Is it possible to separate ischemic and bleeding risk in patients with non-ST segment elevation acute coronary syndromes?

Albert Ariza-Solé *, José C. Sánchez-Salado, Victoria Lorente, Guillermo Sánchez-Elvira, Guillem Muntané, Joel Salazar-Mendiguchía, Ángel Cequier.

Hospital Universitario de Bellvitge, L’Hospitalet de Llobregat, Barcelona, Spain

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Dear editor:

Both intensive antithrombotic therapy and an early invasive strategy reduce the incidence of ischemic events in patients with non-ST segment elevation acute coronary syndromes (NSTE-ACS), at the expense of increasing the rate of bleeding complications. Current recommendations [1] emphasize the use of an early invasive strategy in patients at higher risk. However, most registries show a more conservative management in these patients [2].

Most of the predictors of ischemic events in patients with NSTE-ACS are also predictors of bleeding complications. These variables are part, both of bleeding risk scores and ischemic risk scores [3–7]. We hypothesized that due to similarities in the composition of both types of scores a close linear relationship between them might exist and, therefore, this can make the selective prediction of bleeding or ischemic complications in this clinical scenario difficult.

Thus, the aim of this study was to assess the relationship between current available ischemic and bleeding risk scores and their ability for predicting both ischemic and bleeding events in a cohort of consecutive patients with NSTE-ACS admitted in a tertiary care Coronary Care Unit.

Informed consent was given for all the patients before their inclusion in this prospective study. The confidential information of the patients was protected according to national normative. This manuscript has been revised for its publication by the Clinical Research Ethics Committee of Bellvitge University Hospital (IRB00005523).


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* Corresponding author at: Coronary Care Unit, Hospital de Bellvitge, Feixa Llarga s/n, 08907 Hospitalet de Llobregat, Barcelona, Spain. Tel.: +34 932607924; fax: +34 932607918.

E-mail address: aariza@bellvitgehospital.cat (A. Ariza-Solé).

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Fig. 2. An apical 4-chamber view showed the contrast filled in the left ventricular chamber. There is no contrast within the pericardial sac at the mean time.

The intrapericardial flow pattern could also be demonstrated by pulsed-wave Doppler examination. The authors hypothesize that in their case, probably secondary to anticoagulation, the viscosity of the intrapericardial fluid was low enough to demonstrate, by way of fluid shifts within the confines of the pericardium, the changes of volume and pressure of the heart chambers throughout the cardiac cycle.

Nevertheless, the small amount of effusion can be commonly seen in post-radiofrequency ablation, which should be general fluid without red blood cells and could not generate Doppler signal.

In our case, the patient has only a small amount pericardial effusion. The flow was clearly demonstrated by color and pulse Doppler which might be due to mild injury around the pulmonary vein during radiofrequency ablation operation. The absence of red blood cells prevents the reflection of the ultrasound beam and, therefore, generates a Doppler signal.

This case indicated that in patients with pericardial effusion post-procedure, we should pay more attention to find if there is any flow signal by color and pulse Doppler, which can early detect the communication between chambers and pericardium.

Reference

were included in the case report form. All these scores were calculated for each patient. The incidence of death or reinfarction at 30 days was also collected.

Relationship between ischemic and bleeding risk scores was analyzed by linear regression. The ability of these scores for predicting ischemic events (30-day death or reinfarction) and bleeding events (in-hospital CRUSADE major bleeding [1]) was assessed by binary logistic regression, calculating ROC curves and the corresponding areas under the curve (AUC). Comparative analysis between different AUC was performed by the non-parametric method described by DeLong [8].

We prospectively included 558 patients (407 (72.9%) males), with a mean age of 62.9 years. Prevalence of cardiovascular risk factors was as follows: 383/558 (68.6%) hypertension, 368/558 (65.9%) dyslipidemia and 210/558 (37.6%) diabetes mellitus. 130 patients (23.3%) had signs of heart failure at admission. 142 patients (25.4%) had creatinine clearance <60 ml/min. Mean values of the risk scores were as follows: CRUSADE 28.6; Mehran 14.9, ACTION 27.3, TIMI 3.6 and GRACE 135.2. Coronary angiography was performed during admission in 527 patients (94.4%), with percutaneous coronary intervention in 347 cases.

The incidence of major CRUSADE bleeding was 27/558 (4.8%), 19 patients (3.4%) died during hospitalization. We obtained data on follow up in 521 patients (93.3%). The incidence of death or reinfarction at 30 days was 26/558 (4.99%). A close linear relationship was observed between ischemic and bleeding risk scores. The GRACE score showed a close linear relationship with these 3 bleeding risk scores (B CRUSADE coefficient 0.708, p < 0.001; Mehran B coefficient 0.652, p < 0.001; ACTION B coefficient 0.714, p < 0.001). The analysis of the predictive ability of the different risk scores showed interesting findings. All the scores similarly predicted both ischemic and bleeding complications, supporting previous data [9]. Interestingly, the score that best predicted bleeding complications was the GRACE score (designed for predicting ischemic events). Likewise, the score that best predicted ischemic events was the ACTION score, which was designed for predicting haemorrhagic complications.

Table 1 shows the predictive ability of the different risk scores for predicting both ischemic and bleeding complications.

Our study has the inherent limitations of being a single centre registry. Ours was a relatively young population, with a high rate of early invasive strategy. Therefore, our findings might not be applicable to other populations. In addition, the number of events was relatively small. Finally, we did not collect data about frailty and other comorbidities [10], which could have provided interesting information about ischemic and bleeding risk in this clinical setting.

However, we believe that our findings illustrate the enormous difficulty to separate ischemic and bleeding risk in this clinical scenario, which in turn might be a possible explanation for the lower use of an early invasive strategy in patients at higher risk, as described in most registries. Developing new tools for a selective stratification of bleeding and ischemic risk might significantly contribute to improve clinical management of these patients.

### Table 1

<table>
<thead>
<tr>
<th>Area under the curve</th>
<th>Comparison of scores</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prediction of death or reinfarction at 30 days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GRACE</td>
<td>0.716 (0.673–0.760)</td>
<td>GRACE vs CRUSADE 0.315</td>
</tr>
<tr>
<td>TIMI</td>
<td>0.656 (0.609–0.700)</td>
<td>GRACE vs Mehran 0.059</td>
</tr>
<tr>
<td>CRUSADE</td>
<td>0.770 (0.727–0.808)</td>
<td>CRUSADE vs ACTION 0.253</td>
</tr>
<tr>
<td>Mehran</td>
<td>0.745 (0.701–0.785)</td>
<td>TIMI vs CRUSADE 0.018</td>
</tr>
<tr>
<td>ACTION</td>
<td>0.785 (0.743–0.823)</td>
<td>TIMI vs Mehran 0.099</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TIMI vs ACTION 0.005</td>
</tr>
<tr>
<td><strong>Prediction of major CRUSADE bleeding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GRACE</td>
<td>0.818 (0.778–0.853)</td>
<td>CRUSADE vs GRACE 0.287</td>
</tr>
<tr>
<td>TIMI</td>
<td>0.712 (0.667–0.754)</td>
<td>CRUSADE vs TIMI 0.226</td>
</tr>
<tr>
<td>CRUSADE</td>
<td>0.781 (0.739–0.819)</td>
<td>Mehran vs GRACE 0.032</td>
</tr>
<tr>
<td>Mehran</td>
<td>0.741 (0.697–0.782)</td>
<td>Mehran vs TIMI 0.620</td>
</tr>
<tr>
<td>ACTION</td>
<td>0.743 (0.699–0.783)</td>
<td>ACTION vs GRACE 0.099</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACTION vs TIMI 0.561</td>
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</tbody>
</table>

### References


Various morphological-types of all and fragmented ventricular premature beats on a 12-lead Holter-ECG had positive-relationship with occurrence of LV fibrosis on CT in HCM subjects

Koya Ozawa a,1, Nobusada Funabashi a,8,1, Hiroyuki Takaoka a, Masae Uehara a, Marehiko Ueda a, Yuji Murakawa a, Yoshio Kobayashi a

a Department of Cardiovascular Medicine, Chiba University Graduate School of Medicine, 1-8-1 Inohana, Chuo-ku, Chiba City, Chiba 260-8670, Japan
b The 4th Department of Internal Medicine, Teikyo University School of Medicine, Mizokuni Hospital, 3-8-3 Mizokuni, Takatsuki-ku, Osaka 565, Japan

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Various morphological types of ventricular premature beats (VPBs) with fragmented QRS waves (fragmented VPBs) are often observed among patients with hypertrophic cardiomyopathy (HCM) but their significance is unknown.

In this study, to study the significance of the number of various morphological types of fragmented VPBs on 12-lead Holter electrocardiogram (ECG) in patients with HCM, we evaluated the correlations between the numbers of morphological types of all VPBs/those of fragmented VPBs with patient characteristics and multislice computed tomographic (CT) findings.

Retrospective analysis of a total of 49 consecutive patients with HCM (37 male, mean 61 ± 13 yrs) who underwent enhanced ECG-gated CT (Aquillion one, Toshiba Medical or Light Speed Ultra 16, GE Healthcare) and 12 lead Holter ECG (RAC-2103, Nihon Koden) was conducted within 3 months from July 2007 to April 2012 (Table 1 and Fig. 1). Evaluation of coronary arteries and characteristics of left ventricular (LV) myocardium was performed.

A fragmented VPB was defined as a VPB with one or more notches in the R or S waves on a routine 12-lead Holter ECG (Fig. 2). Obvious complete right or left bundle branch block shaped VPBs were excluded from fragmented VPBs in this analysis. The numbers of morphological types of all VPBs and fragmented VPBs were counted automatically, but were manually revised by experienced technologists. After that, an experienced cardiologist blinded to the CT findings confirmed the results of the printed results.

ECG gated multislice CT was performed in all subjects to evaluate characteristics of the coronary arteries [1–3], myocardium and cardiac function [4,5]. If there was a contrast defect in the left ventricular (LV) myocardium in the early phase, late phase acquisition was added, and if abnormal late enhancement was observed at the corresponding site, we diagnosed myocardial fibrosis (Fig. 3). If contrast defect continued in the late phase with CT values of <0 Hounsfield Units, myocardial fatty change was diagnosed (Fig. 4).

Numbers of morphological types of all VPBs were 6.9 ± 7.8 and those of fragmented VPBs were 2.6 ± 2.3. >50% stenosis of any coronary arteries was observed on CT in 3 (6%) subjects. Fibrosis and fat in LV myocardium were observed on CT in 29 (59%) subjects and 9 (18%) subjects, respectively (Table 2).

Age did not significantly correlate with the numbers of morphological types of all VPBs or those of fragmented VPBs (Fig. 5).

There were no significant differences in the numbers of morphological types of all VPBs and those of fragmented VPBs between males and females (Fig. 6).

There were no significant differences in the numbers of morphological types of all VPBs and fragmented VPBs between subjects with and without diabetes mellitus (Fig. 7).

There were no significant differences in the numbers of morphological types of all VPBs and those of fragmented VPBs between subjects with or without hypertension (Fig. 8).

There were no significant differences in the numbers of morphological types of all VPBs and those of fragmented VPBs between subjects with or without hyperlipidemia (Fig. 9).

Table 1
Patient characteristics.

<table>
<thead>
<tr>
<th>All patients (n = 49)</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Hypertrophic obstructive cardiomyopathy</td>
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<td>Dilated phase hypertrophic cardiomyopathy</td>
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* Corresponding author. Tel.: +81 43 222 7171x5264.
E-mail address: nobusada@w8.dion.ne.jp (N. Funabashi).

1 These authors contributed equally to this work.