	4·4 (1·4)	25	27	-0·5 (1·7)	56 (1·2%)	38 (0·8%)	4·0 (2·1)
100 +	2375	2382	15	4	4·6 (1·8)	16	21	-2·1 (2·6)	31 (1·3%)	25 (1·0%)	2·6 (3·0)
Prior MI											
Yes	4413	4309	22	4	4·1 (1·2)	36	17	4·2 (1·7)	58 (1·3%)	21 (0·5%)	8·3 (2·0)
No	18 424	18 530	109	31	4·2 (0·6)	72	111	-2·1 (0·7)	181 (1·0%)	142 (0·8%)	2·2 (1·0)
Diabetes											
Yes	1706	1730	17	7	5·9 (2·8)	15	16	-0·5 (4·0)	32 (1·9%)	23 (1·3%)	5·5 (4·2)
No	14 603	14 581	85	20	4·4 (0·7)	57	71	-1·0 (0·8)	142 (1·0%)	91 (0·6%)	3·5 (1·0)
All patients	29 315	29 285	166 (0·6%)	39 (0·1%)	4·3 (0·5)	170 (0·6%)	183 (0·6%)	-0·4 (0·7)	340 (1·2%)	224 (0·8%)	3·9 (0·8)

Certain of the presentation features were not recorded in GISSI-1 (heart rate and diabetes) and AIMS (diabetes), so data from these trials could not be included in subdivisions by these features. ASSET, LATE and USIM data were not available for any of these subdivisions.

Even with this data, the authors conclude: "The data do not provide evidence for withholding fibrinolytic therapy from patients on the basis of age." Other authors have strongly expressed similar views. Peter Sleight concludes that "the case for thrombolytic therapy in otherwise fit older patients with acute MI is incontrovertible. Why, then do we discriminate against the older patient in underusing a treatment that is highly cost effective, both in public health and economic evaluation?" (29). Grines and DeMaria state that "age should not be considered an absolute contraindication because the lifesaving potential of thrombolytic therapy in the elderly may be two to three times that of the overall group of patients with myocardial infarction (19)." Table 6 is taken from their review.

Table 6. Mortality: Effect of Age in Previous Trials

Study	Age	% Tx	% Ctrl	Lives Saved*	p value
GISSI-1	<75	8.7	10.6	1.9	0.001
	>75	28.9	33.1	4.2	0.11
ISAM	<70	5.1	6.6	1.5	0.21
	70-75	13.0	9.6	-3.4	0.37
ISIS-2	<70	7.0	9.6	2.6	0.0001
	>70	18.2	21.6	3.4	0.01
ASSET	<66	5.4	6.3	0.9	0.24
	66-75	10.8	16.4	5.6	0.001
AIMS	<65	5.2	8.5	3.3	0.06
	65-70	12.2	30.2	18	0.003
Pooled	**not old**	**7.3**	**9.4**	**2.1**	0.0001
	old	**17.9**	**22.1**	**4.1**	0.0001

*number of lives saved per 100 patients treated. From (19).

Indeed, their analysis of the pooled data of the "not old" versus "old" groups suggests that twice as many lives are saved by treating "old" patients with thrombolytic therapy! In fact, the real benefits in mortality for the "old" subgroups are in those groups which include 65-70 year olds. The evidence for improved mortality in the truly excluded older patients (age > 70 to 75) is marginal.

In summary then, do women have limited access to thrombolytic therapy compared to men and does this constitute a gender bias which compromises the care of women with coronary artery disease? Clearly, less women are eligible for thrombolytic therapy than men because of their different baseline characteristics and at least, based on the data for age, this does not appear to compromise their survival. Are eligible women less likely than eligible men to receive thrombolytic therapy? Perhaps.

Access to Revascularization

Table 7 summarizes 7 studies which report the effect of gender on access to PTCA and CABG (1,6,31-34). These studies were selected because they had large study populations (greater than 1000), gender specific information was available and in studies in which all patients did not undergo catheterization, the medical indication for inclusion in the study was acute myocardial infarction.

In the studies by Bell et al. (30) and Lincoff et al. (6), the study populations were patients who underwent cardiac catheterization for many indications and there were no significant differences in the rates of total revascularization (PTCA plus CABG) procedures by gender. In June this year, Bell and colleagues published the Mayo Clinic experience of 22,795 patients with suspected coronary disease who underwent angiography between 1981 and 1991 and compared the numbers of women and men who underwent PTCA or CABG (30). Table 8 summarizes the findings at diagnostic coronary angiography in these patients. Twice as many women as men had no coronary disease and twice as many men as women had three vessel disease.

Table 8. Summary of Findings at Diagnostic Coronary Angiography in 22,795 Patients

No. of Vessels Diseased	Men No. (%) (n=15237)	Women No. (%) (n=7,558)
0	3,735 (24)	3,605 (48)
1	1,908 (13)	834 (11)
2	3,287 (22)	1,141 (15)
3	6,307 (41)	1,978 (26)

The observed difference in prevalence of coronary disease between men and women was statistically significant ($p<0.0001$) (From ref 30).

Table 7. Gender Differences in Utilization of PTCA and CABG

Study (ref) n= study pop.	Study Period Setting	Cardiac Cath %M/%F	PTCA (all) %M/%F	PTCA (cath) % M/%F	CABG (all) %M/%F	CABG (cath) %M/%F
Bell (30) n=22795	1981-90 Mayo Cl 30 days	100/100	-----------	18/22 *A,C,Y	----------	36/32 *A,C,Y
Lincoff (6) n=1618	1985-90 TAMI in-hosp	100/100	-----------	53/54	----------	22/20.4
Krumholz (31) n=2473	1984-90 B.I. Hosp in-hosp	32/22	-----------	53/51	---------	21/16
Udvar-helyin (32) n=218427	1987 Medicare 90 days	28/18 *A,R	6/4 *A,R	21/22	10/6 *A,R	32/27 *A,R
Kostis (33) n=37921	1986-87 NJ data 3 years	32.3/18.4 *A,R,C,I	6.9/3.5 *A,R,C,I	13.4/12.1	10.4/6.0 *A,R,C,I	32.4/32.3
Giles (34) n=10368	1988-90 N.H Sur in-hosp	32.9/28.4 *A,I	8.3/7.6	25.2/26.9	10.8/6.4 *A,I	32.8/22.3 *A,I
Steingart (1) n=2231	1897-90 SAVE in-hosp	55/55	17/19	---------	9/9	-------

*significant difference end after adjustment for age (A), race (R), insurance (I), co-morbid conditions (C) or year of catheterization (Y) .

Table 9 summarizes the frequency of revascularization by gender according to extent of coronary artery disease. In patients with 3 vessel disease, women were more likely to undergo PTCA while men were more likely to undergo CABG. In analysis of all revascularization procedures, this trend remained. Even after adjustment for age, year of angiography, number of concomitant medial illnesses and the extent of coronary artery disease, women were more likely to undergo PTCA whereas men were more likely to undergo CABG. However, when any revascularization procedure was considered, there was no significant difference between overall use of revascularization procedures between genders.

Table 9. Frequency of Revascularization by Gender According to Extent of Coronary Artery Disease

	No. (%) of Men (n=11,502)	No. (%) of Women (n=3,953)
One vessel disease		
No revascularization	1,057 (55)	439 (53)
Revascularization	851 (45)	395 (47)
CABG	168 (9)	77 (9)
PTCA	683 (36)	318 (38)
Two vessel disease		
No revascularization	1,671 (51)	538 (47)
Revascularization	1,616 (49)	603 (53)*
CABG	848 (26)	304 (27)
PTCA	768 (23)	299 (26)
Three vessel disease		
No revascularization	2,536 (40)	823 (42)
Revascularization	3,771 (60)	1,115 (58)
CABG	3,174 (50)	886 (45)#
PTCA	597 (10)	269 (14)#
Total		
No revascularization	5,264 (46)	1,800 (46)
Revascularization	6,238 (54)	2,153 (54)
CABG	4,190 (36)	1,267 (32)#
PTCA	2,048 (18)	886 (22)#

* $p = 0.03$; #$p<0.0001$. (From ref. 30)

In the remaining 5 studies in Table 7, the study population was patients who had a diagnosis of acute myocardial infarction. In the largest study by Udvarhelyi et al. (32), the mean age of this Medicare population was 76 with almost one-third of the patients older than 80 years. In the study by Giles et al., rates were adjusted age, race, insurance and in-hospital mortality (34). In the study by Steingart et al. which was mentioned in the introduction, women with angina were less likely than men to undergo procedures before the index infarction which qualified them for he SAVE study (1). However, after the index myocardial infarction there was no effect of gender on the rate of procedures (data included in Table 7). The high rates of catheterization in this study probably result from the fact that to be considered eligible for randomization in the SAVE study, patients were required to undergo catheterization and revascularization if they had signs or symptoms of myocardial ischemia after the index infarction. (The study by Ayanian and Epstein (2) was not included in this analysis because it included patients with a diagnosis of angina.)

In the three largest studies, with a pooled population of over 260,000, women were less likely than men to undergo cardiac catheterization even after adjustment for baseline variables. Not surprisingly, in these studies in which women were less likely to undergo cardiac catheterization, they were also less likely to undergo PTCA (with the exception of 34) or CABG. However, in the population which underwent cardiac catheterization, women were as likely as men to undergo PTCA and only slightly less likely to undergo CABG.

Kostis and co-workers examined the Myocardial Infarction Data acquisition System (MIDAS) which included all discharges from 1986 and 1987 with the diagnosis of acute myocardial infarction in New Jersey to evaluate the sex differences in the management and long-term outcome of acute myocardial infarction (3). They examined discharge data from 42,595 patients of whom 25,173 (59%) were men and 17422 (41%) were women to calculate rates of cardiac catheterization, PTCA and CABG during the index hospitalized, within three months of the index hospitalization and at any time during the entire study period as well as the rates of survival at three years. The data shown on Table 7 is for procedures done anytime during the 3 year study period. Women were less likely to undergo cardiac catheterization, PTCA and CABG compared with men. The lower rate of use of procedures in women was observed consistently in different age strata, in the presence and absence of co-morbid conditions and complications, and in different insurance coverage types and races. However, in the patients who underwent cardiac catheterization, women and men had equal rates of PTCA and CABG.

Since access to cardiac catheterization is necessary for access to PTCA and CABG, it is a gatekeeper of sorts. Does the increased rate of catheterization in men represent overuse in men, underuse in women or appropriate use in both? For example, more men may have had rest or provoked ischemia following their myocardial infarction and consequently underwent catheterization more frequently. The survival data presented in this study addresses this issue to some extent.

Figure 5 shows the influence of cardiac catheterization on survival in men and women who underwent catheterization during any time during the study period. Cardiac catheterization was consistently associated with lower mortality in both men and women. Since these patients were not randomized, this better outcome with the invasive strategy could be due to either selection of low risk patients for invasive procedures or due to the beneficial effect of the intervention. However, this lower mortality persisted after adjustment for age and co-morbidity suggesting these interventions may have a beneficial effect on survival. One might conclude that cardiac catheterization is in appropriately underutilized in women compared with men.

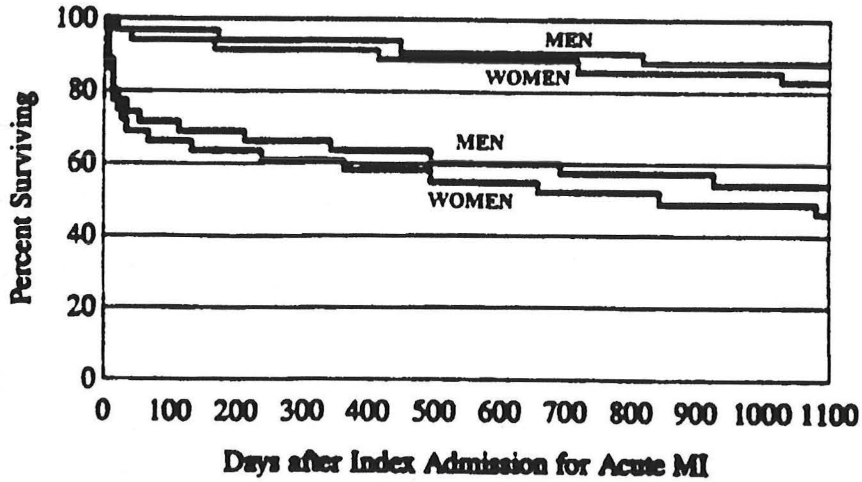

Figure 5. Survival plot showing effect of catheterization in men and women hospitalized with acute myocardial infarction (3).

Bernstein and colleagues retrospectively evaluated the gender-related differences in the appropriateness of use of cardiovascular procedures in a random sample of 3,979 patients in New York State (35). The investigators developed a list of appropriate indications for PTCA and examined whether men and women undergoing PTCA where appropriately selected. They found that the rate of inappropriate use of PTCA was similar in men and women (4% and 3% respectively). What this study does not indicated is the appropriateness of "non-use" of PTCA in men and women. The age adjusted death rate from ischemic heart disease is twice as great in men compared with women but the corresponding age-adjusted rates of PTCA in New York State are over 3 times greater in men than in women: 88 to 27 per 100,000. This suggests possible underuse of these procedures in women.

These studies suggest that women with myocardial infarction may undergo cardiac

These studies suggest that women with myocardial infarction may undergo cardiac catheterization, PTCA and CABG less frequently than men. Furthermore, in patients who have undergone cardiac catheterization, women are less likely than men to undergo CABG. Does this underutilization of revascularization translate into worse outcomes for women?

Gender differences in Outcome following PTCA.
In comparing the mortality in men and women following PTCA, it is critical to understand that there are many important differences in the demographic, clinical and angiographic profiles of women who undergo PTCA compared with men. These important differences (listed in Table 10) should be taken into account when comparing the outcomes of procedures in order to distinguish the effects of gender from the effects of differences in other baseline characteristics of the two groups studied.

Table 10. Distinguishing Features of Women Who Undergo PTCA Compared With Men (Ref)

- ↑ Age (30,36-42)
- ↑ Congestive heart failure (36,39,40,42)
- ↑ Hypertension (30,36,37,40,42)
- ↑ Diabetes mellitus (30,36,37,39,40,42)
- ↑ Hypercholesterolemia (36,39)
- ↑ Unstable angina(36-39,42)
- ↓ Cigarette use(36,39,40,41)
- ↓ Prior CABG(36,42)
- ↓ Multivessel disease(37,38,40)
- ↑ Left ventricular EF (38-40,42)

Using data collected from 16 centers participating in the first National Heart, Lung and Blood Institute's (NHLBI) PTCA registry on 3079 cases through 1982, Cowley et al. reported that PTCA in women was associated with less favorable short-term outcome, lower initial success rate and higher mortality rate than in men (38). Table 11 lists significant differences ($p < 0.05$) in the short-term results of PTCA in 2374 men and 705 women in the Registry. After multivariate analysis, female gender, prior CABG and age > 60 were the factors associated with early mortality. No relationship between body size and mortality was identified in women. There was a significant inverse linear relationship identified between height and mortality rate in men, with higher mortality in shorter men. Eighteen month mean follow-up data were available in 2272 patients.

Table 11 also lists significant differences ($p < 0.05$) in the long-term results of PTCA in 1092 men and 305 women in the Registry. After multivariate analysis, left main disease, male gender, class 3 or 4 angina, hypertension, multivessel disease and smoking history were the factors associated with late mortality.

Table 11. Early NHLBI Registry:
Early and Late Results of PTCA

	F (%)	M (%)
Early Results		
Angio success	60.3	66.2
Unable to pass	25.2	21.8
Unable to dilate	8.4	7.2
Intimal tear	16.5	10.7
Complications	27.2	19.4
Death	1.8	0.7
PTCA mort	1.7	0.3
CABG mort (6.5%)	17.4	3.2
Late Results		
Event-free Surv	79.7	69.0
Repeat PTCA	9.9	17.5
Death	2.2	0.3

In 1993, recent results of the NHLBI PTCA Registry were published by Kelsey et al. who reported data on 2136 patients, 546 of whom were women, who underwent PTCA in 1985 and 1986 on whom 4 year follow-up status was available (39). Table 12 lists selected baseline characteristics and outcome features in men and women. Twice as many women than men were older than 65 years, inoperable or at high surgical risk or diabetic. Women were more likely to have a history of congestive heart failure, hypertension, hypercholesterolemia, unstable angina and preserved left ventricular systolic function. Men and women had the same angiographic profile. The rates of successful dilatation of attempted lesions were 89% for women and 88% for men. The rate of clinical success (defined as all lesions dilated by greater than or equal to 20% without death MI or CABG) was 79% for both women and men. Among complications, coronary dissection and entry-site complications occurred significantly more often among women than men.

Table 12. 1985-86 NHLBI PTCA Registry:
Baseline and Outcome Features by Gender

	F (%)	M (%)
Baseline Characteristics		
Age ≥ 65*	41.7	21.6
History of CHF*	8.6	4.2
History of HTN*	57.8	41.7
History of DM*	20.2	11.0
Co-morbid disease*	9.5	4.6
Unstable angina*	60.4	49.9
EF ≥ 50%*	86.5	79.5
Inoperable*	12.1	6.1
No. targets	1.51	1.58
In-hospital Outcome		
None in laboratory	82.8	87.2
Death*	2.6	0.3
Non-fatal MI	4.6	4.3
Urgent CABG	4.8	3.3
Elective CABG	1.8	2.0
Complete revasc	42.5	44.5
Clinical success	79.5	78.9
Status at 4 Years		
Death*	10.8	6.6
Angina-free*	70.3	81.8
Repeat PTCA	24.0	26.5
CABG	15.8	18.3

*p<0.001

One of the most striking differences listed in Table 12 was the higher in-hospital mortality rate among women. Women were 10.5-fold more likely to have died in-hospital then were men. Besides gender, other risk factors for mortality were age, history of congestive heart failure history of diabetes, inoperable or high risk status and multivessel disease. After adjustment for these independent predictors of mortality, the relative risk for female gender was reduced to 4.53.

The cause of this increased in hospital mortality is unclear. In the past, poorer PTCA results in women have been attributed to women smaller physical size and hence smaller vessels, making the procedure more technically difficult. In the CASS registry, the average diameter of the grafted vessel was inversely related to mortality (43). However, no relation between body size and mortality was found for women in the early NHLBI PTCA Registry nor in the most recent one. Interestingly, rates of procedural complications were related to height for both men and women. The shorter the person the more likely a complication. Only one study of PTCA in men and women evaluated the effect of vessel size on mortality (40); multivariate correlates of in-hospital mortality included short stature but not vessel size. Women experience more complications associated with the procedure and complications were more lethal in women, but even among patients with no complications, mortality was higher in women.

Table 13 shows four-year event rates by gender with odds ratios (39). Compared to early NHLBI PTCA Registry data, after adjustment for independent predictors of mortality such as age, history of congestive heart failure or diabetes, and multivessel disease, female gender was no longer an independent risk factor for death or the combined events endpoint.

Table 13. 1985-86 NHLBI PTCA Registry:
4 yr Event Rates by Gender with F vs M Odds Ratios

	% M	**% F**	**Unadj O R** (95% CI)	**Adj O R** (95% CI)
Death	6.6	10.8	**1.84*** (1.31, 2.60)	**1.20** (0.84,1.73)
Angina	18.2	29.7	**1.69*** (1.30, 2.20)	**1.78*** (1.34,2.36)
Death, CABG, MI or angina	40.3	48.5	**1.36*** (1.09, 1.69)	**1.23** (0.97,1.56)

The 1985-86 NHLBI PTCA Registry data shows that women have higher in-hospital mortality but long-term mortality and clinical outcome were similar in both genders. Many other studies confirm the finding that women have similar long term outcome compared to men following PTCA (34,40, 41,44). Some groups also confirm increased in-hospital mortality for women following PTCA (36,40,44) while others report no difference between men and women (37,41,45). These studies are summarized in Table 14.

Table 14. In-Hospital and Long-Term Mortality in Men and Women Undergoing PTCA.

Study (ref)	No. M/F	In-hosp	Long-term
NHLBI (38)	2374/705	F > M	F > M (18 mos)
NHLBI (39)	1590/546	F > M	M = F (4 yrs)
Kahn (37)	7142/2033	M = F	NE
McEniery (45)	2727/969	M = F	NE
Welty (41)	341/164	M = F	M = F (34 mos)
Bell (36,44)	2203/824	M = F	M = F (5.5 yrs)
Weintraub (40)	7940/2845	F > M	M = F (5 yrs)

M=male; F=female; NE=not evaluated

Women who undergo PTCA may have a higher in-hospital mortality than men, which when present is largely or completely, explained by their worse cardiovascular risk profile and older age. There is still no consensus as to whether there is independent gender risk with PTCA. The long term survival and improvement in symptoms appears to be generally the same for both sexes, particularly after adjustment for baseline differences. Therefore, PTCA should be not be withheld from women who are in need of coronary revascularization and who have suitable anatomy for PTCA.

Gender differences in Outcome following CABG.

As shown in Table 7, many studies, but not all, reported that women with myocardial infarction are less likely than men to undergo CABG even after adjustment for rates of cardiac catheterization. Does this represent underutilization in women or overutilization in men. This is a difficult question to answer because compared with men, there simply aren't sufficient medical versus surgical treatment survival data in women from which to formulate appropriate indications for CABG.

Coronary artery bypass surgery has been shown to improve long-term survival in selected patients: patients with 3 vessel disease with impaired left ventricular function (46,47) or 2 vessel (LAD) and 3V disease with normal LVEF (49). These data come primarily from three randomized trials: the VA CABG Surgery Cooperative Study (46), the Coronary Artery Surgery Study (CASS) (47) and the European Coronary Surgery Study Group (48). Some important features of these trials are listed in Table 15. The number of women enrolled in these trials was very small (4%). Furthermore, the clinical features which are predominant in women undergoing CABG (shown in Table 16) are exclusion criteria in these trials - unstable angina, decompensated heart failure, co-morbid disease. Clearly, the subset of female patients with coronary artery disease who would have survival benefit from CABG have not been identified. Consequently, to make conclusions about whether women who would benefit from CABG are denied access to this procedure is difficult.

Table 15. Features of CABG Surgery Trials

Study	F/M	Excluded	Benefit
VA Coop Study	0/686	CHF, USA DBP >100 MI <6 mos comorbid	3V and 50>EF>25
CASS	76/704	age >65 MI <3wks CHF, USA comorbid	3V and 50>EF>34
Eur CSS Group	0/767	age >64 EF <50 USA	2V (LAD) 3V

Table 11. Distinguishing Features of Women Who Undergo CABG Compared With Men (Ref)

↑ Age(43,49-53)

↑ Congestive heart failure(43,49,50,52)

↑ Hypertension (49-51)

↑ Diabetes mellitus(49-53)

↑ Unstable angina(43,49-53)

↓ Multivessel disease(43,50)

↑ Left ventricular EF(50)

↑ Recent MI(51)

While gender differences in the indications for CABG are uncertain, the relationship between gender and mortality following CABG is also unclear. There does not appear to be a consensus as to the effect on gender if any on in-hospital survival. In some studies, women were more likely to experience in hospital death than men even after adjustment for baseline variables (50-52) while in others, the increase in mortality in women was fully accounted for by differences in baseline variables (43,49). Finally, the fundamental question isn't really whether women treated with CABG so better than men treated with CABG, it is whether women treated with CABG do better than women not treated with CABG. That data remains to be published.

Conclusion

Clearly men and women with myocardial infarction are clearly different clinical subgroups. Women are, in general, older with hypertension, diabetes, unstable angina and heart failure who present later from onset of symptoms than men. Correcting for these baseline differences, appears to offset many of the absolute differences in mortality and access to procedures so that in fact, gender bias may not compromise the treatment of women with coronary artery disease.

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