Continuous multilead ST-monitoring identifies patients with unstable coronary artery disease who benefit from extended antithrombotic treatment

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Aims Prolongation of anticoagulant treatment might reduce subsequent cardiac events in patients with unstable coronary artery disease. Multilead ST-segment monitoring identifies patients with a high risk of adverse outcome. The aim was to assess the value of multilead ST-monitoring in prospectively identifying patients who respond to extended anticoagulant treatment with low-molecular weight heparin when treated by a primarily non-invasive strategy.

Methods and Results In this substudy of the FRISC II trial, ST-monitoring with a continuous 12-lead ECG or vectorcardiography was performed for 24 h in 629 patients with unstable coronary artery disease randomized to receive either the low-molecular weight heparin dalteparin, or placebo for 3 months after at least 5 days’ dalteparin treatment in all patients. Ischaemic episodes were detected in 34% during ST-monitoring. In the group with ischaemic episodes, the extended dalteparin treatment was associated with a lower rate of death, myocardial infarction, or revascularization (35·2% vs 53·4%, relative risk reduction: 34%, P=0·01). In patients without ischaemic episodes, long-term dalteparin treatment had no effect.

Conclusions In patients with unstable coronary artery disease treated primarily with a non-invasive strategy, ischaemic episodes revealed while on multilead ST-monitoring identifies patients who benefit most from extended treatment with anticoagulants.


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Key Words: Electrocardiography, ST-monitoring, troponin T, unstable angina, myocardial infarction, prognosis, low-molecular weight heparin.

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Introduction

Unstable coronary artery disease, i.e. unstable angina or evolving myocardial infarction without ST-elevation, is a heterogeneous condition with a variable risk of subsequent cardiac events. The underlying pathophysiology in most cases involves plaque rupture or erosion with superimposed coronary thrombosis and downstream embolization[1–3]. In the recently reported Fragmin and Fast Revascularisation during Instability in Coronary artery disease (FRISC II) trial, an invasive strategy following 5–7 days’ treatment with the low-molecular-weight heparin dalteparin significantly reduced the rate of death or myocardial infarction compared with a non-invasive strategy[4,5]. However, in practice, not all patients are suitable for revascularization and not all centres are equipped to perform interventions within a few days. This raises the issue of how to manage patients with unstable coronary artery disease who are ineligible or need to wait for early revascularization. In FRISC II, extended treatment with an anticoagulant, the low-molecular weight heparin dalteparin, in addition to aspirin, was shown to reduce the composite of death, myocardial infarction and revascularization during the 3 months treatment and also death or myocardial infarction during the first month of treatment[6]. However, the unstable coronary artery disease population is heterogeneous in terms of both prognosis and response to
antithrombotic treatment. Previous studies have shown that increased levels of troponin T and I identify high risk patients who benefit most from antithrombotic treatment\[^{15-17}\].

Detection of transient ischaemic episodes seems to be one way of identifying high-risk unstable coronary artery disease patients\[^{11-14}\]. Multilead ST-segment monitoring with continuous vectorcardiography or continuous 12-lead electrocardiography improves the detection of transient ischaemic episodes and thereby the early risk stratification of the unstable coronary artery disease patients\[^{11-14}\]. In addition, the occurrence of ischaemic episodes might also identify patients who respond to antithrombotic treatment\[^{15-17}\]. Accordingly, the objective of this pre-specified substudy of the FRISC II trial was to assess the value of multilead ST-segment monitoring in predicting the efficacy of extended treatment with dalteparin in patients treated primarily non-invasively.

**Methods**

**Patients and study design**

The present study was carried out as a substudy of the Fragmin and Fast Revascularisation during InStability in Coronary artery disease (FRISC II) trial. The protocol and primary results of this trial have been published elsewhere\[^{4,6}\]. In brief, the FRISC II trial was a prospective, randomized, factorial, multicentre trial, designed to compare extended treatment with the low-molecular weight heparin dalteparin with placebo, and an early invasive strategy with a non-invasive strategy. In total, 3489 patients were recruited between 17 June 1996, and 28 August 1998, in 58 Scandinavian centres. Patients were eligible for inclusion if they had symptoms of myocardial infarction, with the last episode of ischaemia occurring within 48 h of the start of dalteparin or heparin treatment.

Myocardial ischaemia had to be verified by ECG (ST depression $\geq 0.10$ mV or T-wave inversion $\geq 0.10$ mV) or by raised biochemical markers. Exclusion criteria were: increased risk of bleeding, anaemia, indication for or treatment in the past 24 h with thrombolysis, angioplasty in the previous 6 months, being on a waiting list for coronary revascularization, other acute or severe cardiac disease, renal or hepatic insufficiency, known clinically relevant osteoporosis, other severe illness, hypersensitivity to randomized drug, anticipated difficulties with cooperation, and participation in other trials. In addition, patients in this substudy with an ECG not interpretable for ischaemia, i.e. left bundle branch block and pacemaker-ECG, and those in whom less than 18 h of ST-segment monitoring was performed, were also excluded from the analyses. Written consent was obtained from all patients and the protocol was approved by all local ethics committees.

The FRISC II trial had a factorial design with parallel groups. Eligible patients were started on open-label subcutaneous dalteparin twice daily or infusion of standard heparin. Within 72 h patients were randomly allocated to one of four treatment groups; invasive treatment and 5 days+3 months dalteparin, invasive treatment and 5 days dalteparin+3 months placebo, non-invasive treatment and 5 days+3 months dalteparin, non-invasive treatment and 5 days dalteparin+3 months placebo. Patients with a history of previous open heart surgery, or who were of advanced age, or poor general health, and those included after completion of recruitment of patients to the invasive vs non-invasive arm, were included in the non-invasive arm of the study and randomized to receive dalteparin or placebo. In the present substudy, only the 2267 patients allocated to a non-invasive strategy were included\[^{6}\].

After randomization, all patients were treated with dalteparin 120 IU. kg$^{-1}$ (maximum dose of 10 000 IU) twice daily for at least 5 days. After this initial treatment, patients randomized or included in a non-invasive strategy and with no contraindications performed a symptom-limited bicycle exercise test. If there were signs of severe ischaemia during the exercise test, patients were referred for early angiography and revascularization. Otherwise, patients were discharged, receiving a double-blind treatment with twice-daily subcutaneous dalteparin or placebo for 3 months. Women who weighed less than 80 kg, and men who weighed less than 70 kg, received 5000 IU twice daily, and women and men who weighed more than these values received 7500 IU twice daily. Aspirin and beta-blockade were given to all patients unless contraindicated. Long-acting nitrates, calcium antagonists, statins and angiotensin-converting-enzyme inhibitors were given as needed.

Standard 12-lead ECG readings were obtained at inclusion and interpreted centrally (Department of Cardiology, Department of Clinical Physiology, Uppsala, Sweden) without knowledge of other clinical data.

**ST-segment monitoring**

ST-segment monitoring was performed from admission and for 24 h, with continuous vectorcardiography at 17 centres and continuous 12-lead ECG at seven centres. The ST-trends from continuous vectorcardiography and continuous 12-lead ECG were stored on floppy disks and sent to the central laboratories at Sahlgrenska University Hospital, Östra (Gothenburg, Sweden) and Uppsala University Hospital (Uppsala, Sweden), respectively, where the trends were analysed by well trained observers who were blinded to other clinical data.

Continuous vectorcardiography was performed with the HP-MIDA (Hewlett Packard, Andover, Massachusetts, U.S.A.), MIDA 1000 or Coronet systems (Ortivus Medical AB, Täby, Sweden). ST-segment monitoring using vectorcardiography has been described...
in detail elsewhere\textsuperscript{[13]}. In brief, the system continuously collects electrocardiographic signals from eight electrodes positioned according to \textsuperscript{Frank}\textsuperscript{[18]}. The electrocardiographic complexes are averaged each minute to form mean vectorcardiographic complexes in the three orthogonal leads: X, Y and Z. The ST-vector magnitude is then calculated from the formula: ST-vector magnitude\(= (Xi^2 + Yi^2 + Zi^2)^{1/2}\) where Xi, Yi, and Zi are the deflections of the ST-segments from the isoelectric level 20 ms after the J point in the three orthogonal leads. All electrocardiographic data, including trends are continuously stored and displayed on screen. A transient ischaemic episode is defined as a transient change of ST-vector magnitude of at least 50 \(\mu\text{V}\) compared to the individual baseline, lasting for at least 1 min. Episodes have to be separated by at least 1 min to be considered as two separate episodes.

A 12-lead ECG was performed continuously using the ST-Guard system (GE Marquette Medical Systems, Milwaukee, U.S.A.). This system continuously collects data from all 12 leads, and calculates each minute from the last 10 s of monitoring median QRS-T complexes. From these QRS-T complexes an ST-trend for each lead is constructed, stored and displayed on-line. A transient ischaemic episode is defined as a transient ST-segment depression or elevation in any lead of at least 100 \(\mu\text{V}\) compared to the individual baseline, lasting for at least 1 min. Episodes have to be separated by at least 1 min to be regarded as two separate episodes. In order to reduce the effect of heart rate, ST-segment changes are measured at J-point\(+ (1/16 \times \text{R-R interval})\), corresponding to J-point\(+ 60 \text{ ms}\) at a heart rate of 62.5 beats per minute.

**End-points**

The end-points were death or myocardial infarction, and death, myocardial infarction or revascularization during the 3 months treatment period. In addition, the same events were also assessed at 1 month after the start of treatment. A diagnosis of myocardial infarction was made if two out of the following three criteria were met: typical chest pain, typical electrocardiographic changes (mainly new Q waves) or typically raised biochemical markers of myocardial damage. The definition of typically raised biochemical markers has been published in the main trial\textsuperscript{[9]}. In the present substudy, all patients were allocated to a non-invasive treatment strategy. Thus, in hospital, revascularization was recommended only if refractory unstable angina persisted despite optimal medical treatment, or severe ischaemia was detected at the pre-discharge exercise test. During long-term follow-up, revascularization was considered for patients with incapacitating symptoms, recurrence of coronary instability or reinfarction. The presence of transient ischaemic episodes detected by continuous multilead ST-segment monitoring during the acute phase was not considered a reason for revascularization.

**Statistical analysis**

All statistical analyses were performed on an intention-to-treat basis, using the Statistical Package for Social Sciences (SPSS 9.0) software (SPSS Inc., Chicago, Illinois, U.S.A.). Differences in proportions were judged by chi-square analysis using Yates’ correction and by Fisher’s exact test as appropriate. For continuous independent data the Mann–Whitney U test was used. A significant difference was considered to exist with \(P<0.05\). The Kaplan–Meier method was used to illustrate the timing of events. Risk ratio (RR) with 95% confidence interval (CI) was used to express treatment efficacy. Multiple logistic regression analyses with backward stepwise selection were used to identify independent predictors of outcome. The following terms were included: age \(\geq 67\) years (yes/no), male gender (yes/no), hypertension (yes/no), hyperlipidaemia (yes/no), current smoking (yes/no), diabetes mellitus (yes/no), history of previous myocardial infarction (yes/no), previous percutaneous coronary intervention (yes/no), previous coronary artery by-pass grafting (yes/no), angina pectoris >48 h (yes/no), chest pain at rest (yes/no), ST-depression \(\geq 0.05\) \text{mV} at entry (yes/no), transient ischaemic episodes (yes/no), and medication on admission; aspirin (yes/no), \(\geq 1\) antianginal drug (beta-blocker, calcium-antagonist or long-acting nitrate) (yes/no), and angiotensin-converting-enzyme inhibitor (yes/no).

To assess a possible interaction between treatment and occurrence of transient ischaemic episodes, and to compare it with the interaction between treatment and age, history of previous myocardial infarction and presence of ST-depression at entry, a multiple logistic regression analysis was used. The following terms were included: treatment (dalteparin/placebo), transient ischaemic episodes (yes/no), age \(\geq 67\) years (yes/no), history of previous myocardial infarction (yes/no), ST-depression at entry (yes/no), interaction–term 1 (treatment by transient ischaemic episodes), interaction–term 2 (treatment by age), interaction–term 3 (treatment by history of previous myocardial infarction) and interaction–term 4 (treatment by ST-depression at entry). The end-point used for the interaction-analysis was death, myocardial infarction, or revascularization at 3 months.

**Results**

**General findings**

Out of 2267 patients allocated to a non-invasive treatment strategy, 710 were included in the ST-segment monitoring substudy. Out of these, 81 (12\%) were excluded due to monitoring time <18 h (50 cases), technical problems with floppy disks or poor recording quality (31 cases). Thus, 629 patients were included in the analysis. The baseline characteristics and the event rates in these patients were similar to the total study

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population. Except for a somewhat higher proportion of previous myocardial infarction (30% vs 22%, \(P < 0.05\)) in the dalteparin-treated group, there were no significant differences in terms of baseline characteristics when the 321 patients treated with extended dalteparin and the 308 patients treated with placebo were compared (Table 1). The effect of dalteparin during follow-up in this subgroup is shown in Table 2 and was comparable to the total material.

### Prognostic value of transient ischaemic episodes

A total of 211 (33.5%) patients had transient ischaemic episodes detected as ST-vector magnitude or ST-episodes during the 24 h of ST-monitoring. Patients with transient ischaemic episodes were significantly older and had more often had ST-depression in ECG at entry than patients without transient ischaemic episodes (Table 1).

To evaluate the prognostic value of transient ischaemic episodes, the risk of death, myocardial infarction or revascularization was compared in patients with and without ischaemic episodes in the placebo group. As shown in Table 2, patients with ischaemic episodes in the placebo group had a significantly higher risk of death, myocardial infarction or revascularization both at 1 month (13.6% vs 6.8%, RR (95% CI): 1.99 (0.99-4.02)), and at 3 months this difference was less pronounced (15.5% vs 9.8%, RR (95% CI): 1.59 (0.86-2.94)).

Also concerning the composite of death or myocardial infarction, there was a trend to a higher event rate in patients with episodes of transient ischaemia compared to those without at 1 month (13.6% vs 6.8%, RR (95% CI): 1.99 (0.99-4.02)), but at 3 months this difference was less pronounced (15.5% vs 9.8%, RR (95% CI): 1.59 (0.86-2.94)).

### Treatment effect in relation to presence or not of transient ischaemic episodes

The efficacy of extended treatment with dalteparin in relation to the occurrence of transient ischaemic episodes is shown in Table 2 and in Figs 1 and 2. In the group without transient ischaemic episodes the outcome in the dalteparin and placebo groups was similar, concerning both the composites of death or myocardial infarction, and death, myocardial infarction or revascularization. However, in the group with transient ischaemic episodes, patients randomized to extended dalteparin had at 1 and 3 months significantly lower risk of the triple end-point death, myocardial infarction, or revascularization than patients on placebo, a relative risk reduction of 47% at 1 month (\(P = 0.001\)) and 34% at 3 months (\(P = 0.01\)). Concerning death or myocardial infarction, there tended to be an early separation of the event curves, with a lower event rate in the dalteparin group compared to the placebo group which, however, was not significant at 1 or 3 months.

In a multiple logistic regression model, including patients with transient ischaemic episodes, extended dalteparin treatment (odds ratio (95% CI): 0.43 (0.24-0.76)) and \(\geq 1\) antianginal drug on admission (odds ratio (95% CI): 2.68 (1.48-4.83)) were the only independent predictors of the composite of death, myocardial infarction or revascularization (Table 3).

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### Table 1  Baseline characteristics of the study population (n=629)

<table>
<thead>
<tr>
<th></th>
<th>No transient ischaemic episodes (n=418)</th>
<th>Transient ischaemic episodes (n=211)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=205)</td>
<td>Dalteparin (n=213)</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>66 (42–86)</td>
<td>65 (37–83)</td>
</tr>
<tr>
<td>Men (%)</td>
<td>151 (74)</td>
<td>141 (66)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>69 (34)</td>
<td>72 (34)</td>
</tr>
<tr>
<td>Hyperlipidaemia (%)</td>
<td>27 (13)</td>
<td>38 (18)</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>43 (21)</td>
<td>47 (22)</td>
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<tr>
<td>Diabetes mellitus (%)</td>
<td>31 (15)</td>
<td>28 (13)</td>
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<tr>
<td>Previous MI (%)</td>
<td>48 (23)</td>
<td>63 (30)</td>
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<tr>
<td>Previous PCI (%)</td>
<td>9 (4)</td>
<td>14 (7)</td>
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<tr>
<td>Previous CABG (%)</td>
<td>29 (14)</td>
<td>29 (14)</td>
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<tr>
<td>Angina &gt;48 h (%)</td>
<td>143 (70)</td>
<td>155 (73)</td>
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<tr>
<td>Chest pain at rest (%)</td>
<td>164 (80)</td>
<td>173 (81)</td>
</tr>
<tr>
<td>ST-depression at entry (%)†</td>
<td>92 (45)</td>
<td>72 (34)</td>
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<tr>
<td>Medication on admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>81 (40)</td>
<td>90 (42)</td>
</tr>
<tr>
<td>≥1 antianginal drug (%)</td>
<td>104 (51)</td>
<td>96 (45)</td>
</tr>
<tr>
<td>ACEI (%)</td>
<td>24 (12)</td>
<td>31 (15)</td>
</tr>
</tbody>
</table>

MI=myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass grafting; LVEF=left ventricular ejection fraction; ACEI=angiotensin converting enzyme inhibitor.
†Assessed in 205/210/101/108.
<table>
<thead>
<tr>
<th></th>
<th>Dalteparin (n=321)</th>
<th>Placebo (n=308)</th>
<th>RR (95% CI)</th>
<th>Dalteparin (n=213)</th>
<th>Placebo (n=205)</th>
<th>RR (95% CI)</th>
<th>Dalteparin (n=108)</th>
<th>Placebo (n=103)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 month</strong></td>
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<tr>
<td>Death/MI (%)</td>
<td>24 (7.5)</td>
<td>28 (9.1)</td>
<td>0.82 (0.49–1.39)</td>
<td>16 (7.5)</td>
<td>14 (6.8)</td>
<td>1.10 (0.55–2.20)</td>
<td>8 (7.4)</td>
<td>14 (13.6)</td>
<td>0.54 (0.24–1.24)</td>
</tr>
<tr>
<td>Death/MI/Revasc (%)</td>
<td>76 (23.7)</td>
<td>93 (30.2)</td>
<td>0.78 (0.60–1.02)</td>
<td>48 (22.5)</td>
<td>43 (21.0)</td>
<td>1.07 (0.75–1.55)</td>
<td>28 (25.9)</td>
<td>50 (48.5)</td>
<td>0.53 (0.37–0.78)</td>
</tr>
<tr>
<td><strong>3 months</strong></td>
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<tr>
<td>Death/MI (%)</td>
<td>31 (9.7)</td>
<td>36 (11.7)</td>
<td>0.83 (0.52–1.30)</td>
<td>19 (8.9)</td>
<td>20 (9.8)</td>
<td>0.91 (0.50–1.66)</td>
<td>12 (11.1)</td>
<td>16 (15.5)</td>
<td>0.72 (0.36–1.44)</td>
</tr>
<tr>
<td>Death/MI/Revasc (%)</td>
<td>104 (32.4)</td>
<td>114 (37.0)</td>
<td>0.87 (0.71–1.08)</td>
<td>66 (31.0)</td>
<td>59 (28.8)</td>
<td>1.08 (0.80–1.44)</td>
<td>38 (35.2)</td>
<td>55 (53.4)</td>
<td>0.66 (0.48–0.90)</td>
</tr>
</tbody>
</table>

**MI** = myocardial infarction; **Revasc** = revascularization; **RR** = risk ratio; **CI** = confidence interval.
predictors of death, myocardial infarction or revascularization at 3 months. In a multivariate logistic regression analysis, including treatment, transient ischaemic episodes, age, history of previous myocardial infarction, ST-depression at entry, and interaction terms for treatment and each of the four other variables, only treatment ($P = 0.04$) and the interaction between treatment and transient ischaemic episodes ($P = 0.03$) were independent predictors of death, myocardial infarction, or revascularization at 3 months.

**Discussion**

**Prognostic value of ischaemic episodes**

Previous studies have shown that occurrence of transient ischaemic episodes, detected by multilead ST-segment monitoring, is an important risk marker in patients with unstable coronary artery disease[13,14]. The results of the present study are consistent with these previous findings. Furthermore, ischaemic episodes were shown to be prognostic even in patients with ST-depression at entry, or with raised biochemical markers and a modern therapeutic strategy including at least 5 days of low-molecular weight heparin. However, the possibility of identifying low risk patients using only the absence of ischaemic episodes was less impressive than in the previous studies. In the present study, the risk of death or myocardial infarction and death, myocardial infarction or revascularization at 3 months was still 9.8% and 28.8%, respectively, in patients without ischaemic episodes. Thus, in patients with signs of ischaemia on the ECG or elevated biochemical markers, the absence of transient ischaemia does not necessarily imply a favourable outcome.

**Treatment efficacy in patients with transient ischaemic episodes**

In patients with unstable coronary artery disease, different antithrombotic treatments reduce the occurrence of transient ischaemic episodes[15–17]. This reduction of ischaemia has been associated with a better short- and long-term outcome[15–17]. However, hitherto only elevation of troponin has been proven useful in predicting efficacy of antithrombotic treatment and, hence, useful for identification of patients for a specific therapy[7–9]. The present study is the first to indicate that continuous multilead ST-segment monitoring can be used to prospectively identify patients who benefit from antithrombotic treatment.

The FRISC II trial indicated that 3 months’ treatment with dalteparin reduced the risk of subsequent death, myocardial infarction or revascularization compared to the standard of 5–7 days with dalteparin[6]. The present substudy showed that this treatment effect was most apparent in patients with transient ischaemic episodes detected by continuous multilead ST-segment monitoring. In this group, the risk was reduced during the active treatment period to about the same level as those without transient ischaemic episodes. However, as in the main trial[6], these benefits were gradually lost after cessation of treatment.
As in previous studies\cite{19,20}, the present study showed that patients with transient ischaemic episodes were older and had a higher prevalence of ST-depression at entry. However, in the interaction analysis, including transient ischaemic episodes, age, history of previous myocardial infarction, ST-depression at entry, and the interaction between these variables and drug-treatment, only the drug treatment and the interaction between drug treatment and transient ischaemic episodes were independent predictors of outcome.

Reasons for the difference in treatment effect

The difference in treatment effect may be due to different pathophysiology in patients with and without transient ischaemic episodes. In unstable coronary artery disease, transient ischaemic episodes are caused by a decreased myocardial oxygen supply rather than increased demand\cite{21–23}. Both anticoagulant and platelet inhibitory therapies have been shown to lower the incidence of these episodes\cite{15,24}. These findings indicate that transient ischaemic episodes are associated with thrombus formation and are therefore more likely to respond to antithrombotic treatment.

Previous studies have shown that elevated troponin levels also identify high-risk groups who benefit from anticoagulant or platelet inhibitory therapy\cite{7–9}. Thus, troponin has been put forward as a marker of coronary thrombus and subsequent microembolization\cite{3,25}. However, these two methods seem to identify somewhat different populations, with the highest risk in the group with both elevated troponin T and ischaemic episodes and the lowest in the group without these risk indicators\cite{19,20}. Unfortunately, the present study did not have the power to examine the possibility that these methods might be complementary in the identification of responders to extended antithrombotic treatment. This needs to be examined in forthcoming studies.

Although the lack of treatment effect in patients without transient ischaemic episodes is noteworthy, it should be interpreted with caution because of the low number of patients and low event rates. However, it might be speculated that these patients have a somewhat different pathophysiology, with fewer ischaemic episodes caused by coronary thrombus formation, and with subsequent less likely to benefit from extended antithrombotic treatment.

Limitation

In the present study, two different kinds of multilead ST-segment monitoring systems, continuous vectorcardiography and continuous 12-lead ECG, were used. However, these two systems have, in a previous study, been shown to identify the same high-risk population\cite{26}. Therefore, it seems appropriate to analyse patients identified to have ischaemic episodes by continuous vectorcardiography or by continuous 12-lead ECG as one group.

Conclusions

In patients with unstable coronary artery disease treated by a primarily non-invasive strategy, the occurrence of transient ischaemic episodes during continuous multilead ST-monitoring is associated with a higher rate of subsequent coronary events. The occurrence of transient ischaemia also identifies patients who benefit from extended treatment with a low-molecular weight heparin. Continuous multilead ST-monitoring may therefore be an additional tool with which target anti-
thrombotic therapy in the heterogeneous population of patients with unstable coronary artery disease.

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References


Appendix


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