Factors affecting the therapeutic choice in patients with multivessel coronary artery disease

Stefano De Servi, Stefano Galli, Marco Onofri, Enrico Boschetti, Rossella Oberti, Luigi Niccoli, Anna Maria De Biasi, Gianni Rovelli, Massimo Carini, Francesca Regalia, Paolo Valentinii, Antonio Bartorelli, for the Studio Lombardo Angiografia Multivasali (SLAM) Study Group

Abstract

Objective—To assess how clinical and angiographic findings are related to the decision to carry out coronary angioplasty (PTCA) or coronary bypass grafting in patients with multivessel coronary artery disease.

Design—Prospective survey carried out in 14 centres in the Lombardia region of Italy.

Patients—1468 consecutive patients under going coronary arteriography for known or suspected ischaemic heart disease between May and October 1994, who were found to have multivessel coronary artery disease.

Main outcome measures—Multivariate analysis was undertaken using stepwise logistic regression to identify the clinical and angiographic variables correlated with revascularisation (α medical treatment) in all of patients, and with surgery (α angioplasty) in the subset of revascularised patients.

Results—in all patients the clinical decision after coronary arteriography was made by physicians of each participating centre on the basis of their experience and clinical judgment: 53% of patients had bypass surgery, 28% had PTCA, and 19% continued medical treatment. The choice of a revascularisation procedure was directly related to a clinical diagnosis of unstable angina (P < 0.001), the presence of left anterior descending artery disease (P < 0.001), and to an ejection fraction ≥ 40% (P < 0.001), and inversely related to history of previous coronary bypass surgery (P < 0.001). In revascularised patients, bypass surgery was the preferred treatment in patients with left anterior descending artery disease (P < 0.001), three-vessel disease (P < 0.001), and in those with at least one occluded vessel (P = 0.008). The choice of PTCA was significantly related to history of previous PTCA (P < 0.001) or coronary bypass surgery (P < 0.001), to a clinical diagnosis of non-Q wave myocardial infarction (P = 0.002), and to the possibility of implanting an intracoronary stent (P = 0.01).

Conclusions—Bypass surgery is still the most widely used treatment for patients with multivessel coronary artery disease. This analysis provides a basis for comparison with future developments in the treatment of such patients. Further advancements in PTCA technology are needed to tilt the balance in favour of this less invasive procedure.

Keywords: coronary artery disease; coronary angioplasty; coronary bypass surgery; clinical decision making

Patients with multivessel coronary artery disease often undergo revascularisation procedures. Recent randomised trials have compared the immediate and long term effects of percutaneous transluminal coronary angioplasty (PTCA) and bypass surgery in such patients, but only a small minority of patients could be randomised and enrolled in those studies, since most patients underwent either PTCA or bypass surgery on the basis of clinical and angiographic considerations. However, there are no published data showing how clinical and anatomical features may affect the therapeutic decision in an unselected population of patients with multivessel coronary disease. The purpose of this prospective survey in 14 centres in the Lombardia region of Italy was to verify the relative impact of each revascularisation procedure in a consecutive series of patients undergoing coronary arteriography who were found to have multivessel coronary disease, and to assess which clinical and angiographic factors were related to the decision making process.

Methods

PATIENTS

Between May and October 1994, 4212 patients underwent coronary arteriography for known or suspected ischaemic heart disease in 14 centres in the Lombardia region of Italy. The clinical indication for coronary arteriography included stable or unstable angina in most patients. Stable angina was defined as exercise induced chest pain confirmed by a positive exercise test (development of ST segment depression of > 1 mm 0·08 ms after the J point, with or without chest pain). The severity of anginal complaints was classified according to the Canadian Cardiovascular Society. Unstable angina was defined as angina of recent onset (occurring within the last four weeks) or exacerbation of previously stable symptoms including chest pain at rest. Refractory unstable angina was defined as recurrent chest pain at rest despite full
antianginal treatment including heparin infusion, nitrates, β-blockers, calcium antagonists, and aspirin.

CORONARY ARTERIOGRAPHY
Coronary arteriography was performed in all patients in multiple projections by Sones or Judkins technique. A lesion was considered significant when it occluded the lumen by more than 50%. Multivessel coronary artery disease was defined as the presence of a significant lesion in at least two major coronary arterial systems: the left anterior descending artery (LAD), the right coronary artery, and the circumflex branch. When the right coronary artery failed to supply any left ventricular myocardium, the first two moderate or large sized obtuse marginal branches of the circumflex were considered to supply one vascular territory, and the distal marginal branches and the posterior descending coronary artery were said to supply a different vascular territory.8 Patients with left main disease were not included in this study. All lesions were classified according to the modified AHA/ACC criteria.8,9 For any lesion it was considered possible to implant a stent if the vessel had a lumen diameter of at least 3 mm without proximal tortuosity or diffuse distal disease.11 12 Ejection fraction was calculated from left ventriculograms performed in the right anterior oblique projection.13

TREATMENT CHOICE
In all patients the therapeutic decision after coronary arteriography was made by physicians of each participating centre on the basis of their clinical judgment and experience as well as patient preference. Patients were made aware of their health conditions and informed about the scientific evidence concerning the success and failure of the therapeutic options, including the immediate and long term results of bypass surgery and coronary angioplasty in the various clinical and anatomical settings. No attempt was made to standardise criteria for treatment choice or to alter the therapeutic decision in any case.

STATISTICAL ANALYSIS
Univariate analysis for categorical variables was performed by χ² test with Yates' correction for continuity. Multivariate analysis was undertaken using stepwise logistic regression to identify the clinical and angiographic factors respectively correlated with revascularisation (versus medical treatment) in the overall set of patients, and with surgery (versus PTCA) in the subset of revascularised patients. The independent variables investigated in both these multivariate analyses were: LAD stenosis, more than one occluded vessel, possibility of implanting a coronary stent, ejection fraction, extent of coronary disease (three-vessel versus two-vessel), type of angina (unstable versus stable), type of myocardial infarction (Q wave versus non-Q wave), previous PTCA, previous coronary bypass grafting, stenosis complexity, presence of a proximal coronary lesion, and age. Adjusted odds ratios were calculated from each regression coefficient (only in the case of a binary variable) in order to show the approximate relative probability of a therapeutic choice (revascularisation versus medical treatment in the whole patient population, and surgery versus PTCA in revascularised patients) associated with the presence of a significant correlate, when all other independent factors are absent. Confidence interval (95%) was employed, where appropriate. A P value < 0.05 was considered significant.

Results
CLINICAL FINDINGS
Of the 4212 patients undergoing coronary arteriography, 1468 had multivessel coronary artery disease. There were 1229 men and 239 women with a mean age of 62 years (range 33 to 89). Clinical findings are shown in table 1. Unstable angina was present in 631 patients (refractory to medical treatment in 31% of such patients), stable angina in 582, and no angina in 255. Most of these asymptomatic patients had a positive exercise test after a myocardial infarction or documented silent ischaemia by Holter monitoring. A previous myocardial infarct was found in 920 patients (61%), 120 patients (9%) had previous bypass surgery, and 93 patients (6%) had previous coronary angioplasty.

ANGIOGRAPHIC FINDINGS
Of the 1468 patients included in the study, 698 had two-vessel disease and 770 had three-vessel disease. LAD disease was found in 1148 patients, 1304 patients had right coronary artery disease, and 869 had circumflex branch disease. At least one complex lesion (B2-C according to the AHA/ACC criteria) was found in 1127 patients (79.5%). A low ejection fraction (< 40%) was found in 219 patients (16.5%).

FACTORS AFFECTING THERAPEUTIC CHOICE
After coronary arteriography, medical treatment was continued in 19% of patients whereas a revascularisation procedure was done in 81% (1189 patients). Of these 1189 patients, 782 had bypass surgery and 407 had PTCA. Among patients with two-vessel disease, PTCA was done in 39% of patients and bypass surgery in 41%, whereas 20% continued medical treatment. Among patients with

Table 1 Clinical characteristics of 1468 patients with multivessel coronary disease

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men/women</th>
<th>Mean age (years)</th>
<th>Mean age (range)</th>
<th>Mean age (range)</th>
<th>Previous myocardial infarct</th>
<th>Previous non-Q wave myocardial infarct</th>
<th>Stable angina</th>
<th>CCS I</th>
<th>CCS II</th>
<th>CCS III</th>
<th>No angina</th>
<th>Unstable angina</th>
<th>Refractory unstable angina</th>
<th>Previous CABG</th>
<th>Previous PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1229/239</td>
<td>62 (range 33 to 89)</td>
<td>Previous myocardial infarct</td>
<td>744</td>
<td>Stable angina</td>
<td>582</td>
<td>CCS I</td>
<td>69</td>
<td>CCS II</td>
<td>291</td>
<td>CCS III</td>
<td>222</td>
<td>No angina</td>
<td>255</td>
<td>Unstable angina</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CCS, Canadian Cardiovascular Society; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty.
Factors affecting the therapeutic choice in patients with multivessel coronary artery disease

Table 2 Treatment choice in patients with previous CABG or PTCA

<table>
<thead>
<tr>
<th></th>
<th>MT</th>
<th>CABG</th>
<th>PTCA</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous CABG</td>
<td>42.5</td>
<td>25.8</td>
<td>31.7</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>No previous CABG</td>
<td>16.5</td>
<td>56.2</td>
<td>27.3</td>
<td></td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>27.5</td>
<td>27.5</td>
<td>45.0</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>No previous PTCA</td>
<td>18.1</td>
<td>55.4</td>
<td>26.5</td>
<td></td>
</tr>
</tbody>
</table>

MT, medical treatment; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty.

Table 3 Treatment choice in patients with two-vessel disease. Importance of proximal LAD involvement

<table>
<thead>
<tr>
<th></th>
<th>MT</th>
<th>CABG</th>
<th>PTCA</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prox LAD involvement (% of patients)</td>
<td>14.9</td>
<td>52.0</td>
<td>33.1</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Prox LAD involvement (% of patients)</td>
<td>32.7</td>
<td>16.6</td>
<td>50.7</td>
<td></td>
</tr>
</tbody>
</table>

MT, medical treatment; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; Prox LAD, proximal left anterior descending artery.

Table 4 Treatment choice in patients with three-vessel disease. Importance of proximal LAD involvement

<table>
<thead>
<tr>
<th></th>
<th>MT</th>
<th>CABG</th>
<th>PTCA</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prox LAD involvement (% of patients)</td>
<td>13.5</td>
<td>72.5</td>
<td>14.0</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>No prox LAD involvement (% of patients)</td>
<td>37.2</td>
<td>35.3</td>
<td>27.5</td>
<td></td>
</tr>
</tbody>
</table>

MT, medical treatment; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; Prox LAD, proximal left anterior descending artery.

Three-vessel disease, bypass surgery was performed in 70% of patients, PTCA in 15%, and 15% continued medical treatment. Patients with unstable angina more often had revascularisation procedures than patients with stable angina (88% vs 75.5%, P < 0.001). Previous bypass surgery, on the other hand, favoured medical treatment, though patients with previous PTCA more often had a new PTCA procedure than other treatments (table 2). Proximal LAD involvement significantly increased the need for bypass surgery in both two-vessel and three-vessel disease (tables 3 and 4). The possibility of implanting a stent in at least one lesion of the three major branches significantly increased the number of PTCA procedures in patients with two vessel disease (stent implantable: PTCA 54%, bypass surgery 35%, medical treatment 11%; stent not implantable: PTCA 31%, bypass surgery 44%, medical treatment 25%, P < 0.001; fig 1) but not in patients with three-vessel disease (stent implantable: PTCA 18%, bypass 71%, medical treatment 11%; stent not implantable: PTCA 13%, bypass surgery 69%, medical treatment 18%, P = NS) (fig 2). The presence of a complex lesion in at least one major vessel, on the other hand, did not affect treatment choice. However, the presence of at least one occluded vessel affected the therapeutic decision in patients with two-vessel disease (one or more occluded vessel: PTCA 34%, bypass 42%, medical treatment 24%; no occluded vessels: PTCA 47%, bypass 38%, medical treatment 15%, P < 0.001) but not in three-vessel disease (one or more occluded vessel: PTCA 15%, bypass 69%, medical treatment 16%; no occluded vessels: PTCA 16%, bypass 74%, medical treatment 10%, P = NS).

Patients with a low ejection fraction (EF) more often had medical treatment than patients with an ejection fraction of more than 40%.

Figure 1 The possibility of implanting a stent favoured percutaneous transluminal coronary angioplasty (PTCA) in patients with two-vessel disease (P < 0.001), but not in patients with three-vessel disease. Bypass, coronary artery bypass grafting; Med treat, medical treatment.

Figure 2 In patients with three-vessel disease, surgery was the preferred treatment, irrespective of the possibility of implanting a stent in a coronary vessel. PTCA, percutaneous transluminal coronary angioplasty; Bypass, coronary artery bypass grafting; Med treat, medical treatment.

Figure 3 In patients with ejection fraction ≤ 40%, bypass surgery was preferred in the presence of left anterior descending coronary artery (LAD) disease, while medical treatment was the preferred treatment in the absence of LAD disease (P < 0.001). PTCA, percutaneous transluminal coronary angioplasty; Bypass, coronary artery bypass grafting; Med treat, medical treatment.
Among revascularisation procedures, bypass surgery was the preferred treatment in the presence of LAD disease (P < 0.001), three vessel disease (P < 0.001), and in the presence of at least one occluded vessel (P = 0.008). The choice of PTCA was related to history of previous PTCA (P < 0.001), a clinical diagnosis of non Q wave myocardial infarction (P = 0.002), and to the possibility of implanting an intracoronary stent (P = 0.01).

Discussion

Randomised trials have shown that bypass surgery increases survival in patients with extensive coronary disease, such as those with left main disease, triple vessel disease, and two-vessel disease with LAD involvement. Therefore it is not surprising that bypass surgery was the preferred treatment in our population of patients with multivessel coronary disease. Medical treatment without a revascularisation procedure was chosen in only a minority of patients and multivariate analysis showed that previous bypass surgery was the only variable related to the decision to continue medical treatment; this therapeutic choice may be accounted for by the high mortality and morbidity rate associated with re-intervention on one hand, and by the unsuitability of PTCA in the majority of these patients because of the presence of occluded or degenerated venous grafts in most cases.

In our population, bypass surgery was accomplished in 61% of patients and PTCA in 27%. Therefore, although PTCA is increasingly used in patients with multivessel disease, bypass surgery remains the mainstay of treatment in such patients. Recent randomised trials have compared the clinical efficacy of either procedure in selected patients with multivessel disease. The German angioplasty bypass surgery investigation showed that the two treatments were equally effective in relieving angina at one year follow up. These results, however, were achieved with a greater need of new revascularisation procedures in the PTCA group, but patients treated with PTCA had fewer major cardiac events (death, myocardial infarction) than surgically treated patients. Other randomised trials, such as the Emory angioplasty versus surgery trial (EAST), the randomised intervention treatment of angina (RITA), and the coronary angioplasty bypass revascularisation investigation (CABRI), have reported final or interim data showing a similar mortality among patients with multivessel disease who are undergoing surgery or angioplasty. All these studies confirm that patients initially treated with PTCA more often need a new revascularisation procedure in the follow up period.

A common finding in those trials was the small number of enrolled cases compared with the number of screened and clinically eligible patients. In the GABI trial, 359 patients were enrolled out of the 8981 initially screened patients (4%). The recommended treatment for those who were not randomised was bypass.

### Multivariate Analysis

The results of the multivariate analysis are shown in tables 5 and 6. The choice of a revascularisation procedure was related to a clinical diagnosis of unstable angina (P < 0.001), presence of left anterior descending artery disease (P < 0.001), and an ejection fraction of more than 40% (P < 0.001), whereas previous bypass surgery was the only factor related to the medical treatment choice (P < 0.001).

**Table 5** Variables related to therapeutic choice (revascularisation vs medical treatment in the whole population)

<table>
<thead>
<tr>
<th>Variable</th>
<th>b</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD disease</td>
<td>1.33</td>
<td>3.80</td>
<td>2.63 to 5.49</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>EF &gt; 40%</td>
<td>0.78</td>
<td>2.19</td>
<td>1.46 to 3.28</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>UA</td>
<td>1.04</td>
<td>2.82</td>
<td>1.96 to 4.07</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>1.70</td>
<td>0.18</td>
<td>0.11 to 0.30</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

b, regression coefficient; OR, odds ratio (adjusted for all the other variables); CI, confidence interval; LAD, left anterior descending artery; UA, unstable angina; EF, ejection fraction; CABG, coronary artery bypass grafting.

**Table 6** Variables related to therapeutic choice (CABG vs PTCA in revascularised patients)

<table>
<thead>
<tr>
<th>Variable</th>
<th>b</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD disease</td>
<td>1.81</td>
<td>6.14</td>
<td>4.01 to 9.39</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>EF &gt; 40%</td>
<td>0.94</td>
<td>1.79</td>
<td>1.27 to 2.52</td>
<td>0.008</td>
</tr>
<tr>
<td>Three vessel</td>
<td>1.24</td>
<td>3.46</td>
<td>2.46 to 4.87</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Stent</td>
<td>-0.42</td>
<td>0.66</td>
<td>0.48 to 0.91</td>
<td>0.01</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>-1.10</td>
<td>0.33</td>
<td>0.18 to 0.63</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>-2.05</td>
<td>0.13</td>
<td>0.07 to 0.24</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Non-Q MI</td>
<td>-0.53</td>
<td>0.59</td>
<td>0.38 to 0.91</td>
<td>&lt; 0.002</td>
</tr>
</tbody>
</table>

b, regression coefficient; OR, odds ratio (adjusted for all the other variables); CI, confidence interval; LAD, left anterior descending artery; Stent, possibility of implanting a coronary stent; MI, myocardial infarction; OV, >1, one occluded vessel; CABG, coronary artery bypass grafting.
surgery in 53%, PTCA in 15%, and medical treatment in 32%. Similarly, in the EAST study of the 5118 screened patients with multivessel disease, only 392 (7.7%) were finally enrolled. In the RITA study, 1011 patients were randomised, of whom 555 (55%) had two or three vessel disease. They represented the 3% of all screened patients with angiographically proven coronary artery disease. Of the 17 239 patients in whom myocardial revascularisation was considered necessary, 70% were referred for bypass surgery, 25% were referred for PTCA, and 5% were randomised in the trial. In the bypass angioplasty revascularisation investigation (BARD), whose data on five year clinical outcome have not yet been published, 12 530 patients were considered clinically eligible for the study because of severe angina or ischaemia warranting coronary revascularisation. Nearly 34% of them were suitable for both PTCA and bypass surgery, whereas 60% were considered technically unsuitable for PTCA, 3% for bypass surgery, and 3% for both procedures. In the end, 1829 patients out of a total of 25 200 patients with multivessel coronary artery disease (7.3%) were recruited for the study. All these data show that in the great majority of patients with multivessel coronary disease, treatment is chosen on the basis of patients’ clinical and angiographic features. No papers, however, have so far analysed the detailed clinical and anatomical characteristics leading to the therapeutic choice in patients with multivessel coronary disease.

Our data show that clinical and angiographic factors may affect the therapeutic decision in such patients. The choice of a revascularisation procedure was significantly related to a diagnosis of unstable angina, and multivariate analysis showed that a diagnosis of non Q wave myocardial infarction favoured the use of PTCA. In both these clinical conditions, successful dilatation of only the “culprit lesion” may result in a good outcome, even in the presence of multivessel coronary disease. Thus the high clinical efficacy of the procedure achieved with a partial revascularisation procedure may account for the predominant use of PTCA in such patients. As far as angiographic characteristics of the coronary lesions are concerned, the presence of at least one occluded vessel affected treatment choice, favouring bypass surgery. Interestingly, the possibility of implanting an intracoronary stent was significantly related to the decision to perform PTCA rather than bypass surgery, especially in patients with two vessel disease. This technical consideration retained statistically significant in the multivariate analysis. Deployment of intracoronary stents is now extensively used as a rescue operation for present or threatened vessel closure, thus reducing the need for urgent bypass surgery. Moreover, recent studies show that stent implantation, as compared with angioplasty, increases angiographic and clinical success rate and reduces the incidence of restenosis and the need for subsequent revascularisation of the treated lesion. We believe that the possibility of implanting a stent in a diseased coronary artery may prompt the operators to perform PTCA rather than refer the patient for surgery, because they feel more confident of being able to cope with complications that could arise during the procedure.

The therapeutic decision was also affected by left ventricular ejection fraction. Interestingly, a low value of this variable prompted bypass surgery in the presence of LAD disease; on the other hand, in the absence of LAD disease, depressed left ventricular function was a contraindication to a revascularisation procedure. These conflicting effects of low ejection fraction on the therapeutic decision may explain why this variable did not attain statistical significance in the multivariate model.

In conclusion, this prospective survey confirms that bypass surgery is still the most widely used kind of treatment in patients with multivessel coronary disease, although recent technical improvements have broadened the indications for PTCA in severe forms of coronary artery disease. This analysis also provides a basis for future development in the treatment of multivessel coronary disease. However, further advancements in PTCA technology, possibly including the successful opening of completely occluded coronary vessels and the effective prevention of restenosis, are needed to tilt the balance in favour of this less invasive procedure.

This study was supported in part by a grant from Cordis Italia, Milan.

Appendix
The following institutions and investigators participated in the SLAM study: Policlinico San Matteo, Pavia (Stefano De Servi, Paolo Valenti, Anna Maria Costanzo, Enrico Boschetti); Centro Cardiologico Fondazione Monzino (Stefano Galli, Antonio Bartorelli); Ospedale Multizionale di Varese (Marco Onofri, Sergio Repetto); Ospedali Riuniti di Bergamo (Angelo Cassar, Rossella Oberti); Ospedale Civile di Rovigo (Luigi Nocelli); Centro De Gasperi, Ospedale Niguarda, Milano (Anna Maria De Biase, Luigi Campolo); Ospedali di Rho (Gianni Rovelli, Lucia Picheca); Ospedale di Cremona (Massimo Carini, Rino Distante); Ospedale S. Carlo, Milano (Francesca Regalia, Marco Savioni); Istituto San Raffaele, Milano (Sergio Chierchia, Gabriele Vicedomini); Ospedale di Legnano (Francesco Caflero); Ospedale S. Gerardo, Monza (Virgilio Colombo); Ospedale di Como (Santino Zerboni); Ospedale di Lodi (Alessandro Oddone).
18 Foster ED. Reoperation for coronary artery disease. Circulation 1985;72:99-64V.