Point of View

Computerized Tabulation of Cine Coronary Angiograms
Its Implication for Results of Randomized Trials

René G. Favaloro, MD

"Because numbers are 'the language of science,' the work will need new forms of biostatistical creativity. Because any language, however, depends on basic information and reasoning, the fundamental activities will require that clinical investigators expand their creative horizons to give that scientific language a proper derivation, a sensible grammar, and a meaningful content.'"

The introduction of cine coronary angiography in 1958 clarified the anatomy of the coronary artery tree and as a consequence enabled clarification of the natural history of coronary arteriosclerosis, correlation with the clinical spectrum, selection of candidates for coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA), and proper evaluation of the results with similar medically treated patients.

Proudfit and coworkers clearly demonstrated, as corroborated by others, that patients with one-, two-, or three-vessel disease or left main trunk obstruction had different prognoses. Analysis of cine ventriculograms emphasized that the status of the left ventricle also plays a significant role in conjunction with the number of vessels involved. The standardization of patients with coronary arteriosclerosis into one-, two-, or three-vessel disease or left main trunk obstruction has been very helpful and still is the framework in which different treatments are compared. However, as previously noted, this classification is not sufficient because it does not take into consideration the following significant features of the coronary circulation that deepen our understanding of prognoses among patients with coronary arteriosclerosis: location of obstruction, size of the vessel involved, morphology of the distal vessel beyond the obstruction, and collateral circulation.

Proximal Obstruction
The importance of proximal obstruction was clearly demonstrated by Mock and collaborators, who found that a prominent decline on survival compared with nonproximal obstruction. The most important report from the Coronary Artery Surgery Study (CASS) concerns the prognostic value of angiographic indexes of coronary artery disease. Ringqvist et al presented for the first time in 1983 a superb analysis of the cine angiograms on 8,535 registry patients during a 6-year period. Although the authors used the Cox proportional hazards or regression model and stratified life-table or actuarial analysis, they concluded that simple indexes of severity (number of vessels diseased, left ventricular score, and number of proximal stenosis) are preferable to the more complex ones, and they suggested that the combination of these three simple indexes of severity are powerful predictors of prognosis. As a result of this study, survival rate is shown to comprise a range of 92±2% to 16±14%. Table 1 shows that the location of the obstruction plays a significant role in survival. In addition, a recent CASS study of 2,023 patients with two-vessel disease placed particular emphasis on the role of proximal obstruction, and another study examined 22 aspects of left anterior descending morphology in relation to anterior myocardial infarction. Recently, three CASS reports by Myers et al on patients with three-vessel disease presented data that divided patients into those with no, one, two, or three proximal obstructions. This method of classifying proximal obstructions would have been useful in every CASS report to give a more realistic interpretation of the results and clues as to the causes of the extremely low mortality rate among patients under medical treatment in the randomized series.

Collateral Circulation
Nearly three decades after the introduction of coronary angiography by Sones and Shirey, it is discouraging to see that the collateral circulation is not properly interpreted or even mentioned,
Although it can be clearly identified by the improved quality of cine angiography. The important concerns are whether the donor artery is normal or mildly diseased or whether it has a severe obstruction proximal to the origin of collaterals. An example is presented in Figure 1A–D. The lack of comprehensive information about coronary artery collaterals is evident in reports on this subject\(^\text{22–25}\) and in the CASS protocol,\(^\text{26}\) which states, “Collaterals are not specifically described because they are often poorly visualized; however, their presence or absence are noted. No attempt is made to estimate the quantity of collateral flow.” The use of coronary angioplasty and intracoronary thrombolysis introduced a new field in which collaterals can be properly investigated. Recent reports\(^\text{27–34}\) revealed that collaterals can limit myocardial ischemia.

**Coronary Artery Size and Distal Runoff**

As pointed out in 1978,\(^\text{12}\) the importance of the size of the coronary artery which determines the area of myocardial muscle perfused is exemplified in Figure 2. The runoff of the distal segments beyond the obstruction should be carefully established because it will predict the flow of the vessel under medical treatment or after revascularization (CABG or PTCA). It is logical to think that diffuse atheromatous changes, distal to the site of the severe obstruction, will impair even further coronary flow and blood reserve and that the vessel will be at risk of becoming totally occluded.

**Left Ventricular Status**

The status of the left ventricle is a very important factor—perhaps the most important predictor of survival—in relation to the natural history of coronary patients, and this status is recognized by all cardiologists and cardiovascular surgeons. Originally, in The Cleveland Clinic, only the right anterior oblique projection was used. Due to observations during surgery, mainly among patients with poor ventricular contraction or a ventricular aneurysm, the author suggested to Sones that the left anterior oblique projection was also necessary to obtain a proper visualization of the lateral wall and septum. Both projections allowed analysis of the overall architecture of the left ventricle and multiple segments around the left ventricular circumference. It is unacceptable at the present time that evaluation of the left ventricle be performed only throughout analysis of the right anterior oblique projection. As an example, “Even though the clinical sites were encouraged to obtain a 60–70% left anterior oblique, only the right anterior oblique is utilized in CASS publications because left anterior oblique is seldom available, as can be demonstrated by the data of one of the regular Consensus reading sessions of the Quality Control Subcommittee established from four of the participating centers recognized for their expertise

<table>
<thead>
<tr>
<th>TABLE 1. Six-Year Survival Percentages±1.96 by Number of Diseased Vessels, Number of Proximal Diseased Arterial Segments, and Left Ventricular Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseased vessels (n)</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
</tbody>
</table>

Numbers in parentheses are the numbers of patients at enrollment.  
Zero includes patients with minimal or moderate disease.  
Left ventricular score: 5–11, normal to mild; 12–16, moderate; 17–30, severe (CASS nomenclature\(^\text{26}\)).
and special interest in angiography (Boston University, Miami Heart Institute, Montreal Heart Institute, and St. Luke's Hospital Center)." As a result, wall motion score, left ventricular score, corrected left ventricular score in the original protocol of CASS, and myocardial jeopardized index included later are of limited value.

A coronary artery clinical research protocol that takes into account the above landmarks is presented.

**Computerized Tabulation**

The computerized tabulation program was developed for the Macintosh Plus computer with a File Maker program. Figures 3–5 describe the data base of the program.

As shown in Figure 3A, the program includes the clinical diagnosis, risk factors, catheterization technique, and revascularization procedure (PTCA or CABG). The clinical diagnosis tabulation that we follow in Buenos Aires (a detailed description has been published) is similar to others with the exception of unstable angina, which is mainly divided into progressive angina classes III and IV and intermediate syndrome.

Figure 3B lists the terminology used to tabulate the lesion in the coronary tree, the morphology of the lesion, and the morphology of the distal vessel. The classification of the different coronary segments follows the CASS protocol with minor changes and categorizes the lateral branch of the right coronary...
artery as lesion 11, which is an important source of collaterals toward the anterior descending in many patients, and the obstruction of the midcircumflex as lesion 20. The morphology of the lesion has become very important and should be codified properly to classify the results of PTCA.

Figure 3C tabulates the percentage of the obstruction in different coronary segments, the morphology of the lesion and of the distal vessel, and the dominance of the coronary circulation. In most patients, the size of the coronary artery is related to the dominance of the circulation. For instance, the right coronary artery is small when it does not have a posterior descending artery, medium in a balanced circulation, and large when it perfuses portions of the left ventricle (dominant right). The anterior descending branch sizes are clearly exemplified in Figure 2; it is small when it perfuses only the upper portion of the anterolateral wall, medium when it does not reach the apex of the left ventricle, and large when it perfuses the entire anterolateral wall, including the apex and sometimes part of the diaphragmatic wall of the left ventricle. The circumflex coronary artery is small when it perfuses only the lateral wall of the left ventricle, medium in a balanced circulation, and large when the left coronary artery is dominant.

Figure 3D describes the tabulation of collateral circulation. First, it is important to point out the segment in which collaterals originate and the segment at which they are connected, but this is not sufficient. It is essential to state whether collaterals are compromised. The collateral flow is compromised if there is a significant obstruction in the proximal segment of the coronary artery that pro-
vides the collateral vessels, and it is not compromised if the donor artery is free of significant proximal obstruction. Collaterals are totally adequate when the area contracts normally at rest and at exercise, partially adequate when the area contracts normally only at rest, and not adequate when contractions are abnormal.

In Figure 3E, information regarding the status of the left ventricle is carefully tabulated, following CASS nomenclature, in both right and left anterior oblique projections with 10 different segments. The wall motion is described as normal, hypokinetic (reduced inward motion of the segment during systole), akinetic (complete absence of systolic inward motion), dyskinetic (systolic outward motion), or aneurysmatic (an area that clearly protrudes from the expected outline of the left ventricular chamber during systole and remains so during diastole). The ejection fraction is coded as normal or mildly (>0.4), moderately (0.3–0.4), or severely (<0.3) reduced. The use of Doppler echocardiography is very helpful if the findings by cine angiography are insufficient to calculate the ejection fraction.

Figure 4 shows the tabulation of the surgical protocol, including the nature of the graft, the site of the proximal anastomosis, the type of distal anastomosis, the location at which the distal anastomosis is performed (following the terminology shown in Figure 3B), the quality of the graft, and the state of the bypassed coronary artery as observed by the surgeon during the operation. In addition, endarterectomies are coded if they are used. Finally, perioperative myocardial infarction, including location and causes of death, is also tabulated.

Figure 5 shows the tabulation of the PTCA protocol, which indicates the location at which dilatation is performed, following the terminology shown in Figure 3B, the amount of the initial obstruction, the morphology of the lesion and of the distal vessel, the type of catheter used, the size of the balloon, the pressure, the time used, the number of attempts, and the percentage of residual obstruction. The complications described include acute occlusion and myocardial infarction. Finally, thrombolytic therapy is mentioned because PTCA is performed on patients with acute myocardial infarction after thrombolytic agents are administered.

Implications

Our own research on myocardial revascularization began in 1962. Since then, we have witnessed innumerable controversies related to the results of several randomized studies that compare CABG-treated with medically treated patients and, more recently in nonrandomized series, with angioplasty-treated patients. We believe that the controversies, discrepancies, and confusion among reports in the literature or from national and international meetings concerning these studies are the result of inadequate interpretation of the cine coronary angiograms leading to incorrect patient classification and hence to incorrect conclusions and discrepancies among studies. The randomized CASS trial and the angioplasty literature are discussed as examples.

CASS Randomized Trial

The message from the CASS randomized reports released in 1983 is incomplete. Few cardiologists and cardiovascular surgeons realize the extremely low-risk status of the population, as shown in Table 2. From this data, it is logical to think that the majority of patients must have no or one proximal obstruction because only 31.5% show proximal obstruction of the left anterior descending branch, and there is no information about proximal obstruction of the circumflex or right coronary artery. (Later, we found
that left main equivalent comprises only 5.25% and that three-vessel disease with three proximal obstructions comprises 1.03%. In addition, 100 patients of the medically treated group were operated on with two deaths (crossover factor). Of these 100 patients, 52 had three-vessel disease, that is, 38% of the patients with three-vessel disease (high-risk group) in the medical series were benefited by CABG; thus, surgery becomes an important factor for the survival in the medically assigned group. As a consequence, it is not surprising that at 7 years, both medical and surgical groups had a 91% survival rate, and at 10 years, the overall survival rate was 81% for the surgically treated group and 78% for the medically treated group because most patients were low risk with no or one proximal obstruction. Of course, patients with three-vessel disease and ejection fraction between 0.5 and 0.35 were benefited by surgery. Furthermore, in our view, much confusion and discussion has been created by an editorial by Braunwald in which the results of the CASS randomized trial (4.7% of the originally screened patients) were extrapolated to the overall population of patients with coronary arteriosclerosis. He stated, “Despite these questions, I consider CASS to be an excellent clinical trial and the most up-to-date examination of the important question of the effects of CABG on survival and on the occurrence of myocardial infarction in patients with coronary-artery disease. . . . The lack of statistical evidence in CASS that survival is improved after surgical treatment in any patients other than those with disease of the left main coronary artery . . .”.

The survival rate and the number of late myocardial infarctions in patients with angina class I or II or three-vessel disease became, to our belief, more realistic and clarified by using 51 Cox variables and propensity score in two recent nonrandomized CASS reports when cine coronary angiography was properly tabulated following Ringqvist et al’s contribution.

**Angioplasty Literature**

The introduction of PTCA by Gruentzig was a major contribution to the treatment of coronary arteriosclerosis; however, to our knowledge, the results and indications are still not properly defined, even among patients with one-vessel disease and mild angina. Snyder and colleagues reviewed 630 patients...
in the latter category and emphasized that "mildly symptomatic patients have a significant incidence of recurrent symptoms, hospitalization, morbidity and potentially expensive medical follow-up after PTCA. Randomized studies will be needed before recommending PTCA in this population, with a favorable prognosis on medical therapy." More recently, Emory University and the CASS Coordinating Center joined efforts to compare patients with one- and two-vessel coronary disease with left anterior descending coronary involvement. The 5-year actuarial survival rate of all patients treated medically (865 patients) was not different from that for all patients treated initially with PTCA (627 patients) (93% vs. 96%). However, patients with baseline left ventricular ejection fraction of less than 50% (4-year survival rate of 86% vs. 100%) showed a potential survival benefit after PTCA, as did patients with two-vessel disease. Although Cox's analysis and stratified life-table were used, the distribution of the proper anatomical variations was not carefully defined. In this study, the CASS protocol was followed, and the patients were finally divided into only two categories—above or below the first perforator. The CASS original protocol considered left anterior descending involvement to be when the obstructions were present before the first perforator branch (n=12), below the first perforator (n=13), more distal (n=14), first diagonal (n=15), and second diagonal (n=16). Of course, the size of the vessels, distal runoff, and collaterals were not mentioned. It would be worth considering a comparison only among patients with single obstructions in a dominant right coronary, dominant circumflex, and large left anterior descending artery. Possibly a different outcome could be obtained.

In patients with multiple-vessel disease, the subject became more complicated. Do we really know the location of the obstruction and the status of the left ventricle of patients in whom PTCA is attempted? Hartzler et al. have stated, "Based upon a large experience with predominantly complex coronary angioplasty, we recognize coronary anatomic features which are uniquely better treated with PTCA as opposed to bypass surgery: 1. small arteries. 2. relatively small or inaccessible branch vessels. 3. very distal lesions such as those at the apex of the LAD, the left AV groove branch of the circumflex, or those located in the posterior descending or posterolateral branch circulation of the right coronary artery. 4. diffuse segments of disease, particularly in distal vessels. . . . When diffuse proximal disease is present in association with suitably bypassable distal vessels, we favor an operative approach assuming that procedural risk is not excessively elevated by associated anatomic or medical factors." These concepts are further highlighted by two reports from the same group. First, 3,100 PTCA's reported between 1981 and 1985, only 45 patients (1.45%) had left main equivalent (obstructions at the proximal segment of the left anterior descending and circumflex branches of the left coronary artery). In this selected group, complete revascularization (both obstructions) was accomplished in only 64% of the patients. In the second report from November 1987, 1,310 of 5,000 consecutive PTCA's were performed in patients with three-vessel disease ("each of the three major coronaries of their branches"). (In this particular group, the primary success rate was 82%, 14% lower than that of the overall population.) Thus, it is fair to believe that 3,590 PTCA's were performed in another anatomical location, maybe the majority in "small arteries and distal lesions." The finding that proximal obstruction has a lower primary success rate was
corroborated with findings from Emory University in 300 consecutive PTCA patients with acute myocardial infarction: The success rate at proximal obstructions was 69.6% compared with 84% among nonproximal sites. In addition, the overall experience of Emory University showed an increased rate of restenosis in proximal obstruction (left anterior descending, 37% proximal vs. 26% nonproximal; right coronary artery, 28% vs. 19%; circumflex, 24% vs. 13%).

The definition of multiple-vessel disease of the series of patients treated by PTCA in the literature is subject to criticism because authors include in the same category patients with two- and three-vessel disease, and it is well known from the natural history of coronary arteriosclerosis that the prognoses of two- and three-vessel disease differ significantly. As an example, in a study related to multiple-vessel disease performed at Emory University among 280 patients, 84% of the patients had two-vessel disease, but the results and follow-up at 2 and 4 years were reported together as from patients with multiple-vessel PTCA. Sometimes the confusion can even be greater; Vandormael and associates considered multiple-vessel disease as when more than 70% luminal diameter is present at least in one major coronary vessel and more than 50% stenosis is present in one or two more major vessels. An exception is the contribution of Deligonul and associates, who separated patients into those with two- and those with three-vessel disease. The restenosis rate in more than one lesion was 26% in patients with three-vessel disease compared with 9% in patients with two-vessel disease.

There are a few reports that compare patients with multiple-vessel disease treated with PTCA or CABG, but no useful conclusions can be reached because of inadequate patient tabulations. For example, Finci and associates presented, to our knowledge, the first report that compared multivessel PTCA with CABG with both internal mammary arteries, and the series are not comparable—the incidence rate of two-vessel disease was 80% in PTCA compared with 39% in surgery, and the incidence rate of three-vessel disease was 20% in PTCA compared with 61% in surgery. A recent report comparing socioeconomic and other outcomes after multiple-vessel PTCA or CABG repeats the same error—three-vessel disease comprises 47% of patients treated with PTCA compared with 88% in the surgically treated group. As a consequence, conclusions are impossible to compare.

The use of the computerized tabulation program will compound the problem because it will be impossible to compare any of the multiple-vessel series of patients treated by PTCA reported in recent years with, for example, 100 consecutive patients with three-vessel disease operated on in 1987 and another 100 operated on in 1988 who demonstrated the pattern of our present surgical population (Table 3). It is important to emphasize that it will be mandatory in the future to separate patients treated with multiple-vessel PTCA into at least two- and three-vessel disease categories.

The status of the left ventricle has not been properly tabulated in patients who underwent PTCA. For example, reduced left ventricular function is included when the ejection fraction is 40% or less and even 45% or less, and they constitute part of the group classified as complex coronary angioplasty in the majority of the reports. In regard to the status of the left ventricle, it is important to differentiate three categories: normal or mildly impaired left ventricle with an ejection fraction of more than 40%, moderately impaired with an ejection fraction between 40% and 30%, and severely deteriorated with an ejection fraction of less than 30%. Prognosis is different in each group as demonstrated by Ringqvist et al and our own surgical experience.

We are aware that the natural history of arteriosclerosis is predicted not only by the anatomy but also by coronary spasm, as described by Osler, confirmed angiographically by Gensini et al and emphasized by Masera and the characteristics of the plaque (the "missing link"), endothelial ulceration, platelet aggregation, and thrombus formation. Furthermore, the introduction of quantitative coronary arteriography and the calculation of the coronary flow reserve and the stenosis flow reserve will add more information to our understanding of the pathophysiology of coronary arteriosclerosis and are not discussed in depth because they are not the subject of this report. Nevertheless, to obtain realistic data, the angiographic characteristics of the coronary artery tree, as carefully analyzed here, will always be the framework to which the other factors should be related.

The use of exercise tests with or without the addition of radioisotopes helps in the selection of

---

**Table 3.** One Hundred Consecutive Patients With Three Vessel Disease Operated on Between May 2 and July 10, 1977, and Between May 2 and August 5, 1988

<table>
<thead>
<tr>
<th>Proximal coronary segments (%)</th>
<th>Left main equivalent (%)</th>
<th>Total occlusions (%)</th>
<th>Ventricular status (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>One</td>
<td>Two</td>
<td>Three</td>
</tr>
<tr>
<td>1987</td>
<td>10</td>
<td>13</td>
<td>40</td>
</tr>
<tr>
<td>1988</td>
<td>0</td>
<td>17</td>
<td>50</td>
</tr>
</tbody>
</table>

1V, one vessel; 2V, two vessels; 3V, three vessels.

Patients with left main obstruction were excluded.

Left main equivalent: all patients showed three-vessel disease; Two: proximal obstruction of anterior descending and circumflex coronary branches; Three: proximal obstruction of right coronary artery, anterior descending and circumflex coronary arteries.
patients for revascularization procedures, as clearly indicated by Weiner and collaborators from the CASS Registry: "Surgical benefit was greater in the 789 patients who exhibited at least 1 mm ST depression and who could exercise only into stage 1 or less. Among the 398 patients with three-vessel disease with these characteristics the seven-year survival was 58% for the medically treated group and 81% for the surgically treated group (p<0.0001). In the 137 patients with three-vessel disease and in a lower risk exercise classification, however, there was no difference in 6 year survival between the medical and surgical cohorts (83 versus 88%, respectively; p=0.31)." It would be a significant contribution to obtain from the CASS bank data the angiographic characteristics of both groups and tabulate them following Ringqvist's protocol and the ideas discussed in this paper.

Summary

The quality of cine angiography is excellent in our days, and as a consequence some of the pitfalls encountered in previous randomized trials are not currently present. An example can be found in the CASS analysis of the reproducibility of coronary arteriographic reading by the Quality Control Committee Sessions: “There is an indication that different clinics” involved in the CASS trial “can reduce the variability between their readings by concerted effort to improve both the quality and the completeness of the angiographic examination.” The introduction of electronic calipers to judge the severity of the obstruction can eliminate human errors.

The computerized protocol has the disadvantage that it takes longer to tabulate cine coronary angiography and it will depend on its pattern, but it certainly will not be as long as filling in the CASS protocol. However, this effort is justified because it will enrich our knowledge of coronary arteriosclerosis. As a result, patients will be divided into proximal (1, 2, 12, 13, and 19), middle (mainly, 3, 14, and 20), and distal (remainder) segments. Sometimes midsegments can be important. For example, in the report from CASS related to the left main equivalent lesions, the 5-year survival rate was 48% if the obstruction on the left anterior descending was proximal and increased to 71% if it was more distal.

Several randomized studies to compare PTCA with CABG as suggested by Gruentzig et al in 1979 are underway, and it is hoped that the data will be properly analyzed. However, if cine coronary angiography and the status of the left ventricle are not carefully tabulated (classification of patients into left main trunk or one-, two-, or three-vessel disease is not sufficient), the results of the randomized trials comparing PTCA with CABG will add more confusion instead of clarifying proper therapeutic implications.

Acknowledgments

I express my appreciation to Dr. Miguel Alberto Borruel and Dr. Roberto René Favaloro for their assistance in preparing this manuscript.

References

18. Ellis S, Alderman EL, Cain K, Wright A, Bourassa M, Fisher L, and the participants of the Coronary Artery Surgery Study


24. de Belder MA, Skhean JD, Pumpheary CW, Rothman MT, Mills PG: Relation of collateral vessels to left ventricular damage and extent of coronary disease following infarction: Influence on exercise testing and clinical outcome (abstract). Circulation 1988;78(suppl II):I–256


Key Words • coronary artery • proximal obstruction • circulation • multiple-vessel disease • catheterization • angioplasty
Computerized tabulation of cine coronary angiograms. Its implication for results of randomized trials.
R G Favaloro

doi: 10.1161/01.CIR.81.6.1992

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/81/6/1992