



Q/Elevated troponin but no CVD: What's the prognosis?

EVIDENCE-BASED ANSWER

A PATIENTS WITH ELEVATED TROPONIN LEVELS and chronic renal disease, pulmonary hypertension, pulmonary embolism, chronic obstructive pulmonary disease, sepsis, or acute ischemic stroke have a 2- to 5-fold increased

risk of death, even in the absence of known cardiovascular disease (TABLE)¹⁻⁶ (strength of recommendation: **B**, meta-analysis, multiple prospective and retrospective observational studies.)

Evidence summary

To investigate the prognostic value of troponin on overall mortality, a multicenter prospective study followed 847 patients 18 years and older (mean age 59 years) with end-stage renal disease whose troponin T levels were measured 3 months from the start of peritoneal dialysis or hemodialysis until transplantation or death.¹ At enrollment, 566 patients had a troponin level of ≤ 0.04 ng/dL, 188 had a value between 0.05 and 0.10 ng/dL, and 93 had a level of more than 0.10 ng/dL.

Using Cox regression, patients whose troponin levels were more than 0.10 ng/dL had an increased hazard ratio (HR) for all-cause mortality of 2.2 (95% confidence interval [CI], 1.7-2.8) compared with patients who had levels ≤ 0.04 ng/dL. Cardiovascular mortality also was higher (HR=1.9; 95% CI, 0.9-3.7) with troponin elevations, but didn't reach statistical significance. Investigators found no significant differences in mortality risk between patients on peritoneal or hemodialysis, patients with or without a history of acute myocardial infarction, or patients who suffered cerebrovascular accidents.

Elevated troponin raises risk of death 5-fold in pulmonary embolism patients

A meta-analysis of 20 trials with a total of 1985 patients assessed the prognostic val-

ue of troponin for short-term mortality in patients admitted with acute pulmonary embolism.² Sixteen studies (1527 patients) were prospective trials and the remainder (458 patients) were retrospective trials. Investigators obtained troponin levels for all patients at admission. They used several different troponin assays (both I and T), but most of the studies used the assay manufacturers' cutoff points (exceeding the 99th percentile).

High troponin levels were associated with a 5-fold increased risk of short-term death, defined as in-hospital death up to 30 days after discharge (19.7% with elevated troponin vs 3.7% with normal troponin; odds ratio [OR]=5.24; 95% CI, 3.3-8.4).

Increased risk of death among those with pulmonary hypertension, COPD

A prospective single-center study of 56 patients with chronic pulmonary hypertension found that the 14% of those whose troponin T was elevated (≥ 0.01 ng/mL) had a lower survival rate than the other patients. Patients who either had a positive troponin on initial assessment or developed troponin elevation within the 2-year follow-up period had a cumulative 24-month survival rate of 29%, compared with 81% for their troponin T-negative counterparts ($P=.001$).³

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The views expressed herein are those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense, or the US government.

➤ **Patients with elevated troponin levels and certain conditions have a 2- to 5-fold increased risk of death, even without known cardiovascular disease.**

TABLE

Elevated troponin and mortality risk by disease

Disease	Risk (95% CI)
Chronic renal failure	HR 2.2 (1.7-2.8) ¹
Pulmonary embolus	OR 5.2 (3.3-8.4) ²
Pulmonary hypertension	HR 4.9 (1.2-20.3) ³
Chronic obstructive pulmonary disease	HR 1.6 (1.2-2.3) ⁴
Sepsis	OR 2.0 (1.2-3.5) ⁵
Cerebrovascular accident	OR 2.9 (1.7-4.8) ⁶

CI, confidence interval; HR, hazard ratio; OR, odds ratio.

In a retrospective single-center observational study of 396 patients hospitalized from 2000 to 2003 for an exacerbation of chronic obstructive pulmonary disease and followed until 2005, troponin T levels ≥ 0.04 ng/mL within 24 hours of admission were associated with increased all-cause mortality (HR=1.64; 95% CI, 1.15-2.34; $P=.006$).⁴

Elevated troponin I is an independent predictor of mortality in severe sepsis

A double-blind, placebo-controlled, phase 3 trial evaluated the effect of drotrecogin alfa (activated)—withdrawn from the market in 2011—on survival of patients with severe sepsis.⁵ Investigators used positive troponin I levels (≥ 0.06 ng/mL) as a prognostic indicator of mortality. Patients who were troponin-positive had a 28-day mortality rate of 32%, compared with 14% in the troponin-negative group ($P<.0001$).

A bias of this study is that the patients with positive troponin levels tended to be older and more critically ill. However, in a multivariate model, troponin I still remained an independent predictor of mortality.

Elevated troponin predicts increased death risk in up to 20% of stroke patients

A systematic review of 15 trials with a total of 2901 patients evaluated the relationship between troponin levels and stroke.⁶ Investigators assessed the prevalence of elevated troponin in acute stroke patients, the association of elevated troponin levels with electrocardiographic changes, and the overall morbidity and mortality associated with troponin levels. Thirteen of the 15 studies used a

troponin T or I level obtained within 72 hours of admission and a cut-off level of 0.1 ng/mL. The remaining 2 studies used troponin I cut-off levels >0.2 and 0.4 ng/mL.

Overall, 18% of acute stroke patients had elevated troponin levels. Studies that excluded patients with known cardiac disease had a lower prevalence of elevated levels (10% vs 22%). Patients with elevated troponin levels had an associated overall increased risk of death (OR=2.9; 95% CI, 1.7-4.8) and were 3 times more likely to have ischemic changes on electrocardiogram (OR=3.0; 95% CI, 1.5-6.2). Investigators concluded that elevated troponin levels occur in as many as one in 5 patients and are associated with an increased risk of death.

Troponin elevations may be observed in congestive heart failure, chest wall trauma, cardioversion/defibrillator shocks, rhabdomyolysis, and ultra-endurance activities.⁷ However, this analysis didn't address prognostic implications of elevated troponins.

Recommendations

No recommendation exists for biochemical testing of troponins in various medical conditions except in the presence of signs and symptoms consistent with acute coronary syndrome. The American College of Cardiology and American Heart Association recommend routine testing of cardiac troponins in patients hospitalized for worsening congestive heart failure symptoms.⁸

The European Society of Cardiology recommends measuring troponin levels to further stratify risk in non-high-risk patients

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with confirmed pulmonary embolus.⁹

The National Academy of Clinical Biochemistry recommends using cardiac troponins to help define mortality risk in end-stage renal disease and critically ill patients.¹⁰ **JFP**

References

1. Havekes B, van Manen J, Krediet R, et al. Serum troponin T concentration as a predictor of mortality in hemodialysis and peritoneal dialysis patients. *Am J Kidney Dis.* 2006;47:823-829.
2. Becattini C, Vedovati MC, Agnelli G. Prognostic value of troponins in acute pulmonary embolism. *Circulation.* 2007;116:427-433.
3. Torbicki A, Kurzyna M, Kuca P, et al. Detectable serum cardiac troponin T as a marker of poor prognosis among patients with chronic precapillary pulmonary hypertension. *Circulation.* 2003;108:844-848.
4. Brekke PH, Omland T, Holmedal SH, et al. Troponin T elevation and long-term mortality after chronic obstructive pulmonary disease exacerbation. *Eur Respir J.* 2008;31:563-570.
5. John J, Woodward DB, Wang Y, et al. Troponin I as a prognosticator of mortality in severe sepsis patients. *J Crit Care.* 2010;25:270-275.
6. Kerr G, Ray G, Wu O, et al. Elevated troponin after stroke: a systematic review. *Cerebrovasc Dis.* 2009;28:220-226.
7. Korff S, Katus HA, Giannitsis E. Differential diagnosis of elevated troponins. *Heart.* 2006;92:987-993.
8. Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the International Society for Heart and Lung Transplantation. *J Am Coll Cardiol.* 2009;53:e1-e90.
9. Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology. *Eur Heart J.* 2008;29:2276-2315.
10. Wu AH, Jaffe AS, Apple FS, et al. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure. *Clin Chem.* 2007;53:2086-2096.

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information about managing missed doses; and has high consumer ratings. The Contra-ceptive Pill has similar features, although it has fewer reminder options and is available in fewer languages than myPill.

We urge providers caring for adolescents to stay abreast of contraceptive reminder apps and to discuss them during counseling sessions. Given the prevalence of smartphone use among adolescents, these apps have the potential to improve contraceptive consistency.

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1. Singh S, Darroch JE. Adolescent pregnancy and childbearing: levels and trends in developed countries. *Family Planning Perspectives.* 2000;32:14-23.
2. Pew Research Center. Teens and technology 2013. Available at: http://www.pewinternet.org/-/media/Files/Reports/2013/PIP_TeensandTechnology2013.pdf. Accessed April 29, 2013.

Too little training in acute care

I read Dr. Hickner's editorial, "Have family physicians abandoned acute care?" (*J Fam Pract.* 62;7:333) shortly after graduating from residency and starting my job as a full-spectrum family physician at a federally qualified health center, and it really resonated with me.

In the residency program, we managed many patients with chronic conditions. But they tended to use the emergency department or urgent care for acute conditions, at least in part because we could never figure out a way to offer extended hours.

Now I see many acute care patients, especially among the uninsured. I've come to see that my residency training was a bit weak in this area, but I'm learning on the job. I've discovered that chronic conditions tend not to improve without first addressing the things the patient acutely cares about.

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