



Published Studies Supporting Aspirin Response Testing

Urinary 11-dehydrothromboxane B₂ levels have been utilized as a measurement of in-vivo platelet activation in a wide variety of clinical situations.

“Considering that an estimated 26 million patients in the United States alone currently take aspirin for thromboprophylaxis, and assuming a conservative aspirin resistance rate of 15%, almost 4 million patients are at risk of a breakthrough thrombotic event because they do not receive an antiplatelet benefit from aspirin.” Martin C, et al. *Aspirin Resistance: An Evaluation of Current Evidence and Measurement Methods*. Pharmacotherapy 2005;25(7):942-953.

“discovery of aspirin resistance in individuals might be important in order to devise better antiplatelet strategies and improve our ability to prevent acute thrombotic complications.” Macchi, L., et al. *Aspirin Resistance: Definitions, Mechanisms, Prevalence, and Clinical Significance*. Curr Pharm Design 2006; 12(2):251-258.

“the clinical benefits of adding clopidogrel to aspirin may be greatest in patients whose platelets are least inhibited by aspirin.” Eikelboom JW., et al. *Enhanced antiplatelet effect of clopidogrel in patients whose platelets are least inhibited by aspirin: a randomized crossover trial*. J Thromb Haemost 2005;3(12):2649-55.

“acute atherothrombotic events, including ACS and ischemic strokes, are severe diseases associated with poor clinical outcomes. Even a minor reduction in the frequency of these clinical events may affect healthcare costs and the quality of life for a wide array of patients.” Poulson TS, et al. *A Critical Appraisal of the Phenomenon of Aspirin Resistance*. Cardiology 2005;104:83-91.

“Aspirin-resistant patients as a group have reduced response to clopidogrel. Furthermore, we have identified a unique group of dual drug-resistant patients who may be at increased risk for thrombotic complications after PCI.” Lev EI, et al. *Aspirin and Clopidogrel Drug Response in Patients Undergoing Percutaneous Coronary Intervention*. J Am Coll Cardiol 2006;47:27-33.

Outcomes data from patients enrolled in the Heart Outcomes Prevention Evaluation (HOPE) Study, recently published in Circulation, showed that “in aspirin treated patients, urinary concentrations of 11-dehydro thromboxane B₂ predict the future risk of myocardial infarction or cardiovascular death. These findings raise the possibility that elevated urinary 11-dehydrothromboxane B₂ levels identify patients who are relatively resistant to aspirin and who may benefit from additional antiplatelet therapies or treatments that more effectively block in vivo thromboxane production or activity.” Eikelboom JW., et al. *Aspirin-Resistant Thromboxane Biosynthesis and the Risk of Myocardial Infarction, Stroke, or Cardiovascular Death in Patients at High Risk for Cardiovascular Events*. Circulation 2002;105:1650-1655.

Cardiology

“the natural history of aspirin resistance in a stable population, documenting a greater than threefold increase in the risk of major adverse events associated with aspirin resistance. Our study demonstrates it to be significantly associated with major adverse events during long-term follow up. The availability of safe, alternative long-term antiplatelet agents makes screening for aspirin resistance in cardiovascular patients a potentially important and useful diagnostic test.” Gum P., et al. ***A Prospective, Blinded Determination of the Natural History of Aspirin Resistance Among Stable Patients With Cardiovascular Disease.*** J Am Coll Cardiol 2003;41:961-5.

“In the aspirin-alone group, urinary 11-dehydrothromboxane B₂ was reduced prior to PTCA, less than the levels that are seen in non-cardiac patients, 221 to 361 pg/mg creatinine vs 454 to 650 pg/mg creatinine, and there was no rise in levels following PTCA.” “The optimal suppression of TxA₂ is achieved with the use of aspirin alone during PTCA. The addition of a selective COX-2 inhibitor does not result in any additional suppression of TxA₂ generation.” Kearney D., et al. ***Optimal suppression of thromboxane A₂ formation by aspirin during percutaneous transluminal coronary angioplasty: No additional effect of a selective cyclooxygenase-2-inhibitor.*** J Am Coll Cardiol 2004;43:526-531.

“On the day they presented to the emergency room, the MI group had significantly higher levels of 11-dehydrothromboxane B₂ in their urine than all other patients, 1667 pg/mg creatinine and 692 pg/mg creatinine.” “The measurement of thromboxane metabolites in the urine may provide a more rapid, accurate and cost-effective means of diagnosing MI in patients presenting with chest pain.” Foegh ML. ***Urinary thromboxane A₂ metabolites in patients presenting in the emergency room with acute chest pain.*** J Int Med. 1994;235:153-161.

“Urinary 11-dehydrothromboxane B₂ amount in unstable angina was significantly increased compared to the stable angina group, 627 – 1402 pg/mg creatinine vs 363 – 713 pg/mg creatinine. These findings suggest that platelet activation in vivo is more pronounced in unstable angina than in stable angina, and that the measurement of urinary 11-dehydrothromboxane B₂ may be useful for evaluating and treating angina.” Hattori KT., et al. ***Elevation of 11-dehydrothromboxane B₂ levels in unstable angina.*** J Cardiol 1991;21:899-904.

“Patient variability in response to treatment was defined by the coefficient of variability. Patients with diabetes were more frequently ASA resistant. In conclusion, ASA resistance is associated with increased platelet reactivity in patients on long-term dual antiplatelet treatment.” Angiolillo DJ., et al. ***Influence of aspirin resistance on long-term aspirin and clopidogrel after precutaneous coronary intervention.*** Am J Cardiol. 2006 Jan 1;97(1):38-43

Stroke

“In patients taking daily aspirin at any dose, the median urinary 11-dehydrothromboxane B₂ was 783 pg/mg creatinine compared with 1386 pg/mg creatinine in patients not taking daily aspirin.” “In African American stroke patients, aspirin use is associated with significantly lower urinary 11-dehydrothromboxane B₂ independent of other vascular factors, and there does not appear to be a dose-response effect for aspirin doses of 325 to 1300 mg daily.” Bruno A., et al. ***Aspirin and urinary 11-dehydrothromboxane B₂ in African American stroke patients.*** Stroke 2002;33:57-60.

“Aspirin resistance in stroke patients is not uncommon. It seems not enough to supply stroke patients with aspirin because about 10% of patients either show initial ASA non-response or develop secondary ASA non-response.” Berrouschot J., et al. ***Aspirin resistance in secondary stroke prevention.*** Acta Neurol Scand 2006;113:31-35.

Diabetes

“The amount of 11-dehydrothromboxane B₂ in the urine of pregnant women with diabetes, 551 – 1103 pg/mg creatinine was significantly higher than in women with normal pregnancies, 33 – 323 pg/mg creatinine.” “Our findings support a role for thromboxane in the pathogenesis of preeclampsia.” Van Assche FA., et al. *Increased thromboxane formation in diabetic pregnancy as a possible contributor to preeclampsia*. Am J Obstet Gynecol 1993;168:84-87.

“Although a daily dose of 100 mg aspirin effectively inhibited platelet function in a majority of diabetics, a considerable portion of patients showed a greater platelet inhibition with the use of 300 mg aspirin.” Abaci A., et al. *Effects of increasing doses of aspirin on platelet function as measured by PFA-100 in patients with Diabetes*. Thromb Res 2005;116(6):465-70.

“Everyday clinical practice shows that antiplatelet pharmacological approach may not always be efficient enough in people with diabetes.” Watala C., et al. *Blood platelet abnormalities and pharmacological modulation of platelet reactivity in patients with diabetes mellitus*. Pharmacol Rep 2005;57 Suppl:42-58.

“Resistance to aspirin was detected in 18.7% of diabetic aspirin users, with similar rates in T1D (21.7%, p=0.5) and T2D (16.2% p=0.6).” Mehta SS., et al. *Comparison of aspirin resistance in type 1 versus type 2 diabetes mellitus*. Am J Cardiol. 2006 Feb 15;97(4):567-70.

Chronic Obstructive Pulmonary Disease

“The urinary excretion of 11-dehydrothromboxane B₂ was significantly higher in patients with COPD than in control subjects: 277 – 4409 vs 129 – 612 pg/mg creatinine.” Davi, G., et al. *Enhanced thromboxane biosynthesis in patients with chronic obstructive pulmonary disease*. Am J Respir Crit Care Med 1997;156:1794-1799.

Metabolic Syndrome

“Women with android obesity had higher levels of 11 dehydrothromboxane B₂, 729 – 1296 vs 184 – 253 pg/mg creatinine than non obese women.” Davi, G., et al. *Platelet activation in obese women*. JAMA 2002;288:2008-2014.



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