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Risk of Major Complications From Coronary Angioplasty Performed Immediately After Diagnostic Coronary Angiography: Results From the Registry of the Society for Cardiac Angiography and Interventions

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Objectives. **This study was designed to determine the risk of performing percutaneous transluminal coronary angioplasty (PTCA) at the time of diagnostic catheterization ("combined procedures").**

Background. **Health care providers are under increasing pressure to combine diagnostic and interventional coronary procedures to reduce costs. However, the risk associated with combined procedures has not been rigorously assessed.**

Methods. **A multicenter cohort study of 35,700 patients undergoing elective PTCA from 1992 through 1995 was performed to determine the risk of major complications (myocardial infarction, emergency coronary artery bypass graft surgery or death) from combined relative to staged procedures (i.e., performing PTCA at a session subsequent to diagnostic catheterization).**

Results. **The risks of major complications from combined and staged procedures were 2.0% and 1.6%, respectively (unadjusted odds ratio [OR] 1.28, 95% confidence interval [CI] 1.05 to 1.57). After adjusting for clinical and angiographic differences and clustering by laboratory, the risk from combined procedures was not significantly elevated (multivariable OR 1.18, 95% CI 0.89 to 1.55). However, several subgroups of patients did have an increased risk from combined procedures: patients with multivessel disease (multivariable OR 1.64, 95% CI 1.13 to 2.39); women (multivariable OR 1.64, 95% CI 1.05 to 2.55); patients >65 years old (multivariable OR 1.40, 95% CI 1.02 to 1.93); and patients undergoing multilesion PTCA (multivariable OR 1.53, 95% CI 1.06 to 2.21). The risk of combined relative to staged procedures decreased over the 4-year period (multivariable p = 0.029).**

Conclusions. **Combining PTCA with diagnostic catheterization appears to be safe in many patients. However, several subgroups of patients may be at increased risk. Careful patient selection will most likely remain critical to ensuring the safety of combined procedures.**

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There are >400,000 percutaneous transluminal coronary angioplasty (PTCA) procedures performed each year in the United States, at an estimated cost of 6 billion dollars (1). Health care providers are under intense pressure from third-party payers to reduce the cost associated with PTCA (2). One proposed cost reduction strategy is to perform PTCA at the time of the initial diagnostic catheterization ("combined," "ad hoc" or "add-on" procedures [3,4]). Along with the potential for decreasing length of hospital stay and costs (3), these "combined" PTCAs may also reduce the risk of peripheral vascular complications and patient exposure to radiation and contrast agents (3).

However, the potential benefits of performing combined procedures must be weighed against their possible risks. Performing PTCA immediately after a diagnostic procedure involves prolongation of the catheterization procedure and may not allow for as careful an assessment of the indications for or technical difficulty of the procedure as may occur in "staged" procedures (i.e., performing the diagnostic catheterization and subsequently having the patient return to the catheterization laboratory for PTCA if clinically indicated [5]). The American College of Cardiology (ACC) and American Heart Association (AHA) recommend that combined PTCA is "particularly suited" for patients with unstable angina who cannot be stabilized, patients with restenosis after previous angioplasty and patients undergoing PTCA for acute myocardial infarction (AMI). However, in the many other patients who might be

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Abbreviations and Acronyms

ACC = American College of Cardiology
AHA = American Heart Association
AMI = acute myocardial infarction
CABG = coronary artery bypass graft surgery
CI = confidence interval
OR = odds ratio
PTCA = percutaneous transluminal coronary angioplasty
SCA&I = Society for Cardiac Angiography and Interventions

candidates for combined PTCA, there are few data to support the use of this procedure. Studies that have assessed the risk of combined procedures in these patients have been limited by their small sample sizes (3,4,6–9), their lack of a control group (6,7,9), their performance in only single institutions (many of which had specific protocols to try to ensure the safety of combining PTCA with diagnostic angiography [8,9]) and their highly selected patient groups (6,7). Thus, there remains debate (8–11) over the proper use of combined procedures at a time when economic forces are creating increasing pressure to do more (3,4,8,9). Before recommendations are made to encourage the routine use of combined procedures, it is critically important to assure that patients are not unknowingly placed at increased risk.

Thus, this study was designed to 1) determine if the performance of combined procedures increases the risk of major complications compared with staged procedures; and 2) explore which patient subgroups may be at higher risk from combined relative to staged procedures.

Methods

Data base. This study used the 1992 through 1995 registries of the Society for Cardiac Angiography and Interventions (SCA&I). The SCA&I Registry, established in 1979, is a voluntary, prospective, multicenter, data collection instrument allowing individual laboratories and operators to track their activity. Details of the participating laboratories, data collection techniques and variable definitions have been previously reported (12–14). An independent review of 18 laboratories contributing 56% of procedures to the 1992 Registry confirmed that more than 99% of procedures performed at these laboratories were entered into the data base.

Patient groups and laboratories. From January 1, 1992 through December 31, 1995, a total of 54,607 balloon angioplasty procedures were performed in 61 centers participating in the SCA&I Registries. Twenty-three centers contributed data to all 4 years of the Registry. Because of intrinsic differences in the risk of complications with devices other than balloon catheters (15) and the lack of information in the data base on whether stents (the most commonly used "other device") were used as planned or bailout therapy, only balloon procedures were included in this analysis. Repeat PTCAs (13,594 procedures) also were excluded because 1) patients undergoing a repeat PTCA represent a lower risk group than patients undergoing a first PTCA (16); and 2) it was not possible to determine if these repeat PTCAs were performed on restenotic or de novo lesions (a potentially important predictor of complications [17]). To eliminate the bias that could result from including combined procedures that were performed either because of hemodynamic instability or a complication that occurred during diagnostic angiography or because of indications that could be associated with an increased risk of complications, we excluded patients undergoing emergency PTCA (any unplanned PTCA [14]), patients in shock (any hemodynamic instability before PTCA [14]) and PTCAs performed within 24 h after an AMI, regardless of whether PTCA was combined or staged (total of 5,313 patients excluded, leaving 35,700 patients for this study). To identify subgroups that might be at increased risk from combined procedures, patients were further divided into prespecified risk groups on the basis of age, gender, ACC/AHA Task Force classification of lesion type (5), number of lesions attempted, laboratory volume and the presence or absence of heart failure, diabetes mellitus, AMI within 2 to 14 days before PTCA, unstable angina and multivessel disease.

Study variables. Combined procedures were defined as coronary angioplasty performed during the same session as a diagnostic catheterization. All other procedures were considered "staged" procedures. The data entry system used for this Registry required that this variable be recorded for all patients.

The primary outcome variable, "major complication," was defined as any one or more of the following: 1) emergency coronary artery bypass graft surgery (CABG) as a result of the procedure; 2) death occurring any time during the hospital period; or 3) myocardial infarction, as evidenced by a rise in serum creatine kinase, MB fraction to at least twice the normal level or development of new Q waves on the electrocardiogram within 24 h of the procedure. Patients with more than one complication were counted only once.

The procedure type (combined vs. staged) was recorded for all patients, and complete data for all potentially confounding variables (Table 1), other than "multivessel disease," were available for 99% of patients. Detailed data on the variable "multivessel disease" were available in the angioplasty data bases for only 14,679 patients (41.1%) because the complete information on coronary anatomy in all patients was recorded in separate diagnostic catheterization data bases that could not be linked to patient records in the angioplasty data bases. Although information on the contrast volume used and arterial time required for any PTCA was recorded, these data represented the *total* contrast volume and time required both for the procedure and for the management of any complications resulting from the procedure; because the amount of contrast volume and arterial time recorded were thus determined by the occurrence of complications, it was not appropriate to include these variables as potential confounders in the analyses of complications.

Table 1. Clinical Characteristics of Patients by Procedure Type

Clinical Characteristic	Total Sample (n = 35,700)	Procedure Type [% (no.) of pts] Combined (n = 6,152)	Staged (n = 29,548)	p Value*
Age >65 years	42.8 (15,272)	41.6 (2,561)	43.0 (12,711)	0.046
AMI within last 2 to 14 days	17.9 (6,391)	27.8 (1,711)	15.8 (4,680)	< 0.0001
Aortic valve disease	0.1 (50)	0.6 (36)	0.04 (14)	< 0.0001
Congestive heart failure	3.7 (1,327)	4.0 (244)	3.7 (1,083)	0.27
Chronic renal insufficiency	1.8 (626)	1.8 (108)	1.8 (518)	1.00
Dialysis	0.4 (160)	0.5 (30)	0.4 (130)	0.60
Diabetes mellitus	16.9 (6,020)	17.0 (1,047)	16.8 (4,973)	0.72
Geographic region†				< 0.0001
Northeast	43.1 (15,377)	13.8 (2,120)	86.2 (13,257)	
South	20.9 (7,446)	18.0 (1,338)	82.0 (6,108)	
Midwest	23.1 (8,256)	24.3 (2,005)	75.7 (6,251)	
West	1.9 (686)	34.3 (235)	65.7 (451)	
Canada	10.9 (3,900)	11.6 (453)	88.4 (3,447)	
South America	0.1 (35)	2.9 (1)	97.1 (34)	
Graft attempted	4.7 (1,668)	4.3 (264)	4.8 (1,404)	0.13
Hypertension	40.3 (14,400)	42.5 (2,615)	39.9 (11,785)	0.0001
LMCA attempted	0.5 (162)	0.4 (25)	0.5 (137)	0.60
Laboratory volume ≤200 cases/year	12.1 (4,332)	15.4 (948)	11.5 (3,384)	< 0.0001
Lytic therapy before PTCA	6.7 (2,403)	11.0 (674)	5.9 (1,729)	< 0.0001
Mitral valve disease	0.4 (138)	1.7 (105)	0.1 (33)	< 0.0001
Multilesion PTCA	24.7 (8,818)	18.8 (1,159)	25.9 (7,659)	< 0.0001
Multivessel disease‡	33.3 (4,891)	34.8 (1,851)	32.5 (3,040)	0.004
Previous CABG	10.8 (3,63)	10.2 (627)	11.0 (3,236)	0.075
Previous valve surgery	0.3 (103)	0.3 (21)	0.3 (82)	0.43
Unstable angina	35.2 (12,573)	42.5 (2,613)	33.7 (9,960)	< 0.0001
Women	32.3 (11,529)	32.5 (2,001)	32.2 (9,528)	0.67
Worst lesion type attempted				
Type A	36.5 (13,026)	36.8 (2,261)	36.4 (10,765)	0.018
Type B	50.6 (18,054)	51.4 (3,162)	50.4 (14,892)	
Type C	12.9 (4,620)	11.8 (729)	13.2 (3,891)	

*Chi-square test for differences in clinical characteristics between combined and staged procedures. †Percentages are row percentages for geographic region (e.g., 13.8% of coronary angioplasties performed in the Northeast were done during a diagnostic catheterization). Geographic region was defined as in a previous study (1). ‡For subset of patients with known multivessel disease status (n = 14,769). AMI = acute myocardial infarction; CABG = coronary artery bypass graft surgery; LMCA = left main coronary artery; PTCA = percutaneous transluminal coronary angioplasty; pts = patients.

Statistical analysis. The univariate association between PTCA timing (combined vs. staged) and major complications was determined using odds ratios (ORs) with 95% confidence intervals (CIs) and the chi-square or Fisher's exact test. Staged procedures were the reference group.

To determine if the effect of combined procedures on outcomes was due to differences in characteristics of patients treated with combined versus staged procedures, multivariable logistic regression (18) was performed. Along with the timing of PTCA, all variables in Table 1 (initially excluding multivessel disease) plus year of procedure were included in all models to provide as complete control of confounding as possible (19). In addition, the standard errors of the regression coefficients were corrected for clustering by laboratory (20,21). A secondary analysis was also performed in which a series of indicator variables for individual laboratories was included to assess the effect of laboratory as a confounder. Separate models that included multivessel disease also were derived in the subset of patients with known multivessel disease status. Interactions between PTCA timing and the prespecified risk groups were assessed using the relevant product-term in the multivariable models. The changes in complication risk and PTCA timing over the 4 years of this study were assessed using the Mantel-Haenszel test for linear association (18). To determine the change in complication risk over time, the variable "year" (which as a continuous variable demonstrated an inverse linear association with complications in univariate analyses) was included as a continuous variable in the multivariable models.

All statistical analyses were performed using the SPSS (version 6.1) and Stata (version 5.0) statistical programs, and statistical significance was defined as a two-sided p value < 0.05.

Results

Patient and procedural characteristics. There were 6,152 combined procedures (17.2% of all elective PTCAs) performed in the 4 years of this study. The proportion of

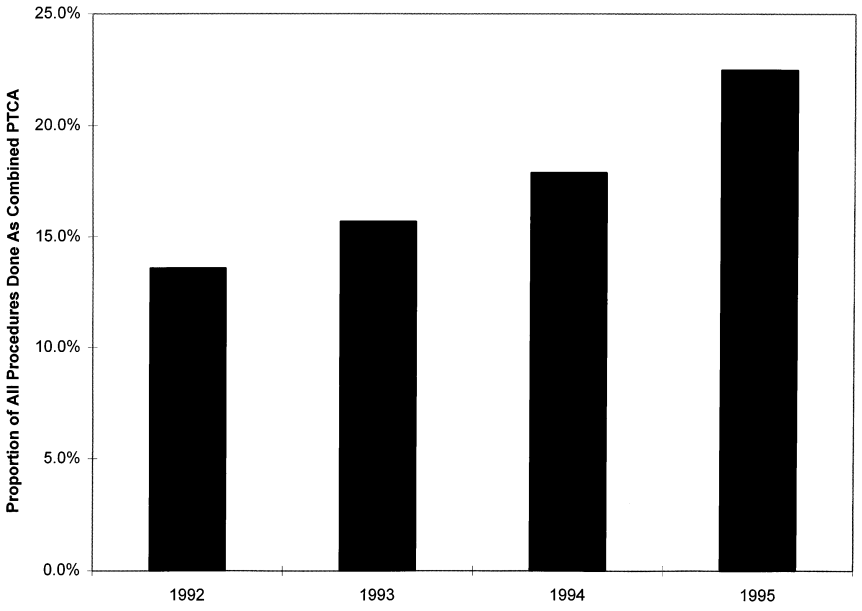

Figure 1. Percentage of all procedures that were done as combined percutaneous transluminal coronary angioplasty (PTCA) in each year.

combined procedures performed per year in any one laboratory ranged from 0% to 86%, and there was an increase in the proportion of combined procedures from 13.6% in 1992 to 22.5% in 1995 ($p < 0.0001$) (Fig. 1). An increasing proportion was also found when the analysis was restricted to laboratories contributing data to all 4 years ($p < 0.0001$), suggesting that the proportion of combined procedures increased within laboratories, not that laboratories that did more combined procedures entered the Registry in later years.

The clinical characteristics differed between patients undergoing combined versus staged procedures (Table 1). Although some potential risk factors were more prevalent in patients undergoing combined procedures (e.g., multivessel disease, unstable angina, lower laboratory volume, aortic valve disease and recent infarction or thrombolytic therapy), others were more prevalent in patients undergoing staged procedures (e.g., older age, multilesion PTCA and complex lesion PTCA).

Relation between PTCA timing and outcomes. The overall risks of complications were mortality 0.2%, emergency CABG 1.1%, AMI 0.5% and major complications 1.6%. In unadjusted analyses, there was a statistically significant 28% greater relative risk of major complications (a 0.4% absolute risk difference) from combined procedures compared with staged procedures in all patients (Table 2), and a 35% greater relative (0.6% absolute) risk in the subset of patients with known multivessel disease status (OR 1.35, 95% CI 1.06 to 1.72). There was no significant difference in the OR for combined procedures in those with known multivessel disease status compared with those with unknown status (multivariable $p = 0.2$ for interaction). After adjusting for the year, the effects of clustering on laboratory and all variables in Table 1 except multivessel disease, there was no detectable association between PTCA timing and complications (OR 1.18, 95% CI 0.89 to 1.55) (Table 2). Including multivessel disease in the model produced similar results (OR 1.23, 95% CI 0.95 to 1.58). In a model that corrected for clustering but that did not adjust for confounders, the OR was 1.28 (95% CI 0.92 to 1.80), and in a model adjusting for confounders but that did not correct for clustering, the OR was 1.21 (95% CI 0.99 to 1.49). In the analysis that included indicator variables for laboratory as covariates, the OR was 0.89 (95% CI 0.70 to 1.12). The test for an interaction between laboratory and PTCA timing was not significant ($p = 0.9$), indicating that the relative risk of combined versus staged procedures was statistically indistin-

Table 2. Univariate and Multivariable Association Between Outcomes and Procedure Type

			OR (95% CI)	
Outcome	Incidence (%) in Combined Procedures (n = 6,152)	Incidence (%) in Staged Procedures (n = 29,548)	Univariate OR for Combined Relative to Staged Procedures	Multivariable OR*
In-hospital death	0.29 (0.17–0.46)	0.16 (0.12–0.21)	1.84 (1.07–3.17)	1.62 (0.90–2.93)
Emergent CABG	1.34 (1.07–1.66)	1.09 (0.98–1.22)	1.22 (0.96–1.56)	1.15 (0.86–1.56)
AMI	0.73 (0.54–0.98)	0.15 (0.11–0.70)	1.56 (1.11–2.18)	1.40 (0.72–2.72)
Major complication	2.01 (1.67–2.39)	1.57 (1.43–1.71)	1.28 (1.05–1.57)	1.18 (0.89–1.55)

*All variables in Table 1 are in the model, except for multivessel disease, and confidence intervals are adjusted for clustering by laboratory. CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

Table 3. Association of Procedure Type With Major Complications for Different Risk Groups of Patients*

Risk Group	Procedure Type [% (no.) of pts with major complications]		OR for Combined Relative to Staged Procedures (95% CI)*	p Value for Test for Interaction†
	Combined (n = 6,152)	Staged (n = 29,548)		
Total patients (n = 18,568)	2.0 (123)	1.6 (463)	1.18 (0.89–1.55)	
Age				0.057
≤65 years (n = 20,409)	1.7 (62)	1.6 (264)	1.02 (0.73–1.41)	
>65 years (n = 15,272)	2.4 (61)	1.6 (199)	1.40 (1.02–1.93)	
Gender				0.02
Female (n = 11,529)	2.6 (52)	1.5 (141)	1.64 (1.05–2.55)	
Male (n = 24,171)	1.7 (71)	1.6 (322)	0.98 (0.75–1.28)	
Multivessel disease‡				0.03
Yes (n = 4,891)	3.0 (55)	1.6 (49)	1.64 (1.13–2.39)	
No (n = 9,788)	1.7 (60)	1.6 (102)	1.02 (0.76–1.37)	
Number of lesions attempted				0.11
One (n = 26,882)	1.9 (93)	1.6 (345)	1.09 (0.80–1.49)	
More than one (n = 8,818)	2.6 (30)	1.5 (118)	1.53 (1.06–2.21)	

*Only statistically significant results are shown (see text for results of all subgroups). †Adjusted for all other variables in Table 1, except for multivessel disease, and adjusted for clustering by laboratory. ‡For subset of patients with known multivessel disease status. Abbreviations as in Tables 1 and 2.

guishable from laboratory to laboratory. Similar to the results using the composite outcome of major complications, there was a statistically significant increased risk of death and AMI from combined procedures in univariate but not multivariable analyses (Table 2).

Risk in subgroups of patients. There was no significant difference in the risk of combined procedures relative to staged procedures when patients were stratified by annual procedural volume in the laboratory performing the PTCA or by the presence or absence of a recent infarction, congestive heart failure, diabetes mellitus, unstable angina and complex lesion type (type A vs. B or C) PTCA (all tests for interaction $p > 0.10$). In addition, none of these individual low or high risk subgroups exhibited a significant difference in risk from combined compared with staged procedures.

However, the relative risks of combined versus staged procedures did differ by age, gender, multivessel disease status and number of lesions attempted (Table 3). Older patients had an increased risk from combined relative to staged procedures that was different from younger patients (test for interaction $p = 0.057$ when multivessel disease was excluded from the model and $p = 0.020$ when multivessel disease was included). The multivariable OR from combined procedures in patients >65 years old was significantly elevated whether multivessel disease was included in the model (Table 3) or not (OR 1.52, 95% CI 1.09 to 2.10). The increased risk in older patients was also statistically indistinguishable across the 4 years of the study (multivariable $p = 0.11$ for interaction by year).

Women also had an increased relative risk from combined procedures that was significantly different (interaction $p = 0.02$) from the risk in men. The OR from combined procedures relative to staged procedures was significantly elevated in women but not in men (Table 3). This increased risk persisted in women when further adjusting for multivessel disease in the subset of patients with known multivessel disease status (OR 1.84, 95% CI 1.24 to 2.72). The increased risk in women was statistically indistinguishable across the 4 years of the study (multivariable $p = 0.09$ for interaction).

The OR in multilesion PTCA was significantly elevated and was different from the OR in single-lesion PTCA (Table 3). After adjusting for multivessel disease status, the relation persisted (test for interaction $p = 0.15$, multivariable OR 1.63 in multilesion PTCA, 95% CI 1.04 to 2.57). The risk from multilesion PTCA was statistically indistinguishable across the 4 years of the study (multivariable $p = 0.40$ for interaction). Similarly, the OR for combined procedures in patients with multivessel disease was both significantly elevated and significantly different ($p = 0.031$) from the OR in patients with single-vessel disease (Table 3). The multivariable ORs in patients with multivessel disease were similar in each year of the study (multivariable $p = 0.80$ for interaction). In those patients with multivessel disease undergoing ad hoc multilesion PTCA, the risk of complications was more than twofold greater compared with similar patients undergoing staged procedures (multivariable OR 2.30, 95% CI 1.34 to 3.98).

Change in patient group and complication risk over time by procedure type. The prevalence of several risk factors for complications (diabetes mellitus, recent infarction, complex lesion PTCA and unstable angina) increased in patients undergoing both combined and staged procedures over the 4 years of the study (all p values <0.01). The mean age increased somewhat ($p < 0.01$), and the prevalence of multivessel disease increased dramatically (23% in both 1992 and 1993 and 47% in 1994 and 1995; $p < 0.0001$) in staged procedures but not in combined procedures ($p = 0.54$ for age; $p = 0.88$ for multivessel disease). Women were somewhat more likely to undergo combined ($p = 0.05$) but not staged ($p = 0.23$) procedures in later years.

There was a significant overall decrease in the risk of major complications over time (1.9% in 1992, 1.7% in 1993, 1.4% in 1994 and 1.5% in 1995; test for trend $p = 0.006$). Although the

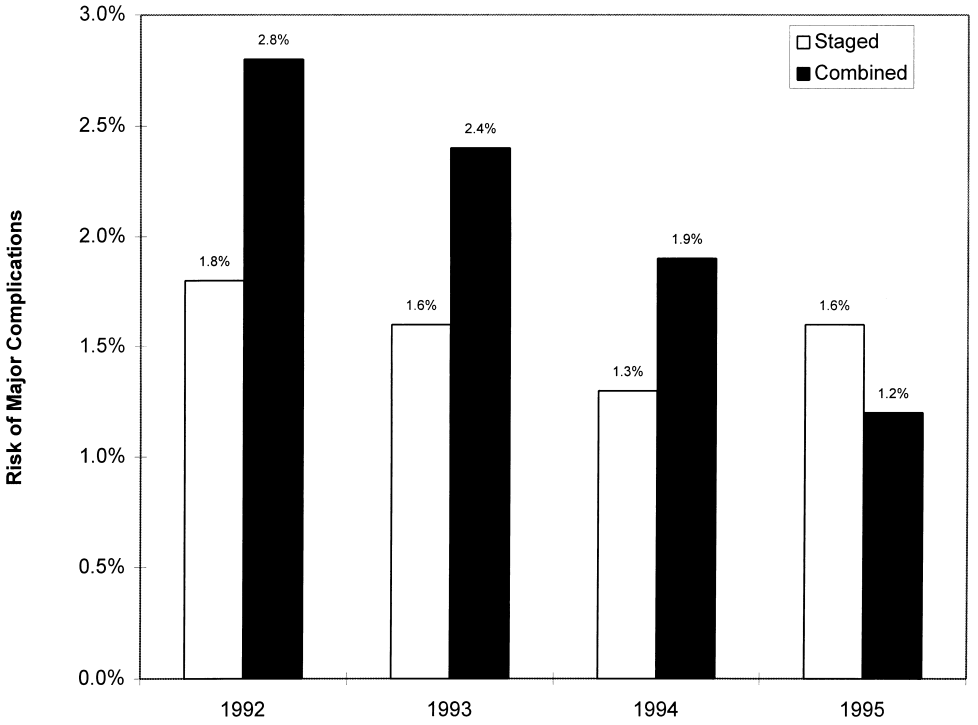

Figure 2. Risk of major complications (%) by year among patients undergoing coronary angioplasty in all participating laboratories.

absolute risk from combined procedures decreased over time (multivariable $p < 0.001$), the risk did not decrease from staged procedures over time (multivariable $p = 0.13$) (Fig. 2). Consequently, the *relative* risk decreased over time; for each year of the study, the multivariable ORs (95% CIs) for major complications from combined versus staged procedures decreased: 1.43 (0.89 to 2.30), 1.32 (0.80 to 2.20), 1.16 (0.75 to 1.78) and 0.70 (0.44 to 1.09) in 1992, 1993, 1994 and 1995, respectively. This decrease in relative risk was statistically significant when adjusting for laboratory and all variables in Table 1 except multivessel disease (test for linear interaction of procedure timing by year $p = 0.029$; regression coefficient −0.1740 for interaction term). When also adjusting for multivessel disease in the smaller subset of patients with known multivessel disease status, the test for interaction was no longer statistically significant ($p = 0.24$), although the regression coefficient was similar (−0.1156). Limiting the analyses to only those laboratories that contributed data to all 4 years of the study did not substantively change any of the aforementioned results.

Discussion

Association between combined procedures and complications. In this study, combined procedures were not associated with a greater risk of major complications than staged procedures after accounting for 1) differences in the clinical characteristics of patients undergoing these procedures and 2) clustering of outcomes by laboratories. Furthermore, there was no evidence for interlaboratory variability in the relative risk of combined procedures. An increased risk was also observed for each of the specific outcomes, but, again, after appropriate multivariable adjustments these associations were no longer statistically significant.

This overall negative conclusion must be viewed cautiously, however. It is not known what factors minimize the risk of combined procedures or were responsible for the decrease in risk over time. Other, more intangible variables such as individual operator experience and catheterization laboratory "systems" (e.g., algorithms, clinical pathways) were not included in the present data base but may be critically important in ensuring the safety of combined procedures.

Risk in subgroups. In addition, the risk of combined procedures may be increased in certain subgroups of patients. The data suggest that older patients, women, patients with multivessel disease and patients undergoing multilesion PTCA (all prespecified subgroups) may be at increased risk from combined relative to staged procedures. In the absence of further studies, one can only speculate why this may be so. Combined procedures may increase the risk in these subgroups if the risk or technical difficulty of performing PTCA in these patients is not as well appreciated during combined procedures as during staged procedures (e.g., if cine films are not critically reviewed before angioplasty) or if the performance of a combined procedure results in increased contrast load, more intimal disruption and destabilization of plaque (22,23) and/or inadequate maintenance of anticoagulation or antiplatelet therapy throughout the course of treatment (24–26).

For example, women may be at increased risk because the smaller vessel size in women (27,28) may lead to a higher likelihood of improper balloon sizing or failure to recognize lesion complexity when relying on non–cine film techniques

with lesser resolution (29,30) during a combined procedure. It is also possible that, because of women's smaller body surface area, the amount of contrast used in combined procedures represents an excessive dye load. Similarly, multilesion PTCAs in patients with multivessel disease represent more complex, prolonged procedures; performing them immediately after a diagnostic catheterization could increase the risk if the technical difficulty is not appreciated before proceeding or if the procedure requires excessive time and contrast dye loads. Similar arguments can be made for older patients.

Change in complication risk over time. There was a significant decrease in the absolute risk of complications from ad hoc PTCAs over the 4 years encompassed by this study, despite their use in higher risk patients. Equally important, there was a decrease in the relative risk of combined compared with staged procedures over time. This suggests that improvements in technical abilities, equipment, procedural protocols and/or patient selection procedure may also be important to ensuring the safety of combined PTCA. Our data do not allow us to explore the reasons for this improvement in outcomes, and further studies to determine what factors improve the safety of same-sitting PTCAs will be important to ensure continued improvement in patient outcomes.

Comparison with other studies. Although previous studies have suggested that performing PTCA early after the onset of unstable angina increases the risk of complications compared with delaying the procedure (25,31,32), no studies that have directly compared combined with staged procedures have shown an increased risk from combined procedures. However, many of these later studies focused on carefully selected groups of patients with unstable angina (6,7) or included only repeat PTCAs (33) in which the benefits of known anatomy and previous experience might make combined procedures as safe as staged procedures. Several studies also used specific protocols for combined procedures that required careful assessment of coronary anatomy, patient risk and appropriateness of PTCA before proceeding with the procedure (8,9). In addition, previous studies were of small size and thus could not exclude the possibility of a clinically significant increase in risk from combined procedures. For example, the largest study to date (8) could not exclude a relative risk as high as 2.0 (based on our calculations of the 95% CI). Finally, no previous study has included analyses that adjust for differences in clinical and anatomic characteristics.

Our large, multicenter study included most patients undergoing a first balloon PTCA, excluding only 13% of first angioplasties because they occurred in patients who were clinically unstable, required an emergency PTCA or underwent angioplasty as therapy within 24 h of an AMI. Thus, across numerous clinical settings and laboratories, combined procedures were not independently associated with an increased risk of complications, except in the subgroups described. It is important to note that 71% of all patients had at least one risk factor for increased risk from combined PTCA (age >65 years, female gender, multivessel disease or multilesion PTCA). Thus, increasing the overall use of combined PTCAs, particularly in these groups of patients, could increase the number of complications attributable to this protocol.

Study limitations. There are several important limitations to this study. First, the finding of increased risk in subgroups of patients must be interpreted cautiously because they were observed among numerous subgroup analyses in the setting of an overall negative finding. Nonetheless, these subgroups were specified in advance, and the increased risk is both biologically plausible and consistent over the 4 years of the study, suggesting that these findings are valid and that a substantial proportion of patients may not be appropriate for combined procedures. Second, although the results cannot necessarily be generalized to patients requiring PTCA for restenosis or for conditions refractory to medical therapy, these patients would be expected to be particularly suited for combined procedures, as outlined in the ACC/AHA guidelines (5). Importantly, our results should be applicable to the majority of patients undergoing a first balloon angioplasty, as 87% of all patients undergoing their first angioplasty in participating laboratories were included. It will, of course, be important for future studies to assess the effects of new devices and adjuvant therapies such as stents and IIb/IIIa inhibitors on the relative risk of combined versus staged procedures, particularly in high risk patients. Third, differential misclassification of outcomes ("gaming") could bias the results if laboratories doing more combined procedures tended to underrepresent their complications, thus underestimating the true association between combined procedures and complications. We believe that this is unlikely because the SCA&I Registry data base is confidential and is not used by external auditors. Fourth, combined procedures included complications from both angiography and angioplasty, whereas staged procedures included complications only from angioplasty. However, the rate of major complications that are attributable to diagnostic angiography is extremely low (12), and patients with complications of diagnostic angiography requiring PTCA were excluded from this study. Thus, this would be unlikely to bias the results in favor of staged procedures.

Conclusions. Given the enormous pressure for the medical care system to become more cost efficient, performance of combined procedures has been advocated as a means to reduce costs (3,4,8,9) and is likely to be increasingly encouraged by health care payers and providers. This study suggests that performing PTCA at the time of the diagnostic catheterization is, overall, as safe as performing it later and that the procedure has become safer over time. However, there are subgroups that may be at greater risk with this strategy. In particular, performing more complex procedures such as multivessel PTCA or PTCA in patients with multivessel disease at the same time as the diagnostic procedure appears to be associated with an increased risk of complications. The risk of the combined procedure also appears higher in older patients and in women. Further study is needed to confirm these findings. In the meantime, proper patient selection for combined PTCA and continued consideration of the other risks and benefits of

combined PTCA is likely to remain important in assuring the continued safety of this procedure.

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