Quantitative Results of Baseline Angiography and Percutaneous Coronary Intervention in the COURAGE Trial

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Background—COURAGE compared outcomes in stable coronary patients randomized to optimal medical therapy plus percutaneous coronary intervention (PCI) versus optimal medical therapy alone.

Methods and Results—Angiographic data were analyzed by treatment arm, health care system (Veterans Administration, US non–Veterans Administration, Canada), and gender. Veterans Administration patients had higher prevalence of coronary artery bypass graft surgery and left ventricular ejection fraction ≤50%. Men had worse diameter stenosis of the most severe lesion, higher prevalence of prior coronary artery bypass graft surgery, lower left ventricular ejection fraction, and more 3-vessel disease that included a proximal left anterior descending lesion ($P<0.0001$ for all comparisons versus women). Failure to cross rate (3%) and visual angiographic success of stent procedures (97%) were similar to contemporary practice in the National Cardiovascular Data Registry. Quantitative angiographic PCI success was 93% (residual lesion <50% in-segment) and 82% (<20% in-stent), with only minor nonsignificant differences among health care systems and genders. Event rates were higher in patients with higher jeopardy scores and more severe vessel disease, but rates were similar irrespective of treatment strategy. Within the PCI plus optimal medical therapy arm, complete revascularization was associated with a trend toward lower rate of death or nonfatal myocardial infarction. Complete revascularization was similar between genders and among health care systems.

Conclusions—PCI success and completeness of revascularization did not differ significantly by health care system or gender and were similar to contemporary practice. Angiographic burden of disease affected overall event rates but not response to an initial strategy of PCI plus optimal medical therapy or optimal medical therapy alone. **(*Circ Cardiovasc Qual Outcomes*. 2009;2:320-327.)**

Key Words: coronary angiography ■ ventricular ejection fraction ■ gender identity ■ delivery of health care ■ revascularization ■ stent

The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial was a multicenter randomized clinical trial comparing morbidity, mortality, quality of life, and resource utilization in 2287 patients with stable coronary artery disease randomized to optimal medical therapy plus percutaneous coronary intervention (PCI) or optimal medical therapy alone.[1] There was no difference between treatment arms in the primary com-

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posite outcome of death or nonfatal myocardial infarction (MI).[1] The trial has generated lively debate regarding the role of PCI in stable coronary artery disease.[2–5] Questions regarding the applicability of results to both genders, the results in different health care systems, and adequacy of PCI have been raised. In this article we report the baseline quantitative angiographic disease and PCI procedural success as measured by the angiographic core laboratory according to treatment arm, health care system, and gender. The influence of angiographic burden of disease and completeness of revascularization on outcome is also examined.

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WHAT IS KNOWN

- In patients with chronic stable angina, there was no difference between an initial strategy of optimizing medical therapy versus percutaneous coronary intervention plus optimization of medical therapy for the prevention of death or nonfatal myocardial infraction in COURAGE.

WHAT THE STUDY ADDS

- Angiographic burden of disease was least severe in women and most severe in patients enrolled from the US Veterans Administration.
- Percutaneous coronary intervention performance and completeness of revascularization were not influenced substantially by gender or health care system and did not differ from published norms or National Cardiovascular Data Registry information.
- Although there was no interaction between treatment strategy and either indexes of atherosclerotic burden or completeness of revascularization, event rates trended lower in patients with less severe disease and with complete revascularization post–percutaneous coronary intervention.
- Future trials of this nature should enroll patients with as high an angiographic burden of disease as possible and more women and attempt to achieve complete revascularization.

Methods

The major angiographic inclusion criteria for the trial were (1) patients with a ≥70% diameter stenosis (DS) by visual assessment in 1 or more vessels subtending a large area of myocardium associated with objective evidence of ischemia; (2) presence of at least 1 vessel suitable for PCI; and (3) American Heart Association/American College of Cardiology Joint Task Force Class I and II indications for PCI.[6] Patients with >80% DS and typical angina were also eligible irrespective of availability of functional test results. Lesions suitable for PCI had to meet at least 1 of the following anatomic criteria: (1) right coronary artery (RCA) lesion proximal to the posterior descending artery in a right dominant circulation; (2) left circumflex (LCX) lesion proximal to 2 or more obtuse marginal branches or proximal to the posterior descending artery and posterolateral branches in a left dominant circulation; (3) left anterior descending (LAD) lesion in the proximal or mid segments; or (4) saphenous vein graft or internal mammary artery graft meeting the same criteria as for native artery lesions or subtending a major mass of myocardium. The major angiographic exclusion criteria were (1) coronary arteries technically unsuitable or hazardous for PCI, (2) left ventricular ejection fraction (LVEF) <30%, or (3) LVEF <35% in the presence of 3-vessel disease, including a ≥70% proximal LAD stenosis.

Angiograms were submitted to the Cardiovascular Imaging Research Core Laboratory (CIRCL), Vancouver, Canada. Previously described and validated software[7–8] was used to analyze either digitized films or compact disc recordings (DICOM standard). Contrast-filled angiographic catheters ≥6F were used to calibrate dimensions. Otherwise, only relative measurements (% DS) were made. Vessel disease was defined as the number of coronary arteries or bypass grafts containing at least 1 lesion ≥50% DS by quantitative coronary angiography (QCA). QCA was designed to accommodate both balloon-only and stent procedures (online-only Data Supplement, Figure S1). When stents were deployed, post-PCI analysis included a record of in-stent minimum lumen diameter (MLD) as well as in-segment MLD to calculate in-stent and in-segment % DS, respectively. Proximal reference diameters were used so that balloon-only and stent cases could be amalgamated. Additionally, the in-segment results are based on a branch to branch delimitation which can extend beyond the ±5-mm region typically reported in stent-only trials. Both factors systematically augment the post-PCI % DS severity. Angiographic success after PCI was examined using in-segment DS <50% and in-stent <20%. Area-length measurements of LVEF were undertaken from technically suitable 30° right anterior oblique ventriculograms (n=1605).

Ischemic Jeopardy Score

The Duke Jeopardy Score[9] was modified to create an index of ischemic jeopardy (Figure S2). Because of the complexity of bypass surgery conduits, the scoring was not applied to patients with bypass grafts (approximately 10% of the cohort). No distinction was made between lesions occurring proximal or distal to the first septal perforator in the proximal LAD, as this was not prespecified at the outset of the trial and was not recorded. A point was given for each ischemic zone and summed based on the most proximal stenosis. Perfusion zones subtended by more minor branches than depicted in Figure S2 were assigned a point only if not already counted by virtue of significant stenoses more proximally in the main vessel segments. This was required because some interventions were performed in distal branches that subtended a large ischemic bed. Finally, in addition to the ≥70% DS threshold described originally,[9] we also examined ischemic jeopardy using a ≥50% threshold.

Revascularization Targets and Adequacy of Revascularization

The modified Duke Jeopardy score described above was used to determine the possible number of revascularization targets before PCI and the number remaining after intervention. Complete revascularization was not mandated, but operators were asked to perform as complete a revascularization as possible within the constraints of anatomy and clinical judgment (eg, fixed defects or reversible defects on nuclear scanning, presence of severe wall motion abnormalities, size of vessel, and chronic total occlusion). Revascularization targets were defined as either ≥50% or ≥70% but not totally occluded and not in a vessel <2.5 mm. Complete revascularization was defined as absence of revascularization targets post-PCI. Partial revascularization was defined as persistence of ≥1 revascularization target post-PCI.

For comparison, the American College of Cardiology's National Cardiovascular Data Registry (NCDR; version 3, www.acc.org/ncdr/cathlab/htm) was queried between January 13, 2000, and December 31, 2006, for patients who did not have MI during the hospital admission before PCI.

Statistics

Comparisons were made using *t* tests, Kruskal–Wallis nonparametric analysis of variance, and χ^2 or Fischer exact tests where appropriate.

Table 1. Angiographic Features of Medical and PCI Cohorts

	Medical Cohort		PCI Cohort		
	n (%)	Mean±SD	n (%)	Mean±SD	*P* Value
Total No. of patients	1138		1149		
Total No. of patients with angiograms	1132		1147		
% DS*	1132	35.5±8.0	1147	36.0±8.6	0.13
Reference diameter, mm†	997	2.8±0.4	1018	2.8±0.4	0.91
Minimum lumen diameter, mm†	997	1.8±0.4	1018	1.8±0.4	0.57
Mean lumen diameter, mm†	997	2.5±0.4	1018	2.4±0.4	0.68
No. of patients with lesions ≥50%	1125 (99.4)		1143 (99.7)		0.38
No. of patients with PLAD lesions ≥50%	277 (24.5)		277 (24.1)		0.88
% DS of worst lesion	1132	78.4±16.5	1147	80.2±16.3	0.006
Jeopardy score (≥50%)	1008	2.4±1.3	1024	2.5±1.3	0.027
Jeopardy score (≥70%)	1008	1.0±1.0	1024	1.0±1.1	0.058
No. of patients with CABG	124 (11.0)		123 (10.7)		0.89
EF, %‡	816		786		0.69
No. of patients with EF >50%	713 (87)	62.4±10.0	680 (87)	62.6±10.7	
No. of patients with EF ≤50%	103 (13)		106 (13)		0.66

PLAD indicates proximal left anterior descending.

*Excluding segments with 0% DS: (1) medical cohort, 38.6±7.9; (2) PCI cohort, 39.0±8.4; *P*=NS.

†Excludes uncalibrated studies.

‡EF measured by all methods: (1) medical cohort (n=1137), EF=60.9±10.3; (2) PCI cohort (n=1146), EF=60.8±11.2.

Kaplan–Meier method was used for the time to event plots, and Cox regression was used for the hazard ratios and confidence limits shown in the forest plot. Because of the numerous comparisons in this descriptive and largely posthoc analysis, only probability values <0.01 were considered significant. Findings of importance with probability values ≥0.01 and <0.05 are reported as trends. The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

Table 1 shows the angiographic features of all patients and a comparison between the medical and PCI arms. The results were similar in the 2 groups: the % DS of the worst lesion was trivially but significantly higher in the PCI + optimal medical therapy cohort than in the optimal medical therapy cohort. Accordingly, the Jeopardy Score using a ≥50% DS threshold tended to be higher in the PCI + optimal medical therapy group. Table 2 shows no major differences between the 2 arms with respect to distribution of vessel disease or numbers of vessels diseased. There were an equal number of patients in each arm with proximal LAD disease (277 per arm). There was a trend in the distribution of proximal LAD disease in association with other disease, namely, proximal LAD+LCX disease was more common in the medical cohort and proximal LAD+LCX+RCA was more common in the PCI cohort (*P*=0.02).

Table 3 shows more severe angiographic disease, including more patients with prior CABG and lower LVEF, in the US VA population. The Jeopardy Score using a ≥70% DS threshold was slightly higher in Canadians, but was similar in the 3 health care systems based on ≥50% DS threshold. A slight trend toward more single vessel LAD disease in US non-VA and Canadian patients compared to US VA patients was noted (Table S1).

Table 4 shows that female patients had smaller diameter vessels, less severe stenoses, better preserved LVEF, and a lower frequency of prior CABG (4.2% versus 12.0% in males, *P*<0.0001). Further details are shown in Table S2, indicating that females had a much higher proportion of single vessel disease. Furthermore, single vessel disease involving the proximal LAD was more common in females,

Table 2. Distribution of Vessel Disease of Medical and PCI Cohorts

	Medical Cohort	PCI Cohort	*P* Value
Vessel disease			
Single	447 (40)	394 (34)	
Double	421 (37)	467 (41)	
Triple	250 (22)	275 (24)	0.07
Single vessel disease			
LAD	206 (46)	199 (51)	
LCX	82 (18)	75 (19)	
RCA	159 (36)	120 (30)	0.28
Double vessel disease			
LAD+LCX	126 (30)	110 (24)	
LAD+RCA	161 (38)	199 (43)	
LCX+RCA	134 (32)	158 (34)	0.10
Proximal LAD disease			
PLAD	76 (27)	69 (25)	
PLAD+LCX	55 (20)	31 (11)	
PLAD+RCA	55 (20)	66 (24)	
PLAD+LCX+RCA	91 (33)	111 (40)	0.02

Data are presented as n (%). Twenty-five patients with "no" vessel disease based on quantitative coronary angiography: 14 (1%) medical cohort versus 11 (1%) PCI cohort.

Table 3. Angiographic Features of All Patients According to Site of Recruitment

	US VA	US Non-VA	Canada	*P* Value
Total No. of patients	968	387	932	
Total No. of patients with angiograms	962	385	932	
% DS*	36.7±8.6	35.4±7.9	34.9±8.0	<0.0001
Reference diameter, mm†	2.8±0.4	2.8±0.4	2.9±0.4	0.004
Minimum lumen diameter, mm†	1.8±0.4	1.8±0.4	1.9±0.4	0.0007
Mean lumen diameter, mm†	2.4±0.4	2.4±0.4	2.5±0.4	0.001
No. (%) of patients with lesions ≥50%	955 (99)	382 (99)	931 (100)	0.01
No. (%) of patients with PLAD lesions ≥50%	225 (23)	95 (25)	234 (25)	0.67
% DS of worst lesion	79.2±17.1	77.9±15.9	80.0±15.9	0.10
Jeopardy score (≥50%)	2.4±1.4	2.5±1.4	2.5±1.3	0.22
Jeopardy score ≥70%)	0.9±1.0	0.9±1.0	1.1±1.1	0.0006
No. (%) of patients with CABG	147 (15)	45 (12)	55 (6)	<0.001
No. of patients with left ventriculograms	645	260	697	
EF, %‡	61.3±10.9	64.3±10.9	62.9±9.4	0.0007
No. (%) of patients with EF >50%	536 (83)	235 (90)	622 (89)	0.0008
No. (%) of patients with EF ≤50%	109 (17)	25 (10)	75 (11)	

PLAD indicates proximal left anterior descending.
*Excluding segments with 0% DS: (1) US VA, 39.7±8.4; (2) US non-VA, 38.3±8.1; (3) Canada, 38.1±7.9; $P<0.0001$.
†Excludes uncalibrated studies.
‡EF measured by all methods: (1) US VA (n=966), EF=59.4±10.8; (2) US non-VA (n=386), EF=61.8±11.6; (3) Canada (n=931), EF=62.0±10.0.

whereas in males proximal LAD disease was most commonly seen with LCX and RCA disease ($P=0.0001$). Figure 1 shows that the outcome of death and nonfatal MI (excluding periprocedural MI) generally increased with increasing levels of jeopardy or number of vessels diseased. There was no heterogeneity of the effects of initial treatment strategy.

Table S3 summarizes the PCI procedures. A total of 97% of patients randomized to PCI + optimal medical therapy underwent PCI: 91% of procedures involved placement of at least 1 stent, 26% received 2 stents, and 15% received 3 or more. Drug-eluting stents (DES) became available only toward the end of the recruitment phase. Only 3% of patients received DES. Of the total number of segments treated with PCI, 88% (1705) were treated with stents and 12% with balloon only. A more detailed segment-by-segment analysis of the PCI procedures is provided in Table S4. Cummulative

Table 4. Angiographic Features According to Gender

	Males		Females		
	n (%)	Mean±SD	n (%)	Mean±SD	*P* Value
Total No. of patients*	1947		338		
Total No. of patients with angiograms*	1941		337		
% DS	1941	36.3±8.4	337	32.8±7.1	<0.0001
Reference diameter, mm†	1727	2.8±0.4	287	2.7±0.4	<0.0001
Minimum lumen diameter, mm†	1727	1.8±0.4	287	1.8±0.3	0.01
Mean lumen diameter, mm†	1727	2.5±0.4	287	2.3±0.4	<0.0001
No. (%) of patients with lesions ≥50%	1933 (99.6)		334 (99.1)		0.21
No. (%) of patients with PLAD lesions ≥50%	482 (24.8)		72 (21.4)		0.19
% Diameter stenosis of worst lesion	1941	80.1±16.4	337	74.8±15.8	<0.0001
Jeopardy score (≥50%)	1708	2.5±1.4	323	2.3±1.3	0.03
Jeopardy score (≥70%)	1708	1.0±1.0	323	0.8±1.0	0.003
No. (%) of patients with CABG	233 (12.0)		14 (4.2)		<0.0001
EF, %‡	1379		223		<0.0001
No. (%) of patients with EF >50%	1188 (86)	62.1±10.4	205 (92)	65.0±9.9	0.02
No. (%) of patients with EF ≤50%	191 (14)		18 (8)		

PLAD indicates proximal left anterior descending.
*Two patients had missing gender; 1 had an angiogram, and the other did not.
†Excludes uncalibrated studies.
‡EF measured by all methods: males (n=1943), EF=60.3±10.6; females (n=338), EF=64.2±10.6.

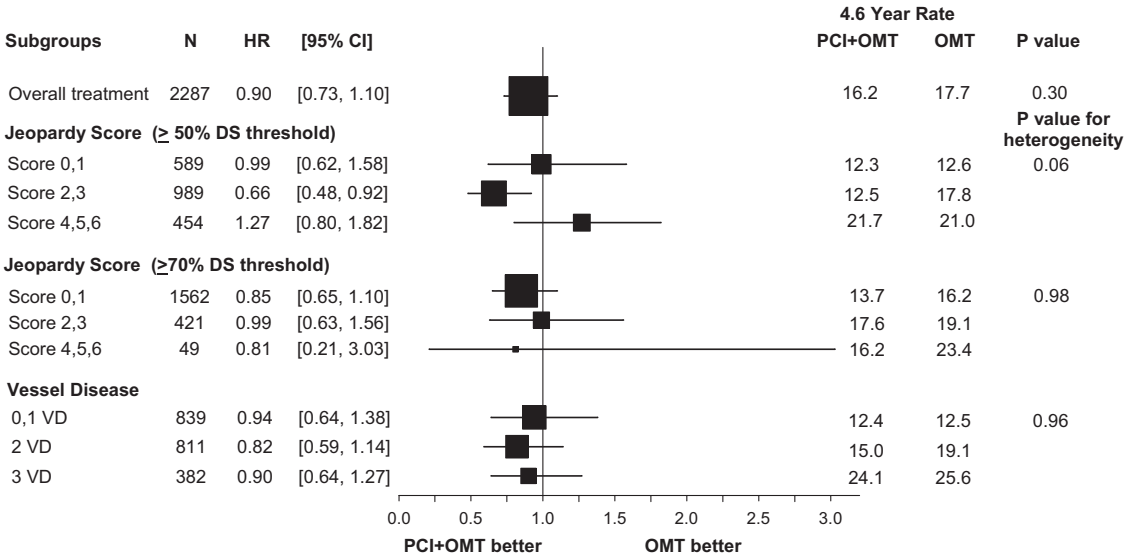

Figure 1. Influence of angiographic burden of disease on the outcome of death and nonfatal MI, excluding periprocedural MI. The rates of death and nonfatal MI during 4.6 years of follow-up are provided to the right of the forest plots. HR indicates hazard ratio.

success rates are plotted in Figure 2 and correspond to the aggregate results detailed in Table S5. There was a 3% rate of failure to cross. Once crossed, the post PCI in-segment % DS was <50% in 93% of all procedures and 95% of stent procedures. Overall PCI angiographic success based on visual analysis was 93% (reported previously).[1] Using quantitative analysis, an in-stent % DS <20% was achieved in 82% of stent procedures. Angiographic success of stents only, based on visual analysis, was 97%.

Table 5 indicates that success rates were comparable among US sites. There was a trend toward greater utilization of stents, a slightly higher aggregate procedural success rate (post balloon-only <50% DS and post stent <20% DS), and a significantly higher frequency of achieving a post-PCI in-stent % DS of <20% in Canada. The self-reported angiographic results after PCI from the NCDR database and from the COURAGE operators are similar except for a lower rate of success in the small number of balloon-only patients. Self-reported results using a <50% DS criterion are similar to the quantitative results, but self-reported frequency of in-stent <20% DS is higher than that based on QCA. There were no significant differences in success between genders (Table S6).

57% and 93% of patients had complete revascularization of ≥50% and ≥70% revascularization targets, respectively (Figure S3). When results were stratified by healthcare system (Table S7), there were no differences in revascularization using the ≥50% DS threshold. Using a ≥70% DS threshold, US non-VA patients had the lowest baseline burden of revascularization targets ≥70% (P=0.008), and this persisted as a trend (P=0.047) after PCI. This may account for the post-PCI trend, suggesting that US non-VA patients had higher complete revascularization (P=0.047). Analyses stratified by gender (Table S8) showed no major differences. Figure 3 shows the influence of revascularization on the outcome of death and nonfatal MI, excluding periprocedural MI in the PCI + optimal medical therapy arm. The analyses indicate no statistical significance, but a trend

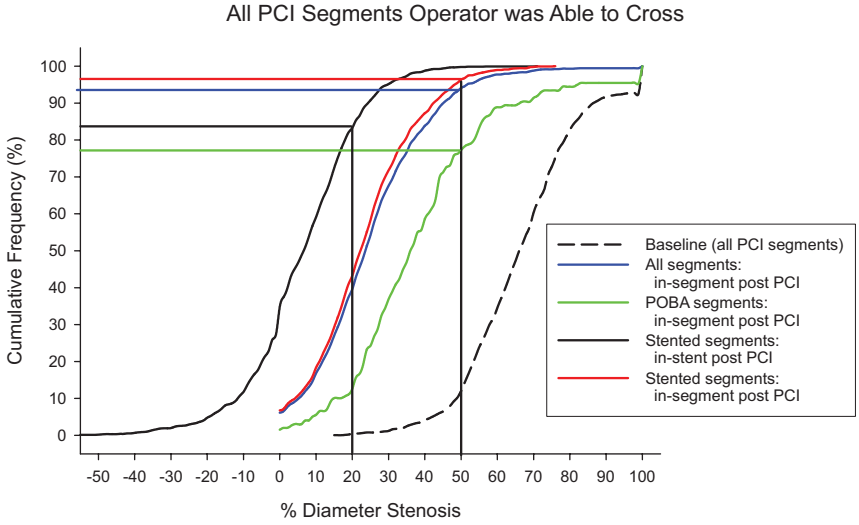

Figure 2. PCI success: cumulative frequency plots of baseline and post-PCI diameter stenosis. POBA indicates plain old balloon angioplasty.

Table 5. Success of Protocol PCI According to Health Care System

	US VA	US Non-VA	Canada	*P* Value	COURAGE	NCDR
No. of PCI segments*	741	288	676		1722	1459008
No. of PCI segments the operator was able to cross	725 (98)	280 (97)	653 (97)	0.36	1669 (97)	1430239 (98)
No. with balloon angioplasty only	96 (13)	42 (15)	60 (9)	0.02	222 (13)	139943 (10)
No. with stents	629 (87)	238 (85)	593 (91)		1447 (87)	1290296 (90)
All PCI segments operator was able to cross	725	280	653		1666	1430239
Post-PCI in-segment % DS <50	680 (94)	254 (91)	611 (94)	0.20	1626 (98)	1409537 (99)
Aggregate success (balloon only post PCI in-segment % DS <50, stent post-PCI in-stent % DS <20)	572 (79)	226 (81)	552 (85)	0.03	1583 (95)	1384549 (97)
Balloon angioplasty only segments	96	42	60		220	139943
Post-PCI in-segment % DS <50	76 (79)	32 (76)	43 (72)	0.56	184 (84)	127554 (91)
Stented segments	629	238	593		1446	1290296
Post-PCI in-segment % DS <50	604 (96)	222 (93)	568 (96)	0.20	1442 (100)	1281983 (99)
Post-PCI in-stent % DS <20	496 (79)	194 (82)	509 (86)	0.006	1399 (97)	1256995 (97)

Data are presented as n (%). Self-reported COURAGE and self-reported NCDR (January 13, 2000, to December 31, 2006) results are also provided in the last 2 columns, respectively.

*No. includes only those with analyzable post-PCI views on the angiogram.

favoring complete revascularization with respect to the ≥50% DS criterion is apparent.

To enrich the insights into the types of patients enrolled in COURAGE, Figure S4 through S10 provide angiograms and clinical details of patients randomized to optimal medical therapy.

Discussion

This is the first comprehensive report of the QCA assessment of patients enrolled in COURAGE. All angiographic variables were well balanced between treatment arms. In the original report, there was no statistically significant heterogeneity in terms of the primary outcome when analyzed according to health care system.[1] This is particularly interesting in view of the current observations that subjects from Canada had less severe disease based on % DS, larger vessel lumen sizes, and the lowest rates of CABG at the time of randomization. These findings may help explain the higher rate of achieving in-stent % DS <20% compared to US patients and the highest rate of complete revascularization of ≥70% target revascularization lesions based on quantitative analysis. Patients enrolled from the VA system were generally comparable to those enrolled in the US non-VA sites except that they had a lower mean LVEF. Even so, outcomes of US VA patients were not significantly different from outcomes for patients from the other health care systems.[1]

Women had smaller coronary arteries as anticipated. However, the less severe % DS of the worst lesion, the higher prevalence of single vessel disease, the higher frequency of isolated proximal LAD not associated with other significant disease, the higher LVEF, and the lower rate of CABG at baseline were not anticipated and indicate that women had slightly less severe disease. Prior studies have suggested differences with respect to patterns of practice and outcomes in women.[10–14] A trend favoring PCI + optimal medical therapy in females was reported in the main trial results,[1] but further assessment suggests that there were no outcome differences when imbalances compared to males were adjusted.[15] Even so, all of these analyses are limited by virtue of the small representation of females (only 15%) in the COURAGE trial.

COURAGE began before the availability of DES, and enrollment terminated shortly after they became available. 88% of patients received bare metal stents, and only 3% received DES. Thus, the outcomes reflect the bare metal stent era. Although DES are effective for reducing restenosis, they have no beneficial impact on death or MI compared with bare metal stents in the management of chronic stable coronary artery disease. In fact, there are data to suggest that DES may increase late stent thrombosis compared with bare metal stents, which causes death or ST elevation MI in nearly all patients in whom it occurs.[16] The results of COURAGE, therefore, reflect the higher restenosis rate associated with bare metal stents but are free of the increased frequency of stent thrombosis that may be associated with DES.

Although the adequacy and aggressiveness of optimal medical therapy in COURAGE is well accepted, the adequacy of PCI and completeness of revascularization has been a common criticism.[2] The current analysis indicates a success rate of 93% in achieving a post-PCI % DS of <50%, a rate of 82% in achieving an in-stent % DS of <20%, and an average in-stent % DS of 7%. These rates reflect an amalgamation of balloon-only and stent procedures and adapted methodologies (ie, use of proximal-only reference diameters and use of vessel branch points to define "in-segment") which systematically inflate the % DS values. These results were not substantially affected by either gender or health care system, and in particular there was no difference in performance between US VA and non-VA sites. The overall success rate reported in this article is based on independent QCA, but it is similar to what was reported in the main article based on visual analysis.[1] Not previously reported is a 97% success

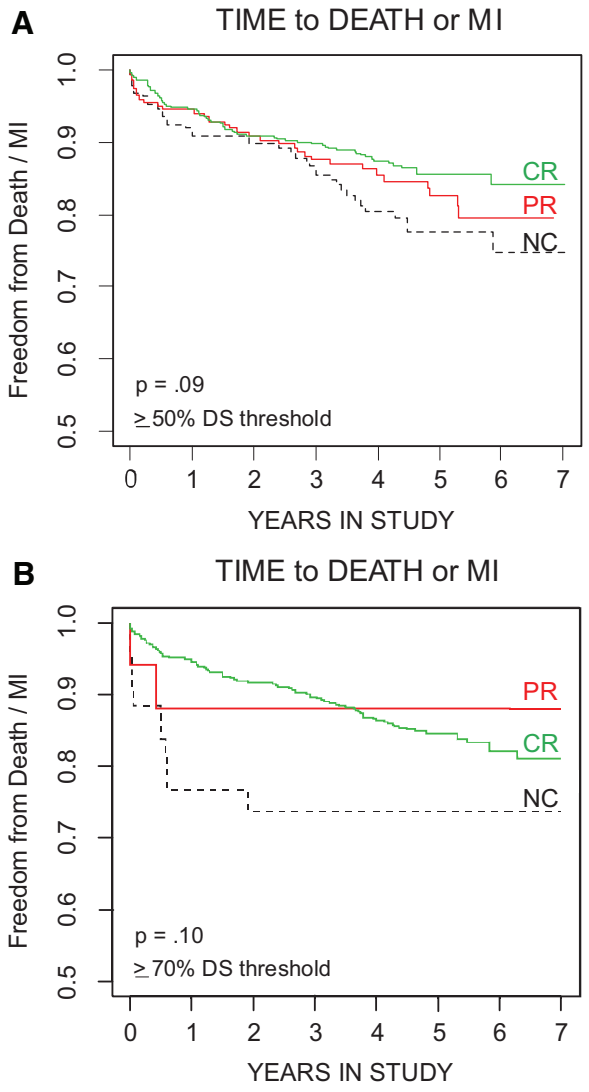

Figure 3. A and B, Influence of revascularization status on the outcome of death and nonfatal MI, excluding periprocedural MI. Panel A reflects revascularization of ≥50% lesions, and panel B reflects revascularization of ≥70% lesions. CR indicates complete revascularization; PR, partial revascularization; NC, no change after procedure.

rate of stenting based on visual analysis. This level of success is similar to the results reported to the NCDR, which also uses visual assessments (Table 5).

The MASS II trial compared medical therapy to angioplasty or surgery and reflects an era of practice that most closely resembles that in which COURAGE was conducted.[17,18] A successful revascularization in MASS II was defined as a residual stenosis of <50% and was achieved in 92% of patients in whom PCI was performed. In COURAGE, this was achieved in 93% of patients. Complete revascularization in the MASS II study was defined as a residual stenosis of <50% in all major vessels with ≥70% stenosis. This definition is somewhat ambiguous in so far as it is unclear how lesions ≥50% but <70% were considered if the operator chose to forego PCI. The complete revascularization rate was reported to be 41%. In a recent meta-analysis of trials comparing PCI to bypass, which included the MASS II trial, the reported rate of complete revascularization was 62%.[19] We analyzed revascularization of lesions ≥50% and ≥70% which yielded complete revascularization rates of 57% and 93%, respectively. Moreover, data from the NCDR indicate that in stable patients with 2- and 3-vessel disease undergoing intervention, PCI in all vessels is unusual. Two vessel intervention is reported in only 33% of patients with 2-vessel disease, and 3 vessel intervention is reported in only 3% of patients with 3-vessel disease. Accordingly, the adequacy of revascularization in the COURAGE trial appears to correspond to prior trials and observational registries[19] and is possibly better than prevailing clinical practice standards.

More important, however, is the potential influence of angiographic features of disease burden and complete revascularization on patient outcome. Although the outcome of death and nonfatal MI (excluding periprocedural MI) was not significantly affected either by initial management strategy or complete revascularization, the rates of events tended to be worse with more severe angiographic disease (Figure 1) and when revascularization was incomplete within the PCI + optimal medical therapy arm (Figure 3). The inability to show clear differences may be attributable to "underpowering" of these posthoc analyses. But the observations underscore that future trials of this nature should be limited to patients with moderate to severe angiographic burden of disease and that complete revascularization should be mandated in the PCI arm.

In conclusion, angiographic features of the treatment arms in COURAGE were well matched, and rates of PCI success and complete revascularization were high and not substantially influenced by health care system or gender. As in other cardiovascular trials, women were underrepresented in COURAGE. Unanticipated differences in disease burden between men and women underscore the imperative that future trials of this nature should recruit a more equal balance between genders. Additionally, such trials should be limited to patients with at least moderate to severe degrees of angiographic burden of disease and ischemic jeopardy in whom complete revascularization is feasible.

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Dr Mancini has received honoraria from GlaxoSmthKline, Merck, Pfizer, and sanofi-aventis. Dr Berman has received research grants and honoraria from Astellas Healthcare, Medtronic, GE, Siemens, and Molecular Insight Pharma; has ownership interest in Spectrum Dynamics; serves as a consultant for Astellas, Fluoro Pharma, and Magellan; and has received software royalties from CSMC. Dr Berger has ownership interest in Lumen and has served on the consultancy/ad board for PlaCor, Accumetrics, The Medicines Company, and Eli Lilly/Daiichi-Sankyo. Dr Spertus has received research

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