The thromboxane A₂ pathway and its components are implicated in the progression of atherosclerosis and cardiovascular diseases. (CAD)

Thromboxane A₂ is clearly involved in CAD due to its acute and chronic role in promotion of vasoconstriction and platelet aggregation.

The success of low-dose aspirin in prevention of CAD is explained by platelet COX-1 inhibiting thromboxane A₂ biosynthesis.

Levels of urinary 11-dehydrothromboxane B₂ reflect activity of components of the thromboxane A₂ pathway that regulate thromboxane A₂ generation.

1. Urinary 11-dehydro-thromboxane B₂ and mortality in patients with stable coronary artery disease
   2017 • Am J Cardiol • Clinical Research • Human • 449 Patients • 11-DHTXB2

   “Urinary concentration of 11DHTXB2 was a strong independent risk factor for all-cause mortality among patients with stable CAD on aspirin therapy and may be a marker for patients with CAD who require more intensive secondary prevention measures.”

2. Urinary 11-dehydro-thromboxane B₂ is associated with cardiovascular events and mortality in patients with atrial fibrillation
   2015 • AHJ • Clinical Research • Human • 837 Patients

   “The novelty of the present study is our demonstration that urinary 11-dehydro-TxB₂ levels were associated with an increased risk of CVEs and CV death in an AF cohort already on OACs.”

3. Incomplete inhibition of thromboxane biosynthesis by acetylsalicylic acid.
   2008 • Circulation • Clinical Research • Human • 3261 Patients • 11-DHTXB2
4. **Urinary 11-dehydro-thromboxane B\textsubscript{2} as a predictor of acute myocardial infarction outcomes: results of leukotriene and thromboxane in myocardial infarction (LTMI) study.**

2016 • JAH/A • Clinical Research • Human • 180 Patients • 11-DHTXB2

“Urinary 11-dehydro-thromboxane (TX)B\textsubscript{2} has been described as a potential predictive biomarker of major adverse cardiovascular events (MACEs) in high cardiac risk patients.”

“11-Dehydro-TXB\textsubscript{2} predicts 1-year cumulative MACEs in AMI patients and provides prognostic information on the left ventricular performance.”

5. **Risk factors for nonplatelet thromboxane generation after coronary artery bypass graft surgery.**

2016 • JAH/A • Clinical Research • Human • 260 Patients • 11-DHTXB2

“A significant finding of our analysis was that U8-iso-PGF\textsubscript{2α} correlated directly with the incidence of early vein graft thrombosis. This suggests that therapies aimed at reducing oxidative stress might be a viable strategy to reduce nonplatelet TXA\textsubscript{2} generation and improve outcomes after cardiac surgery.”

6. **Aspirin-resistant thromboxane biosynthesis and the risk of myocardial infarction, stroke, or cardiovascular death in patients at high risk for cardiovascular events.**

2002 • Circulation • Clinical Research • Human • 488 Patients/488 Controls • 11-DHTXB2

“In aspirin-treated patients, urinary concentrations of 11-dehydro thromboxane B\textsubscript{2} predict the future risk of myocardial infarction or cardiovascular death. These findings raise the possibility that elevated urinary 11-dehydro thromboxane B\textsubscript{2} 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.”

7. **Age-related increase of thromboxane B\textsubscript{2} and risk of cardiovascular disease in atrial fibrillation.**

2016 • Oncotarget • Clinical Review • Human • 11-DHTXB2

“Urinary excretion of 11-dehydro-txb2 increases by advancing age, peaking after 70 years.”
8. **11-Dehydro thromboxane b2 levels after percutaneous transluminal angioplasty in patients with peripheral arterial occlusive disease during a one year follow-up period.**

   2016 • J Physiol Pharmacol • Clinical Research • Human • 175 Patients • 11-DHTXB2

   “Overall the mean TXB$_2$ values immediately after PTA were significantly higher than either before the procedure (1524.4 pg/mg ± 1411.1 vs. 2098.1 pg/mg creatinine ± 1661.8; P=0.00002), the day after PTA, or at any other point during the study.”

   “Moreover, preoperative TXB$_2$ levels correlated well with the composite endpoints of death, myocardial infarction and stroke during the follow-up period.”

9. **Oxidative stress reflected by increased F$_2$-isoprostanes is associated with increasing urinary 11-dehydro thromboxane B$_2$ levels in patients with coronary artery disease.**

   2016 • Thromb Res • Clinical Research • Humans • 11-DHTXB2

   “Elevated 11dhTxB$_2$ was found to increase the risk of adverse events in patients with stable CAD [12] and myocardial infarction.”

10. **The influence of low-grade inflammation on platelets in patients with stable coronary artery disease.**

    2015 • Thromb Haemost • Review Article • Human • 11-DHTXB2

    “Increased levels of hsCRP and IL-6 were independently associated with increased platelet aggregation and urine-11-dehydrothromboxane B$_2$ levels (110). This association may be explained by aspirin-insensitive thromboxane generation derived from cyclooxygenase-2 in non-platelet cells.”

11. **Measurements of thromboxane production and their clinical significance in coronary heart disease.**

    2012 • Thromb Haemost • Review Article • Human • 11-DHTXB2

    “Residual TX production, as revealed by different methods, may derive from COX-1 or COX-2.”

    “Extra-platelet sources may contribute to aspirin-insensitive TX generation: monocytes/macrophages and vascular endothelial cells express COX-2 in response to inflammatory stimuli, and the up regulation of COX-2 activity may account for a TX biosynthesis not sensitive to once daily low-dose aspirin.”
12. **The improvement of walking abilities and endothelial function after the supervised training treadmill program** (STTP) in patients with peripheral artery disease (PAD) is not related to prostacyclin and thromboxane release.  
2016 • Int. J Cardiac • Clinical Research • Human • 59 Patients • 11-DHTXB2

13. **Relation of fish oil supplementation to markers of atherothrombotic risk in patients with cardiovascular disease not receiving lipid-lowering therapy.**  
2015 • Am J Cardiol • Clinical Research • Human • 259 Patients • 11-DHTXB2

“Fish oil supplementation (FOS) is known to have cardiovascular benefits. Patients on FOS had lower urinary 11-dehydrothromboxane B₂ levels regardless of lipid-lowering therapy.”

**Thromboxane A₂ pathway schematics**