recommendations for standardization, recording, and reporting as a core laboratory technique. Proposals for integration in clinical trials. Circ Cardiovasc Int 2012;5:312–7.
6. Pijls NHJ, Tonino PAL. The crux of maximum hyperemia: the last remaining barrier for routine use of fractional flow reserve. J Am Coll Cardiol Int 2011;4:1093–5.

Reply

We thank Dr. Palmer and colleagues for commenting on 1 of the potential important implications of our recently reported finding (1). We demonstrated, in healthy volunteers, that ticagrelor enhanced coronary vasodilatory response to adenosine through increased sensitivity to adenosine, as shown by a greater area under the curve for adenosine dose versus coronary blood flow when ticagrelor was used. A maximum significant additive effect was seen at a submaximal adenosine dose of 80 μg/kg/min. The study was conducted in healthy volunteers to avoid any confounders, such as concomitant medications, etc.

Adenosine is a widely used cardiac stress agent for measurement (e.g., fractional flow reserve [FFR]). However, it has been shown that maximum hyperemia could not be achieved in all patients using the standard intravenous adenosine dose of 140 kg/min (2). Interestingly, the variability in adenosine response could also be partially explained by the genetic polymorphism in adenosine receptors (3).

In patients with various risk factors, impaired coronary flow velocity reserve (CFVR) has been reported and has also shown strong predictive values for future cardiovascular outcomes (4). Thus, it is conceivable that ticagrelor may also enhance the maximum hyperemic response in patients with impaired CFVR through increased hyperemic flow velocity response. If that is the case, this will lead to an increased drop in pressure over a certain stenosis, and thereby, lower the FFR value. As correctly pointed out by Palmer et al., this will likely improve the accuracy and consistency of FFR measurements in the future.

Finally, because our data were generated in healthy volunteers, the concept still needs to be demonstrated in patients with coronary artery disease. Thus, more studies are warranted to prove the hypothesis raised by Palmer et al.

***Li-Ming Gan, MD, PhD**
Ann Wittfeldt, MD
Gunnar Brandrup-Wognsen, MD, PhD
J. J. J. van Giezen, PhD
Jenny Jonasson, PhD
Sven Nylander, PhD
Håkan Emanuelsson, MD, PhD

*AstraZeneca R&D
Pepparedsleden 1
Mölndal
SE-431 83 Sweden
E-mail: li-ming.gan@astrazeneca.com

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REFERENCES

1. Wittfeldt A, Emanuelsson H, Brandrup-Wognsen G, et al. Ticagrelor enhances adenosine-induced coronary vasodilatory responses in humans. J Am Coll Cardiol 2013;61:723–7.
2. Wilson RF, Wyche K, Christensen BV, Zimmer S, Laxson DD. Effects of adenosine on human coronary arterial circulation. Circulation 1990; 82:1595–606.
3. Andreassi MG, Laghi Pasini F, Picano E, et al. Adenosine A2(A) receptor gene polymorphism (1976C>T) affects coronary flow reserve response during vasodilator stress testing in patients with non ischemic-dilated cardiomyopathy. Pharmacogenet Genom 2011;21:469–75.
4. Cortigiani L, Rigo F, Gherardi S, et al. Coronary flow reserve during dipyridamole stress echocardiography predicts mortality. J Am Coll Cardiol Img 2012;5:1079–85.

Choosing Troponin Immunoassays in a World of Limited Resources

We read with interest the report by Korley and Jaffe (1), who elaborated several critical issues as a means of educating clinicians about cardiac troponin immunoassays. Although the investigators should be praised for their effort to synthesize and emphasize the leading problems and drawbacks, another important issue engages the minds of clinicians and laboratory professionals. There is open debate about the different analytical and clinical performance of the different troponin immunoassays (2,3). Because of the ongoing economic crisis and the increasing pressure placed on clinical laboratories to conserve economic and human resources, there is a widespread phenomenon of merging of existing clinical laboratories into larger ones, accompanied by consolidation of different tests within multitasking analytical platforms (4). The in vitro diagnostic industry is continuously developing and marketing integrated instrumentation, where the consolidation of most clinical chemistry and a variety of immunochemistry tests is indeed an efficient and cost-effective solution in a world of limited resources.

What some clinicians often ignore is that the procedures for purchasing instrumentations and reagents in clinical laboratories are challenging and increasingly involve a large number of tests rather than individual parameters (4). Regardless of its unquestionable clinical value for cardiologists and emergency physicians, troponin testing is only a minor part of the game in the context of a large tender for laboratory equipment, so that the acquisition of dedicated instrumentation to measure only troponin is becoming problematic, especially in some European countries. In this perspective, the question as to whether troponin T may be better than troponin I for identifying myocardial injury, and even whether one troponin I immunoassay may perform better than another for diagnosing myocardial infarction, will become virtually academic in the foreseeable future, provided that the methods are straightforward and fulfill basic criteria of analytical quality (5).

All that said, a reasonable solution can be developed. Supported by science, rather than the market, the in vitro diagnostic companies should be encouraged to reach a formal agreement to standardize their immunoassays around 1 molecule (either cardiac troponin I or T) and, even more important, on immunoassays calibrated using an identical reference material and containing a cocktail of antibodies that recognize the same and more analytically suitable epitopes of the proteins. This solution would also be more effective than continuing to pursue a challenging harmonization or an unlikely standardization of the different troponin I methods (6).

***Giuseppe Lippi, MD**
Gianfranco Cervellin, MD