RESEARCH LETTER

On-treatment platelet reactivity in patients with chronic obstructive pulmonary disease undergoing percutaneous coronary intervention

Patients with chronic obstructive pulmonary disease (COPD) show a poor prognosis after myocardial infarction (MI) and percutaneous coronary intervention (PCI). We evaluated on-treatment platelet reactivity (PR) and several gene polymorphisms related to PR in 130 patients undergoing PCI with and without COPD. Those with concomitant COPD showed higher on-treatment PR values both at the time of PCI and 1 month after. This finding may contribute to explain the poor prognosis of COPD patients after MI and PCI.

Patients with myocardial infarction undergoing percutaneous coronary intervention (PCI) with concomitant chronic obstructive pulmonary disease (COPD) are at increased risk for death and hospital readmissions compared with those without COPD.¹ Abnormalities in the on-treatment platelet reactivity (PR) values could be involved in this worse outcome.

In the Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia study we enrolled 1970 patients treated with PCI and stent implantation and all received dual antiplatelet therapy (aspirin+clopidogrel).² In 723 patients (random sample), we assessed on-treatment PR at the time of PCI and after 1 month (by P2Y12 VerifyNow system and Multiplate Analyzer) together with the gene polymorphisms CYP2C19*2, *17, ABCB1 and Q192R PON1.^{3, 4} Sixty-five (9%) patients had a documented COPD (cases). COPD was defined as a history or presence of physician-diagnosed COPD. The patients were required to be on chronic pharmacologic therapy and/or have an forced expiratory volume in the first second (FEV)₁ <75% of predicted value. As control group, sixty-five patients without COPD matched for baseline characteristics were selected (propensity score analysis). Informed written consent was obtained from all patients, and the study was approved by the local ethics review board. All tests used for statistical analysis were reported in the online supplementary file.

At the time of PCI, on-treatment PR was significantly higher in patients with

concomitant COPD as compared with those without (table 1). As expected, on-treatment PR values decreased from baseline to 1 month, both in patients with and without concomitant COPD (table 1). As for baseline values, 1 month on-treatment PR remained significantly higher in patients with concomitant COPD (table 1). These

findings are consistent considering both platelet function assays and using different agonists (table 1). We did not observe differences in gene polymorphisms between the two groups (table 1).

It is known that on-treatment PR can be influenced by age, sex, smoking, diabetes and renal failure;⁵ however, the impact of

Table 1 Characteristics of study population

Variables	without COPD (n=65)	With COPD (n=65)	p Value
Age (years), mean±SD	70±11	71±10	0.4
Cardiovascular risk factors, n. (%)			
Men	52 (80)	50 (77)	0.9
Diabetes mellitus	14 (21)	14 (21)	0.9
Hypertension	53 (81)	55 (84)	0.3
Current smoker	14 (21)	12 (18)	0.5
Hypercholesterolemia	31 (47)	30 (46)	0.7
Prior medical history, n. (%)			
Renal failure	3 (4)	3 (4)	0.6
MI	24 (36)	21 (32)	0.7
PCI	23 (38)	21 (36)	0.6
CABG	2 (3)	3 (4)	0.8
Clinical presentation, n (%)			
ST-segment elevation MI	11 (17)	11 (17)	0.9
No ST-segment elevation ACS	35 (54)	36 (55)	0.7
Stable angina	17 (26)	18 (27)	0.7
Laboratory data, mean±SD			
Platelet count (u×10 ³ /mm ³)	230±65	239±70	0.3
White blood cells (u/mm ³)	8.2±2	8.5±2	0.5
Haematocrit (%)	42±6	43±5	0.5
Cardiac medical therapy, n (%)			
ACE inhibitors	60 (92)	60 (92)	0.9
B-blockers	53 (81)	49 (75)	0.1
Statins	61 (93)	60 (92)	0.9
Clinical outcome at 2 years, n (%)			
Death	9 (13)	10 (15)	0.2
MI	3 (5)	5 (7)	0.3
Heart failure	9 (13)	11 (18)	0.4
Gene polymorphisms, n. (%)			
CYP2C19 *2 carriers	14 (21)	12 (18)	0.4
CYP219 *17 carriers	25 (38)	24 (37)	0.8
ABCB1 CC homozygotes	16 (24)	14 (21)	0.5
PON1 192 RR homozygotes	5 (8)	6 (9)	0.8
P2Y12 VerifyNow (PRU), mean±SD			
Baseline	182±100	226±105	0.01
1 month	148±79	184±77	0.009
Multiplate Analyzer (AU×min), median (IQR)			
Baseline TRAP test	953 (605–1104)	1119 (867–1388)	0.002
ASPI test	235 (139–352)	349 (192–645)	0.02
ADP test	504 (337–800)	679 (438–934)	0.03
ADP HS test	317 (224–535)	514 (287–737)	0.01
1 month TRAP test	796 (589–908)	1054 (763–1123)	<0.001
ASPI test	137 (37–242)	352 (232–427)	<0.001
ADP test	309 (277–543)	677 (324–891)	<0.001
ADP HS test	212 (205–342)	567 (219–752)	<0.001

Multiplate analyzer result is expressed in area under the curve of arbitrary units (AU×min). P2Y12 VerifyNow, ADP test and ADP HS test evaluate the platelet pathway normally inhibited by clopidogrel. ASPI test evaluates the platelet pathway normally inhibited by aspirin. TRAP test evaluates the general platelet function after stimulus with thrombin. ACS, acute coronary syndrome; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; HS, high sensitivity; MI, myocardial infarction; PCI, percutaneous coronary intervention; PON, paraoxonase; PR, platelet reactivity; PRU, P2Y12 reactivity unit; TRAP, thrombin receptor activating peptide.

COPD has been less investigated. This is probably due to different reasons: (i) exclusion of COPD patients from clinical studies; (ii) possible interaction between COPD therapy and on-treatment PR; (iii) poor compliance to antiplatelet drugs in COPD patients. For the first time, our post-hoc analysis showed a significantly higher on-treatment PR in COPD patients undergoing PCI independently from age, sex, cardiovascular risk factor and clinical presentation. This finding is consistent as it occurs at the time of PCI and 1 month after, both in acute coronary syndrome and stable patients. The underlying causes are not known. Genetic determinants were not involved. We may speculate that the proinflammatory nature of COPD could be involved, influencing both platelet function and drug responsiveness. Regardless of the cause, this heightened on-treatment PR may have an important clinical relevance and may influence the long-term outcome. COPD patients undergoing PCI could be candidates for the newer antiplatelet drugs (such as ticagrelor and prasugrel). Contemporaneously, they showed a higher bleeding risk.¹ Further studies should be planned to confirm our suggestion and to

select the best antiplatelet treatment in COPD patients.

Gianluca Campo,^{1,2} Rita Pavasini,¹ Alberto Pollina,¹ Matteo Tebaldi,¹ Roberto Ferrari^{1,2}

¹Department of Medical Sciences, Cardiovascular Institute, Azienda Ospedaliero-Universitaria S. Anna, Cona, Ferrara, Italy

²LTTA Center, Ferrara, Italy

Correspondence to Dr Gianluca Campo, Department of Medical Sciences, Cardiovascular Institute, Azienda Ospedaliera Universitaria S. Anna, Via Aldo Moro, 8, Cona, (FE) 44124, Italy; cmpglc@unife.it

Contributors GC, RP: conception and design; GC, AP, MT: analysis and interpretation of data; GC, MT: drafting the article; RP, AP: revising the article critically for important intellectual content; RF: final approval of the version to be published.

Funding This work was supported by a grant from Fondazione Anna Maria Sechi per il Cuore (FASC), Italy. The funders had no role in the study design, data collection and analysis, decision to publish or the preparation of the manuscript.

Competing interests None.

Ethics approval Comitato Etico Della Provincia Di Ferrara.

Provenance and peer review Not commissioned; externally peer reviewed.

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2013-203608>).

To cite Campo G, Pavasini R, Pollina A, *et al.* *Thorax* 2014;**69**:80–81.

Received 20 March 2013

Revised 13 June 2013

Accepted 23 June 2013

Published Online First 22 July 2013

Thorax 2014;**69**:80–81.

doi:10.1136/thoraxjnl-2013-203608

REFERENCES

- 1 Campo G, Guastaroba P, Marzocchi A, *et al.* Impact of chronic obstructive pulmonary disease on long-term outcome after ST-segment elevation myocardial infarction receiving primary percutaneous coronary intervention. *Chest* 2013. doi: 10.1378/chest.12-2313. [Epub ahead of print].
- 2 Valgimigli M, Campo G, Monti M, *et al.* Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. *Circulation* 2012;125:2015–26.
- 3 Campo G, Ferraresi P, Marchesini J, *et al.* Relationship between paraoxonase Q192R gene polymorphism and on-clopidogrel platelet reactivity over time in patients treated with percutaneous coronary intervention. *J Thromb Haemost* 2011;9:2106–18.
- 4 Sibbing D, Braun S, Morath T, *et al.* Platelet reactivity after clopidogrel treatment assessed with point-of-care analysis and early drug-eluting stent thrombosis. *J Am Coll Cardiol* 2009;53:849–56.
- 5 Angiolillo DJ, Bernardo E, Capodanno D, *et al.* Impact of chronic kidney disease on platelet function profiles in diabetes mellitus patients with coronary artery disease taking dual antiplatelet therapy. *J Am Coll Cardiol* 2010;55:1139–46.