Influence of Balloon Size on Initial Success, Acute Complications, and Restenosis After Percutaneous Transluminal Coronary Angioplasty

A Prospective Randomized Study

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Restenosis after percutaneous transluminal coronary angioplasty (PTCA) is strongly associated with incomplete initial dilatation. To determine if oversized PTCA balloons would reduce the restenosis rate without increasing the risk of arterial dissection and acute complications, we prospectively randomized 336 patients to receive either smaller or larger balloons. Thirty-four percent of patients had multivessel disease and 18% had multisite dilatation. One hundred sixty-nine patients were randomized to PTCA with a larger balloon and 167 to PTCA with a smaller balloon. Balloon:artery diameter ratios were 1.13±0.14 in the larger group and 0.93±0.12 in the smaller group (p<0.001). The trial was halted as clinically important differences in acute complications emerged. Emergency bypass graft surgery, usually for the treatment of arterial dissection, was required in 7.1% of patients in the larger balloon group and 3.6% of patients in the smaller balloon group (p=0.15). Myocardial infarction (Q wave and non-Q wave) complicated 7.7% of procedures in which large balloons were assigned and 3.0% of procedures in which small balloons were assigned (p = 0.056). There were no deaths in either group. The incidence of bypass surgery was 1.7% when the balloon:artery ratio was less than 0.9, 3.1% when the ratio was 0.9-1.1, and 7.8% when it was greater than 1.1. Stepwise logistic regression analysis demonstrated that larger balloon assignment, multiple lesion dilatation, and multivessel coronary artery disease were independent predictors of emergency surgery. Angiographic restudy rates were 50% in the larger group and 60% in the smaller group (p=NS). Mean restudy diameter stenosis was 43±26% versus 47±28% (p = NS). Thirty-three of 84 (39%) restudied patients had restenosis in the large balloon group and 45 of 102 (44%) in the smaller group (p=NS). We conclude that satisfactory initial results can be achieved by conservative sizing of balloon catheters and attention to other dilatation details such as inflation pressure and times. The intention to reduce restenosis by oversizing balloons will result in increased complications, particularly in patients with multivessel disease or complex lesion morphology. (Circulation 1988;78:557–565)

Restenosis after percutaneous transluminal coronary angioplasty (PTCA) is strongly influenced by incomplete initial dilatation.1–4

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Oversizing PTCA balloons may assist the operator in achieving optimal initial results, and studies have implicated a low balloon:artery diameter ratio as being predictive of restenosis.5–7 One retrospective analysis demonstrated a large and highly significant difference in restenosis rates (36% vs. 5%) between procedures in which the balloon was either significantly undersized or oversized.6 Others7 have reported results suggesting the optimal balloon:artery diameter ratio should be 1.1–1.3. Despite the theoretical possibility of causing increased arterial disruption, none of these preliminary studies reported
an increased incidence of arterial dissection or acute complications associated with oversizing of balloons.

Arterial dissection associated with PTCA undoubtedly increases the risk of acute complications. A sevenfold increase in major complications has been associated with intimal tear or dissection,\(^8\) but this outcome is also closely related to lesion morphology,\(^8\) particularly lesion length.\(^9\) Initial experience with oversized balloons led to an increased incidence of arterial dissection and complications, but during this time, the complexity of the lesions being accepted for PTCA had also increased. It, therefore, remained uncertain if the intention to slightly oversize PTCA balloons had increased the incidence of intimal dissection or if the increase in complications was a function of more complex lesion morphology. It also remained uncertain if intending to dilate with an oversized balloon reduced the risk of restenosis. Accordingly, this prospective, randomized trial was undertaken to determine if oversizing PTCA balloons would reduce the restenosis rate without increasing the risk of arterial dissection and acute complications.

Patients and Methods

Patient Population

From February 1985 through March 1986, 336 of 1,411 patients undergoing elective, native-vessel PTCA were entered into the study. Most patients not entered were eliminated either because they were participating in other trials, were not approached by the research fellow or nurse, or refused to participate. Some patients whose arteries were judged to be too small for use of any balloon larger than 2 mm were also eliminated. Patients with high-risk anatomy were not excluded. Participants' mean age was 57 ± 10 years (± SD), and 79% were men. Fifty-six percent had unstable angina defined as recent onset (<2 months) or worsening symptoms, including new rest pain. Twenty-three percent gave a history of current cigarette consumption. 28% gave a history of previous myocardial infarction, 66% had single-vessel disease, and 34% multivessel disease. Eighteen percent had multisite dilatation. The vessels dilated were the left anterior descending artery in 42%, left circumflex artery in 22%, and right coronary artery in 36%. The mean length of lesions dilated was 9 ± 5 mm. Thirty-one percent were single discrete lesions and 22% multiple and complex; 58% were eccentric, and 7% had angiographically evident calcification. The percent PTCA diameter stenosis was 74 ± 13%, and translesional gradient 55 ± 15 mm Hg.

One hundred sixty-nine patients with 205 sites were assigned to dilatation with a larger balloon and 167 with 209 sites to dilatation with a smaller balloon. The baseline clinical and angiographic characteristics of the two groups are shown in Table 1. Apart from a slightly higher proportion of patients in the smaller balloon group having previous myocardial infarction and less PTCA to the proximal left circumflex artery, there were no significant differences between the two groups in any of the baseline variables known to influence risk of acute complications or restenosis.

The study was approved by the Human Investigations Institution Review Board of Emory University, and all patients signed a written informed consent to participate in the study.

Assignment to Therapy

Pre-PTCA angiograms were recorded with 4-in. image magnification. Freeze-frames showing the lesion and proximal and distal arterial segments were displayed on high resolution (1,000 line) video monitors. The diameter of the "normal" lumen of the coronary artery was estimated by direct comparison to the known diameter of the guiding catheter being used (i.e., 8F, 2.6 mm; 9F, 3.0 mm). Having determined this, the operator then nominated the two balloon sizes that bracketed the artery size, one larger and one balloon size smaller than the artery segment to be dilated. If the diam-

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Larger balloons (%)</th>
<th>Smaller balloons (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>57 ± 10 years</td>
<td>56 ± 9 years</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>77</td>
<td>81</td>
</tr>
<tr>
<td>Women</td>
<td>23</td>
<td>19</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>58</td>
<td>53</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>27</td>
<td>37</td>
</tr>
<tr>
<td><strong>Angiographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-vessel disease</td>
<td>65</td>
<td>66</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>PTCA vessel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD (proximal)</td>
<td>42</td>
<td>48</td>
</tr>
<tr>
<td>LCx (proximal)</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>RCA (proximal)</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>Multisite dilatation</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Lesion morphology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 205)</td>
<td>(n = 209)</td>
<td></td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>8.4 ± 5.0</td>
<td>9.3 ± 5.5</td>
</tr>
<tr>
<td>Single</td>
<td>83</td>
<td>84</td>
</tr>
<tr>
<td>Multiple (complex)</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>Eccentric</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>Calcified</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Diffuse</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Pre-PTCA diameter stenosis</td>
<td>74 ± 13</td>
<td>74 ± 13</td>
</tr>
<tr>
<td>Pre-PTCA gradient (mm Hg)</td>
<td>56 ± 14</td>
<td>54 ± 16</td>
</tr>
</tbody>
</table>

PTCA, percutaneous transluminal coronary angioplasty; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery.

*p<0.05.
eter of the artery was estimated, for example, to be 2.7 mm, the operator would notify the control booth technician that the two nominated balloon sizes would be 2.5 mm (smaller) and 3.0 mm (larger).

Most segments fell consistently between two balloon sizes, but if the diameter of the artery was estimated to be close to an available balloon size (i.e., 3.0 mm), the nominated balloon sizes were selected based on the operator’s judgment of the morphological characteristics of the lesion. For long lesions in a tortuous segment, 2.5- and 3.0-mm balloons would be nominated. For short lesions in straight, otherwise normal appearing segments, 3.0- and 3.5-mm balloons may have been nominated.

Patients in whom either very small (≤2.0 mm) or very large (≥3.5 mm) vessel segments required dilatation were not randomized. In cases in which multivessel or multileesion PTCA was performed, a suitable lesion (or lesions) was targeted for the purposes of the study. Only these lesions were considered in analysis of restenosis results.

Randomization

After two appropriate balloon sizes had been nominated by the operator and recorded on the log sheet by the laboratory technician, a randomization card was drawn. To ensure balance between the two treatment groups in lesion characteristics, assignment was stratified according to the vessel to be dilated and the need for either single or multileesion dilatation. Randomization cards were prepared by the Emory University Department of Biometry.

Dilatation Procedure

Angioplasty was performed with a standard guide-wire system that was previously described in detail. In all cases compliant, polyvinyl chloride balloons were used (LPS or LPS II-USCI, Billerica, Massachusetts). For the purposes of the study, the operators were asked to maximize the inflation pressure used (i.e., at least one inflation to 10 bar) and standardize the number of inflations (approximately three) and total inflation time (100–150 seconds). However, the protocol necessarily allowed these parameters to be varied in any way required to achieve an optimal arteriographic and hemodynamic result for the patient. In general, only sufficient pressure was used in the first inflation to remove evidence of balloon indentation. The first inflation was usually the shortest in time. Second, third, and subsequent inflations used increasing increments of pressure and time to achieve the desired result. The final inflation was usually taken to 10 bar or higher if this was felt to be necessary and safe.

The transstenotic pressure gradient was recorded intermittently during the procedure (Meddars, Honeywell) as a guide to completeness of dilatation. Frequent contrast injections through the guiding catheter and dilatation catheter lumens were used to assess interim angiographic results.

If the target lesions could not be crossed with a larger assigned balloon (n=8), the operator was able to change to a smaller size. This proved successful in three of the eight patients. The lesion could also not be crossed in two patients assigned to PTCA with a smaller balloon. If maximum inflation pressures failed to produce optimal results, the operator exchanged the assigned balloon catheter for the next larger size. This was necessary in eight procedures. Complete procedural data (manufacturer’s balloon sizing, measured balloon and artery diameters, number of inflations, total inflation time, maximal inflation pressure, and pre- and post-PTCA translesional gradient) were able to be recorded on 181 sites in the larger balloon group and 182 sites in the smaller balloon group (Table 2). The mean measured artery diameters were 3.0 ± 0.5 and 3.1 ± 0.5 (p = 0.017) for the larger and smaller balloon groups, respectively. The mean measured balloon diameters were 3.3 ± 0.4 and 2.8 ± 0.4 (p<0.001) for the two groups, and mean balloon:artery diameter ratios were calculated out at 1.13 ± 0.14 and 0.93 ± 0.12 (p<0.001), respectively. There was no difference in the number of inflations, but total inflation time was longer in the smaller balloon group. Slightly higher inflation pressures were also used in the patients assigned to dilatation with smaller balloons.

All patients received pretreatment with aspirin (80 or 325 mg orally) and a calcium antagonist. Diazepam and atropine sulphate were administered at the commencement of the procedure as indicated. After arterial access was gained, all patients received heparin 10,000 units i.v. with another 5,000 units i.v. given for each additional hour of the procedure. Intracoronary nitroglycerin (200 μg) was administered in all patients before crossing the lesion with the dilatation catheter. Additional nitroglycerin was given as required for evidence of coronary spasm or myocardial ischemia.

All patients received aspirin (80 to 325 mg daily), 60 mg diltiazem every 6 hours, and topical nitroglycerin after the procedure. Intravenous heparin was administered (usually after sheath removal) for 12–24 hours in those patients with large intimal tears or dissections, possible intralelesional thrombus, or otherwise unsatisfactory angiographic or hemodynamic results.

Patients were routinely discharged on a regimen of aspirin (80–325 mg) daily and a calcium antagonist if there was evidence to suggest that coronary artery spasm played a role in the clinical course or if potentially ischemic areas of myocardium had not been revascularized.

Data Collection and Measurements

Demographic, clinical, angiographic, and procedural data including complications were prospectively recorded on standard forms and, after auditing for accuracy and completeness, were entered into a computerized data base.
Angiographic measurements were done prospectively by experienced angiographers using calibrated electronic digital calipers (Sandhill, Littleton, Colorado). Diameter stenosis pre- and post-PTCA was taken as the mean of the measurement from two near orthogonal views. Arterial diameter was taken as the mean of the diameters of the most normal appearing segments just proximal and distal to the lesion dilated.

Measurements for balloon:artery diameter ratios were taken from a single angiographic view judged to provide the most optimal calibration. This was usually the right anterior oblique projection for the left anterior descending and circumflex marginal arteries and the left anterior oblique projection for the right coronary and circumflex arteries in the atrioventricular groove. Calipers were calibrated against the outer diameter of the guiding catheter seen in the same view. To facilitate accurate calibration, the guiding catheter tip was filmed without containing contrast media. Balloon diameter was measured in the same view with cineangiograms done at the peak inflation pressure. All films were measured with a Siemens projector. For technical reasons, accurate balloon or artery diameters and ratios could not be measured in six patients. Lesion morphology was coded according to coronary arterial segment dilated, length (measured in the least foreshortened view from points indicating a $\geq30\%$ diameter narrowing), eccentricity versus concentricity, presence or absence of angiographically evident calcium, and single discrete versus complex-multiple lesions (long with intermittent segments $\geq30\%$ diameter narrowing). Tortuosity was not routinely coded during the time period of this study.

Multivessel disease was defined as the presence of $50\%$ or more diameter stenosis in two or more of the major epicardial arteries (left anterior descending, left circumflex, or right coronary arteries). Multisite dilatation was defined as dilatation of multiple sites in different coronary artery segments either within the same or different artery. Multivessel dilatation was defined as dilatation of two or more major epicardial arteries.

Intimal tear (intimal disruption limited to the lesion) was defined as the angiographic appearance of an
intraluminal filling defect, extravasation of contrast material, or a linear luminal density or staining within the confines of the original lesion undergoing dilatation. Arterial dissection was defined as the presence of any of these angiographic findings extending proximally or distally beyond the length of the original lesion. Angiographic success was defined as a final diameter stenosis of less than 50%

Patients were monitored postprocedure on a telemetry floor or in an intensive care unit when necessary. An electrocardiogram was recorded after each procedure and on each subsequent day of hospitalization or more often if applicable. Serial creatinine kinase levels including MB fractions were done every 8 hours after the procedure until within normal limits. Myocardial infarction was defined as the appearance of new Q waves (≥40 msec) or a creatine kinase elevation of equal to or greater than 510 (three times the upper limit of normal for our laboratory) including any MB%. Emergency surgery was defined as the need for any bypass graft surgery on the same day of the procedure or on subsequent days for acute or ongoing myocardial ischemia.

Follow-up

At entry into the study, all patients were informed of the requirement for repeat coronary angiography at 4–6 months post-PTCA. Patients and referring physicians were contacted by mail or telephone at 3 months to arrange restudies. Follow-up angiograms performed elsewhere were forwarded to our institution for analysis. All angiograms were measured with electronic digital calipers, and the restudy diameter stenosis was expressed as the mean of two orthogonal views. Restenosis of the target lesion was defined as a diameter stenosis of equal to or greater than 50% at angiographic restudy. If a patient had two target lesions, restenosis of either one or both constituted a patient restenosis.

Of the 336 patients in the study, 302 (90%) had angiographically successful, complication-free procedures. Of these randomized patients eligible for follow-up, 186 patients with 198 lesions (62%) had repeat coronary angiography, a mean of 6±4 months after the index procedure.

Statistical Analysis

Sample size determination was based on the \( \chi^2 \) test statistic. Error levels were set at 0.05 for Type I and 0.2 for Type II (i.e., power=80%). A two-sided test was assumed with anticipated incidence of restenosis of 35% and 20% in the two groups. With standard sample size tables, it was determined approximately 150 patients in each group would need to undergo repeat coronary angiography to satisfy sample size requirements. We anticipated primary success rates of 90% and that approximately 80% of these patients would ultimately undergo repeat angiography. We thus estimated that approximately 210 patients would need to be entered in each study group. The study could not be blinded. The immediate results, particularly with respect to complications, were reviewed periodically by the investigators to determine if differences in results were emerging. The study was halted when the investigators considered clinically significant trends had become apparent. At that time, initial angiographic and hemodynamic results and preliminary restenosis data indicated additional recruitment would also be unlikely to demonstrate meaningful differences in restenosis results.

Comparison between treatment groups was done with \( \chi^2 \) and unpaired Student’s \( t \) tests as appropriate. To determine if imbalance in important baseline covariates between the two groups influenced outcome, stepwise logistic regression analyses were performed, including the covariates and treatment assignment. Primary analysis was done by intention to treat with larger or smaller balloon catheters. Because of the relative limitation in the range of balloon catheter sizes, there was a significant amount of heterogeneity in balloon:artery ratios within the two treatment groups. Therefore, secondary analyses were performed determining the relation between the actual ratios achieved and outcome variables, namely, acute complications and restenosis. Actual balloon:artery ratios were measured and recorded prospectively. Statistical testing was done with BMDP statistical software (BMDP Statistical Software, Los Angeles, California).

Results

Initial Results

Initial angiographic success was achieved in 159 of 169 patients (94%) assigned to PTCA with a larger balloon and 158 of 167 patients (95%) assigned to a smaller balloon. In eight patients randomized to the smaller balloon group (5%), the operator judged it to be necessary to exchange for a larger balloon to achieve an optimal initial result. There was no significant difference in the final mean diameter stenosis (28±17% vs. 31±17%) or final transstenotic gradient (13±11 vs. 12±7 mm Hg) between the larger and smaller balloon groups, respectively.

An intimal tear was present in 44% of patients in the larger balloon group and 42% of patients in the smaller balloon group \( (p=NS) \). Arterial dissection was present in 22 patients (13%) in the larger group and 15 patients (9%) in the smaller group \( (p=0.23) \). Dissections tended to be more severe in the larger balloon group with 12 of 22 (55%) resulting in bypass graft surgery (11 emergency and one elective). This compared with three of 15 (20%) in the smaller balloon group \( (p<0.05) \). The incidence of procedural complications is shown in Table 3. Overall bypass surgery was required in 19 patients (5.7%), 11 of whom suffered a myocardial infarction. An additional seven patients suffered a myocardial infarction in the absence of bypass surgery. Bypass graft surgery was required in 13 patients (7.7%) in the larger balloon group and six patients
TABLE 3. Acute Complications

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 336)</th>
<th>Larger balloon (n = 169)</th>
<th>Smaller balloon (n = 167)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total MI</td>
<td>18 (5.4%)</td>
<td>13 (7.7%)</td>
<td>5 (3%)</td>
<td>0.056</td>
</tr>
<tr>
<td>Q wave MI</td>
<td>4 (1.2%)</td>
<td>3 (1.8%)</td>
<td>1 (0.6%)</td>
<td></td>
</tr>
<tr>
<td>Non-Q wave MI</td>
<td>14 (4.2%)</td>
<td>10 (5.9%)</td>
<td>4 (2.4%)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>19 (5.7%)</td>
<td>13 (7.7%)</td>
<td>6 (3.6%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Emergency</td>
<td>18 (5.4%)</td>
<td>12 (7.1%)</td>
<td>6 (3.6%)</td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>1 (0.3%)</td>
<td>1 (0.6%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
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</table>

MI, myocardial infarction; CABG, coronary artery bypass graft surgery.

(3.6%) in the smaller balloon group (p = 0.15) (Figure 1). Of the 12 patients in the larger balloon group requiring emergency bypass graft surgery, 11 (92%) had arterial dissection. In the remaining patient requiring emergency surgery, the artery closed during attempts to cross the lesion with the balloon. Of the six patients in the smaller balloon group requiring emergency surgery, three (50%) had arterial dissection. Of the other three patients, one had closure associated with wire placement, another had incomplete dilatation, and the third had late closure after cessation of heparin therapy. The incidence of myocardial infarction complicating the procedure was 7.7% in the larger balloon group and 3.0% in the smaller balloon group (p = 0.056) (Figure 1). There were no deaths in either group.

The mean measured balloon:artery ratio was significantly higher in those patients needing emergency bypass graft surgery than in patients not needing surgery (1.17 ± 0.2 vs. 1.03 ± 0.16, p = 0.03).

Descriptors of Acute Complications

Stepwise logistic regression analysis of all preprocedural clinical and morphological descriptors and procedural factors including inflation time, maximal inflation pressure, balloon size, and group assignment showed the independent predictors of emergency bypass surgery were, first, larger balloon assignment (coefficient, 0.69; p = 0.01) and, second, multiple lesion dilatation (coefficient, 0.8; p = 0.026). Independent predictors of myocardial infarction were, first, multisite dilatation (coefficient, 0.57; p = 0.007), second, larger balloon assignment (coefficient, 0.57; p = 0.045), and, third, multivessel disease (coefficient, 0.55; p = 0.058).

The relation between balloon:artery ratio and acute complications is shown in Figure 2. The incidence of emergency surgery was 1.7% when the ratio was less than 0.9, 3.1% when the ratio was 0.9–1.1, and 7.8% when the ratio was more than 1.1 (p = 0.1). The incidence of myocardial infarction was similarly, 1.7% (n = 1), 4.4% (n = 7), and 5.9% (n = 6) (p = 0.47).

Restenosis

Angiographic restudy rates were slightly higher in the smaller balloon size group (50% vs. 60%, p = NS). When baseline characteristics were compared in these two subsets of patients, there was also no difference between any variable known to affect restenosis except for dilatation of a proximal left circumflex artery site, which was more frequent in the larger balloon group (3% vs. 13%, p < 0.01). The mean restudy diameter stenosis was 43 ± 26% in the large balloon size group and 47 ± 28% in the smaller group (p = NS). With the binary outcome, restenosis (≥50% diameter stenosis) versus continued success, 33 of 84 (39%) restudied patients had restenosis in the larger balloon group versus 45 of 102 (44%) in the smaller balloon group (p = NS, Figure 3).

![Figure 1](image1.png)  
**FIGURE 1.** Incidence of bypass graft surgery (CABG) and myocardial infarction in the two groups.

![Figure 2](image2.png)  
**FIGURE 2.** Relation between calculated balloon:artery ratios and emergency bypass graft surgery (CABG). Six patients (including four requiring emergency CABG) could not have balloon:artery ratios calculated for technical reasons, usually failure to film the balloon during inflation.
The relation between balloon:artery ratio and incidence of restenosis is shown in Figure 4. The incidence of restenosis was 36% when the ratio was less than 0.9, 48% when the ratio was 0.9–1.1, and 35% when the ratio was more than 1.1 (p = NS).

Discussion

This prospective, randomized study was instigated with the support of Andreas Gruentzig who was the attending physician for many of the procedures. His intention was to maximize the safety and efficacy of PTCA by subjecting coronary angioplasty technique to rigorous scientific investigation. Randomized studies that concern technique are difficult to perform because most experienced operators find it difficult to subjugate their technical judgment to the discipline of a study protocol. This study emphasizes the importance of prospective trials in studying PTCA technique because the results differ from the results of retrospective studies that had encouraged the oversizing of angioplasty balloons.

In 1984, two preliminary reports suggested restenosis was favorably influenced by increasing the balloon:artery diameter ratio. One retrospective study of 52 patients stated the optimal balloon:artery ratio was 1.1–1.3 and that coronary dissection was not related to balloon size. Another study of 86 patients by Schmitz et al retrovascularly examined patients according to balloon size and found a large difference in restenosis rates at 6 months (36% vs. 19%). When these authors grouped their patients according to balloon-to-artery size, the difference in restenosis rates was even more striking in favor of larger PTCA balloons (5% vs. 36%, p < 0.01). They found the incidence of coronary dissection was similar in both groups (5% vs. 3%) and concluded that “larger balloon size favorably influences the outcome of PTCA.” Neither study reported the incidence of acute complications such as emergency surgery and myocardial infarction, probably because in the small population samples such complications rarely occurred. Recently, Val and Bourassa reviewed their restenosis experience, which demonstrated significantly lower balloon:artery ratios in patients who underwent lesion restenosis. This group also has reported lower balloon:artery ratios predictive of restenosis in patients undergoing double-vessel PTCA.

Apart from the retrospective nature of these previous studies and sample size considerations, the population of patients may have differed from the present investigation. Acute complications from PTCA are closely related to the morphology of the lesions dilated, the presence of multivessel disease, and the number of sites dilated. Lesion length is the most important descriptor of an acute complication, and in the present study, few patients had “short” discrete lesions with the mean lesion length being close to 10 mm. In addition, almost one third had multivessel disease and 18% had multisite dilations. In the present study, multisite dilatation and the presence of multivessel disease were independent predictors of an acute complication. Earlier studies probably included a larger proportion of patients with single-vessel disease, less “complex” lesions, and less diffuse atheromatous plaquing; this may explain the difference in acute results, including the relatively low incidence of arterial dissection.

Both high inflation pressures and prolonged inflation times have also been proposed as methods to optimize initial results and reduce restenosis rates. In the present study, “compliant” polyvinyl chloride balloons were used, and in an attempt to maximize and standardize inflation pressures, the protocol called for at least one 10-atmosphere inflation in each group. For safety reasons, this was not achieved in all cases and inflation pressures were slightly higher in the smaller balloon group where increased pressures were more frequently used to achieve an optimal initial result. In both groups, as expected with compliant balloon materials, the measured balloon sizes were slightly larger than the manufacturer’s stated sizes. Despite the protocol, for the reasons stated, there was a wide range in maximal inflation pressures. However, we found no significant relation between inflation pressures and acute complications or restenosis. Similarly, despite standardization, there was a tendency to use slightly longer total inflation times.
in the smaller balloon group to achieve similar initial results. Because this study was not blinded and operators were obliged to affect the best possible initial result for each patient, longer inflation times and higher inflation pressures in the smaller balloon group were anticipated at the outset of the trial. Total inflation times in this study for both groups were, by “early” PTCA standards, also relatively long (average, over 2 minutes total) but appear to have had no effect on the incidence of angiographic restenosis in this trial. Specific studies are required to determine if prolonged inflation times (two or more ≥3 minutes) will influence restenosis.

In the present study, intention to treat with a larger balloon catheter was independently and significantly related to the risk of a major ischemic complication, either emergency coronary artery bypass surgery or acute myocardial infarction. By univariate analysis, the increase in complications in the larger balloon group did not reach statistical significance, but because of a consistent trend in all complications (approximately twice that seen in the smaller balloon group), it was believed the results were of sufficient clinical significance to halt the trial. It should be noted that the calculated confidence intervals for bypass surgery in the larger balloon group were 3.7–11.7% and for the smaller balloon group were 0.7–6.4%, respectively. However, analysis of data on the basis of prospectively measured balloon:artery ratios and by multivariate, logistic regression demonstrated the adverse influence of both actual balloon size and intention to dilate with a larger balloon.

Overall, complications in the study population tended to be slightly higher than that of nonrandomized patients during the same period. For nonrandomized patients between February 1985 and April 1986, the incidence of emergency coronary artery bypass graft surgery was 3.7% and myocardial infarction 4%. The difference appeared to be attributable to the higher complications in the larger balloon group. Information gained from this study has proved valuable for us in improving the dilatation technique in patients with complex anatomy. From April 1986 through July 1987, the mean balloon:artery diameter ratio has been 1.0±0.16 and incidence of emergency coronary artery bypass graft surgery and myocardial infarction were 2.7% and 2.9%, respectively. Over this most recent time period, 47% of patients have had multivessel disease and 25% multisite dilations with the mean lesion length being 8±5 mm.

The incidence of restenosis was not influenced by balloon size assignment. This finding was not surprising because if balloon size was to influence restenosis, it would probably have done so by improving the initial arteriographic and hemodynamic results. In the present study, patients assigned to dilatation with a slightly smaller balloon had similar diameter stenosis and translesional gradient reductions as patients assigned to larger balloons. These results were obtained by using slightly higher inflation pressures or inflation times when necessary and changing up to a larger balloon in a small number (5%) of patients. This strategy proved to be superior in limiting the incidence of arterial dissection and acute complications. In contrast to the results of Val and Bourassa,13 this trial did not demonstrate a significant increase in restenosis rates when smaller balloons were used. However, in their series,13 inflation pressures averaged 6.67±1.87 bar and total inflation times averaged 60.59±50.5 seconds. Both were considerably lower than the present trial and may explain the difference. In the present study, even analysis of restenosis by actual balloon:artery ratios failed to demonstrate any trend towards increased restenosis rates in the group with smallest balloon:artery ratios.

The most likely explanation for the discrepancy between the results of the present trial and previous studies is the rigor with which prospective trials are conducted. In a recent publication, Von Essen et al20 reported results of their own prospective, but not randomized, study in which they concluded use of larger balloons bears a higher risk of dissection and produces overall, disappointing results with respect to restenosis.20 Numerous studies have shown the importance of optimal initial results in decreasing the risk of restenosis.1,2,13 Geometric considerations alone explain why these relations should exist. Given that the biological response to balloon dilatation results in varying degrees of neointimal proliferation, it is not surprising that large initial lumen dimensions influence late outcome. While larger balloons should theoretically produce larger initial luminal dimensions, the increased intimal and medial disruption produced may be counterproductive. Angiographic evidence of an intimal tear in itself does not predispose to restenosis,21 but in the presence of a suboptimal hemodynamic result, disrupted tissues may produce turbulence, stasis, and thrombosis22–24 and associated regions of reduced shear stress could promote medial cell migration and proliferation.25–27 In the present study, use of smaller balloons with attention to other dilatation details may have reduced these effects.

Overall, the incidence of restenosis was high in both groups and undoubtedly related to the relatively incomplete, but similar, angiographic restudy rates in both treatment groups. Many asymptomatic patients, likely to have continued angiographic success, were reluctant to have repeat angiography despite their consenting to the study protocol. Because angiographic follow-up was incomplete, interpretation of these data on restenosis must be done with caution and with the understanding they can only be applied to a population presenting for angiographic restudy. However, in view of the findings on the initial risk of oversizing balloons, we believed that reporting the results of the study should not await more intensive angiographic follow-
up efforts. Because restudy rates and baseline variables known to influence restenosis were similar in each group, it is likely our conclusion, that the intention to treat with larger balloons will not reduce restenosis rates, will remain valid. The results of this study should not be misinterpreted. If under-sizing of balloons results in inadequate initial results, then acute closure and restenosis may both result. If acute closure occurs in that setting, however, it is usually in the absence of severe dissection and immediate repeat dilatation with a slightly larger balloon or higher pressures usually solves the problem. Balloon catheters should be carefully sized to achieve optimal hemodynamic and angiographic results that should be monitored throughout the procedure. In general, a balloon:artery ratio close to unity is appropriate. The intention to reduce restenosis by oversizing balloons will result in increased complications, particularly in patients with multivessel disease or "complex" lesion morphology.

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References

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