Letters to the Editor

Chest pain unit: do not forget the clinical indexes

Unidad de dolor torácico: no olvidar los índices clínicos

To the Editor,

We have read with considerable interest the article by Piñeiro-Portela et al.,[1] which compares 2 diagnostic imaging tests in the chest pain unit: stress echocardiography and multidetector computed tomography. Given that the included patients had a low-to-intermediate probability of having acute coronary syndrome (ACS), a normal or nondiagnostic electrocardiogram, and normal troponin levels, we believe that some of the participants did not require diagnostic imaging tests. The authors did not provide results on any of the clinical indexes typically applied to patients with ACS (eg, GRACE, TIMI, and HEART) or used in chest pain units.[2–4] It would have been useful to report the results of the CPU-65 risk index (use of aspirin, diabetes, typical pain, age $\geq$ 65 years) and the index described by Sanchis et al.[5] (male sex_1, effort-related $pain_1$, recurrent $pain_2$, and prior ischemic heart disease[2]). Specifically, it would be valuable to know how many patients had index scores ≤ 1 and their outcomes. In addition, the authors should have indicated if high-sensitivity troponin was used, as well as one of the troponin algorithms with proven high sensitivity and negative predictive value for ACS diagnosis. Some evidence indicates that ischemic diagnostic tests might be overused in patients with low or intermediate risk,[6] which is why some very low clinical index scores (0 or even 1) might be sufficient to discharge patients with normal electrocardiogram and troponin results from the emergency department. The overuse of ischemic diagnostic tests in low-risk patients prolongs their stay in emergency departments (and even compels their admission), increases the economic cost, and may even result in invasive procedures with no clear impact on patient prognosis.

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Manuel Martínez-Sellés,[a,*] Juan Sanchis,[b] and Héctor Bueno[c]

[a]*Servicio de Cardiología, Hospital General Universitario Gregorio Marañón, CIBERCV, Universidad Europea, Universidad Complutense, Madrid, Spain*
[b]*Servicio de Cardiología, Hospital Clínico Universitario de Valencia, Universidad de Valencia, Valencia, Spain*
[c]*Servicio de Cardiología, Hospital Universitario 12 de Octubre, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Universidad Complutense, Madrid, Spain*

* Corresponding author:
E-mail address: mmselles@secardiologia.es (M. Martínez-Sellés).

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Chest pain unit: do not forget the clinical indexes. Response

Unidad de dolor torácico: no olvidar los índices clínicos. Respuesta

To the Editor,

We appreciate the interest in our article, comparing stress echocardiography and multidetector computed tomography in a chest pain unit. Although they were not our objectives, we agree that clinical indexes[1] and high-sensitivity troponin determination[2] are useful to reduce the need for techniques to detect ischemia and coronary disease.

Our article reports one of the indexes mentioned in your letter, the TIMI risk score (68% of patients in TIMI I and 32% in TIMI II). We calculated the percentage of patients with a CPU-65 index of 0 to 1 and found it to be 45%, with no significant differences between the 2 strategies. Irrespective of this finding, the high prevalence of the definite diagnosis of acute coronary syndrome (26%) indicates that the techniques to detect ischemia and coronary disease were not overused.

One of the limitations mentioned was the use of conventional troponin determination. The absence of high-sensitivity troponin determination at inclusion may have contributed to a higher pretest probability of acute coronary syndrome and a greater yield of the diagnostic imaging techniques, which might not apply to a more current population.[3]

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In any event, the use of clinical indexes and high-sensitivity troponin does not completely eliminate the need for functional or anatomical tests to detect coronary disease in a part of the population referred to a chest pain unit, and in our opinion, none of the factors mentioned affects the validity of the results of our study.

Miriam Piñeiro-Portela,[a,b,*] Jesús Peteiro-Vázquez,[a,b] Alberto Bouzas-Mosquera,[a,b] and José Manuel Vázquez-Rodríguez[a,b]

[a]*Servicio de Cardiología, Unidad de Imagen y Pruebas Funcionales, Hospital Universitario de A Coruña, A Coruña, Spain*
[b]*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*

[*] Corresponding author:
E-mail address: Miriam.Pineiro.Portela@sergas.es (M. Piñeiro-Portela).

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The use of antiplatelet agents for arterial thromboprophylaxis in COVID-19

El uso de agentes antiplaquetarios para la tromboprofilaxis arterial en la COVID-19

To the Editor,

We read with interest the retrospective study reported by Rey et al.[1] to describe the clinical characteristics and outcomes of patients with novel coronavirus disease 2019 (COVID-19) who developed acute arterial thrombosis. Despite being a small-scale study (n = 87), there are a few clinical trends to be noted. Based on the reported findings, we observed that the proportion of COVID-19 patients with major cardiovascular risk factors who developed acute arterial thrombosis is higher than that of their non-COVID-19 counterparts. Such finding hinted at the possibility that thromboinflammation plays a greater role for the development of arterial thrombosis in COVID-19 patients than traditional cardiovascular risk factors. In addition, the mortality rate of COVID-19 patients with arterial thrombosis was high (44.7%), which indicates a poor prognosis. Therefore, we would like to propose routine antiplatelet therapy (low-dose aspirin, clopidogrel, ticagrelor, prasugrel, ticlopidine, and dipyridamole) for arterial thromboprophylaxis in COVID-19 patients who are deemed at heightened risk for the development of acute arterial thrombosis.

Low-dose aspirin (75–150 mg/d) is sufficient to irreversibly acetylate Ser 530 of COX-1, thus preferentially inhibiting platelet generation of thromboxane A_2, and interfering with the formation of arterial thrombus. On the other hand, for $P2Y_{12}$ inhibitors (clopidogrel, ticagrelor, prasugrel, and ticlopidine), either the parent drug or the active metabolite blocks the $P2Y_{12}$ component of adenosine diphosphate receptors on the platelet surface, which prevents activation of the glycoprotein IIb/IIIa receptor complex, thereby reducing platelet aggregation and subsequent arterial thrombus formation. Dipyridamole inhibits the activity of adenosine deaminase and phosphodiesterase, which causes an accumulation of adenosine, adenine nucleotides, and cyclic AMP; these mediators then inhibit platelet aggregation and the subsequent arterial thrombus formation. Aspirin and dipyridamole may be particularly favored in COVID-19 patients; aspirin possesses antiviral activity related to its ability to inhibit the coronavirus-induced nuclear factor kappa B pathway,[2] while dipyridamole appears to directly suppress severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative pathogen of COVID-19 based on in silico docking analysis and in vitro cell culture study.[3]

There have been limited studies that have demonstrated favorable clinical outcomes in COVID-19 with the use of antiplatelet therapy either alone or in combination with an anticoagulant. In their prospective observational study among critically ill patients with COVID-19, Ranucci et al.[4] reported that a combination of an enhanced prophylactic dose of heparin, clopidogrel, and antithrombin correction returned the parameters of viscoelastic coagulation tests to essentially normal (129). In a proof-of-concept, case control, phase IIb study in 5 patients with COVID-19 and severe respiratory failure treated with a combination of tirofiban, aspirin, clopidogrel, and fondaparinux, Viecca et al.[5] reported superiority in terms of improvement in oxygenation, and weaning time from continuous positive airway pressure therapy compared with controls matched for disease severity who received either prophylactic or treatment-dose heparin. Liu et al.[3] performed a multicenter, parallel, randomized controlled trial of 31 patients with COVID-19 with severe or critical illness, who received either standard of care (n = 17) or dipyridamole at a dose of 50 mg 3 times daily for 14 days in addition to the standard of care (n = 14). Patients randomized to dipyridamole had an increased survival and remission rate that approached statistical significance (odds ratio, 23.75; 95% confidence interval, 0.87-648; $P = .06$), as well as reduced D-dimer levels, and increased lymphocyte and platelet counts.

Nevertheless, at the time of writing, we are not aware of any studies that have reported the outcomes on the use of antiplatelet agents for the prevention of arterial thrombotic events in patients with COVID-19. We urge the performance of a study to evaluate the use of antiplatelet therapy to prevent arterial thrombotic events,

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