Prognostic Value of Cardiac Troponin in Patients With Chronic Kidney Disease Without Suspected Acute Coronary Syndrome

A Systematic Review

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Background: Clinicians face uncertainty about the prognostic value of troponin testing in patients with chronic kidney disease (CKD) without suspected acute coronary syndrome (ACS).

Purpose: To systematically review the literature on troponin testing in patients with CKD without ACS.

Data Sources: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials through May 2014.

Study Selection: Studies examining elevated versus normal troponin levels in patients with CKD without ACS.

Data Extraction: Paired reviewers selected articles for inclusion, extracted data, and graded strength of evidence (SOE). Meta-analyses were conducted when studies had sufficient homogeneity of key variables.

Data Synthesis: Ninety-eight studies met inclusion criteria. Elevated troponin levels were associated with all-cause and cardiovascular mortality among patients receiving dialysis (moderate SOE). Pooled hazard ratios (HRs) for all-cause mortality from studies that adjusted for age and coronary artery disease or a risk equivalent were 3.0 (95% CI, 2.4 to 4.3) for troponin T and 2.7 (CI, 1.9 to 4.6) for troponin I. The pooled adjusted HRs for cardiovascular mortality were 3.3 (CI, 1.8 to 5.4) for troponin T and 4.2 (CI, 2.0 to 9.2) for troponin I. Findings were similar for patients with CKD who were not receiving dialysis, but there were fewer studies. No study tested treatment strategies by troponin cut points.

Limitation: Studies were heterogeneous regarding assays, troponin cut points, covariate adjustment, and follow-up.

Conclusion: In patients with CKD without suspected ACS, elevated troponin levels were associated with worse prognosis. Future studies should focus on whether this biomarker is more appropriate than clinical models for reclassifying risk of patients with CKD and whether such classification can help guide treatment in those at highest risk for death.

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The most important use of troponin testing is to guide treatment of patients with suspected acute coronary syndrome (ACS). However, elevated troponin levels may be due to cardiac injury associated with chronic structural heart disease rather than acute ischemia, especially when levels do not change (1).

Patients with chronic kidney disease (CKD) are more likely than those without it to have elevated troponin levels. Given the high prevalence of CKD in the United States, clinicians need to know how to interpret troponin levels in this population (2, 3). Reduced renal clearance may explain persistently elevated levels in patients with CKD (4), but this hypothesis is controversial (5). Rather, elevated troponin levels most likely indicate myocardial injury (5–7). Also, dialysis may affect troponin T and troponin I levels differently (8).

Studies of patients with CKD without suspected ACS have shown that chronically elevated troponin levels are associated with increased risk for cardiovascular disease morbidity and mortality (9–12). In 2004, the U.S. Food and Drug Administration approved measurement of troponin T levels for prediction of mortality in patients receiving dialysis (13). However, data from studies that rigorously compared risk reclassification with troponin level versus traditional clinical risk markers are limited. Furthermore, whether asymptomatic patients with CKD and elevated troponin levels should be treated differently from those with normal levels is unclear.

We aimed to systematically review studies that assessed the value of troponin testing for risk stratification and treatment of patients with CKD without suspected ACS.

METHODS

This review was part of a larger systematic review commissioned by the Agency for Healthcare Research and Quality (AHRQ). The utility and interpretation of troponin testing differ in patients with and without suspected ACS. Our findings for patients with CKD and suspected ACS are reported separately. The protocol is available at www.effectivehealthcare.ahrq.gov and was registered with PROSPERO (CRD42013004795).

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Data Sources and Searches

We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials from January 1990 through May 2014 (the MEDLINE search strategy is shown in the Appendix Table, available at www.annals.org). Two reviewers independently evaluated titles, abstracts, and full-text articles. We resolved disagreements on exclusion through consensus adjudication.

Study Selection

We included studies that evaluated a troponin assay in adults with CKD who had no symptoms of ACS and that reported on all-cause mortality; cardiovascular mortality; and major adverse cardiovascular events (MACEs), which were defined differently across studies but were generally a composite outcome of myocardial infarction, cardiovascular mortality, and/or revascularization. We included original, peer-reviewed studies regardless of sample size, language, length of follow-up, and setting. We excluded studies published before 1990 because troponin level was not used as a cardiac marker before then.

Data Extraction and Quality Assessment

One reviewer used standardized forms to extract information on study characteristics, troponin assays and cut points, and outcome measures. The prevalence of elevated troponin levels, number of events in each group, and measure of association with the outcome (such as hazard ratio [HR], odds ratio [OR], or relative risk) were abstracted. For studies reporting HRs, the most adjusted HR was abstracted. A second reviewer confirmed the first reviewer’s abstracted data. Two reviewers independently assessed study quality by using the Downs and Black checklist (14). If the reviewers rated study quality differently, they obtained input from a third reviewer if they still disagreed after open discussion.

Data Synthesis and Analysis

We organized abstracted data by outcomes, troponin type, and dialysis status. Results were analyzed separately for troponin T and troponin I and for patients with CKD who were receiving dialysis versus those who were not. We qualitatively summarized studies that were not able to be pooled.

Two reviewers graded the strength of evidence (SOE) on each troponin assay for each outcome by adapting the scheme in the Methods Guide for Effectiveness and Comparative Effectiveness Reviews (15). We rated the SOE in terms of risk of bias, consistency, directness, and precision. Study quality and level of covariate adjustment were considered in the assessment of risk of bias. Strength of associations was determined from the results of the meta-analyses, when available. We classified the SOE as “high,” “moderate,” “low,” or “insufficient.” Details of SOE grading for each outcome are provided in Supplements 1 and 2 (available at www.annals.org).

We conducted meta-analyses when at least 2 studies had sufficient homogeneity of key variables (such as population characteristics or troponin assay type). For studies that reported an HR with a CI, we pooled the HRs by using the profile likelihood estimate. This method provides better accounting of uncertainty in the estimation of between-study variance than the DerSimonian–Laird estimator (16).

Meta-analyses of pooled HRs were stratified by levels of adjustment. We considered adjustment for age and coronary artery disease (CAD) or a risk equivalent (cerebrovascular disease, peripheral vascular disease, reduced left ventricular ejection fraction, heart failure, or diabetes) to be the highest level of adjustment. Supplement 3 (available at www.annals.org) presents details on the specific covariates adjusted for in each study.

If a study reported HRs by tertiles or quartiles of troponin levels, we selected the HR from the comparison of the highest and lowest groups. Studies that only presented troponin level as a continuous variable rather than a cut point could not be included in meta-analyses. For studies that reported incidence of events, we pooled the unadjusted ORs by using a profile likelihood estimate (17). A study could be included in the HR meta-analysis, the OR meta-analysis, or both depending on the type of results it reported. If a study reported on more than 1 troponin assay, we included the most commonly used one in the meta-analysis. If several published studies used the same patient cohort, we included only the most adjusted or most recent results to avoid double counting.

We examined heterogeneity among studies by using the I² statistic, with a value greater than 50% considered an indication of substantial variability (18).

We used Stata/IC, version 12.1 (StataCorp), for all meta-analyses.

Role of the Funding Source

The AHRQ reviewed the key questions, protocol, and draft report but did not have a role in the literature search, analysis, or interpretation of findings. The authors prepared the manuscript, and AHRQ granted copyright assertion.

RESULTS

We identified 98 studies (in 105 publications) that evaluated the use of troponin levels for risk stratification among patients with CKD without ACS symptoms (3, 10, 12, 19–119). A flow diagram of our search results is presented in Figure 1. All studies were observational cohort studies. The median follow-up ranged from 30 days to 5 years. There was marked heterogeneity of the prevalence of elevated troponin levels across studies, even when similar cut points were used.

Among patients receiving dialysis, an elevated troponin level was associated with a higher risk (approximately 2- to 4-fold) for all-cause mortality, cardiovascular
mortality, and MACE. Findings were similar for the association of troponin T level with all-cause mortality and MACE among patients with CKD who were not receiving dialysis. Figure 2 summarizes the results of the meta-analysis of the pooled HRs from only the studies that adjusted for age and CAD or a risk equivalent and the SOE for these findings. Further details are described in the following sections.

CKD = chronic kidney disease.
* Articles could be excluded for >1 reason.
Patients With CKD Receiving Dialysis

Troponin T Level and All-Cause Mortality

Forty-three cohort studies (in 49 publications) examined the association between troponin T level and all-cause mortality (12, 20, 21, 27, 29–32, 36, 38, 40–42, 44, 47, 50, 51, 53, 59, 61, 65, 67–69, 71, 73, 77, 79, 81, 82, 85, 86, 89, 91–97, 99, 100, 102–104, 109, 111, 116). One study (31) tested high-sensitivity troponin T level and did not find a statistically significant association, but we also pooled ORs from 24 studies (Supplement 4, available at www.annals.org) and found a nearly 5-fold increased risk (OR, 4.7 [CI, 3.6 to 6.5]) with significant heterogeneity ($I^2 = 53\%$).

One study (31) tested high-sensitivity troponin T level on a continuous scale rather than by cut point. The age-adjusted risk increased $1.4$-fold (CI, 1.0- to 2.0-fold) for every 2.72-ng/L increase in troponin T level.

Troponin I Level and All-Cause Mortality

We identified 30 studies (in 31 publications) on the association between troponin I level and all-cause mortality (3, 19–21, 25, 30, 32, 36, 43, 47, 48, 51, 56, 67, 68, 72–74, 81, 86, 88, 89, 93, 94, 102–105, 113, 118, 120). We excluded 7 of them from our meta-analyses because they reported insufficient data, presented troponin levels as continuous variables rather than cut points, or did not present results separately for patients receiving dialysis (30, 36, 89, 102, 103, 105, 113). We included 7 studies in a meta-analysis of HRs adjusted for age and CAD or a risk equivalent (Figure 4). The overall pooled HR was 2.7 (CI, 1.9 to 4.6); heterogeneity was not significant. Similar levels of risk were seen in studies that presented HRs that were adjusted for age but not CAD or were unadjusted. In a meta-analysis of 19 studies, we found a pooled OR of 2.6 (CI, 1.9 to 3.6) (Supplement 5, available at www.annals.org).

One study (113) evaluated the risk associated with each 10-ng/L increase in high-sensitivity troponin I level and did not find a statistically significant association, but the study was underpowered for this outcome.

Troponin T Level and Cardiovascular Mortality

Twenty studies (of 16 unique cohorts) addressed the association between troponin T level and cardiovascular mortality (12, 44, 50, 53, 59, 66–68, 77, 79, 91–95, 99, 107, 108, 111, 114). We excluded 2 of these studies from our meta-analyses because they had insufficient data (111, 114).

Five studies were included in a meta-analysis of pooled HRs adjusted for age and CAD or a risk equivalent (Supplement 6, available at www.annals.org). We found a 3-fold increased risk (HR, 3.3 [CI, 1.8 to 5.4]) with significant heterogeneity ($I^2 = 66\%$). We included 9 studies in the meta-analysis of ORs (Supplement 7, available at www.annals.org) and found a 4-fold increased risk (OR, 4.3 [CI, 3.0 to 6.4]).

One study (114) used a high-sensitivity troponin T assay but presented results per 100-U increase in troponin T level as a continuous variable (OR, 1.5 [CI, 1.2 to 1.9]).

Troponin I Level and Cardiovascular Mortality

Thirteen studies addressed the association of troponin I level with cardiovascular mortality (3, 19, 25, 43, 58, 67, 68, 74, 90, 93, 94, 107, 118). One study was excluded...
from our meta-analyses because it had insufficient data (67). We pooled HRs from 3 studies that adjusted for age and CAD or a risk equivalent (Supplement 8, available at www.annals.org) and found an HR of 4.2 (CI, 2.0 to 9.2) with no heterogeneity.

We included 9 studies in the OR meta-analysis (Supplement 9, available at www.annals.org). Two (58, 107) had unusual ORs due to zero events in one of the groups. Pooled results showed a 5-fold increased risk (OR, 5.2 [CI, 2.8 to 9.0]). The estimated risk was similar in a sensitivity analysis that excluded 1 study (90) that used a high troponin I cut point (2.3 μg/L).

We did not identify any studies that reported an association between high-sensitivity troponin I level and cardiovascular mortality among patients receiving dialysis.

**Troponin T Level and MACE**

Twelve studies reported on the association between troponin T level and MACE (12, 42, 46, 51–53, 62, 83, 97, 98, 101, 107). Only 1 presented an HR adjusted for age and CAD or a risk equivalent (HR, 1.9 [CI, 1.0 to 3.4]) (Supplement 10, available at www.annals.org). Another study (62) only presented an adjusted HR per 0.01 μg/L increase in troponin T level as a continuous variable rather than a cut point.

Nine studies with follow-up on MACEs were included in the OR meta-analysis (Supplement 11, available at www.annals.org). The pooled OR was 6.0 (CI, 3.5 to 12.0).

We did not identify any studies that assessed the association of high-sensitivity troponin T level with MACE among patients receiving dialysis.

**Troponin I Level and MACE**

Twelve studies reported on the association of troponin I level and MACE (25, 48, 51, 58, 75, 78, 83, 84, 97, 98, 101, 107), but none presented HRs for this outcome.

Nine studies were included in the OR meta-analysis (Supplement 12, available at www.annals.org). We ex-
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Figure 4. Pooled HRs, stratified by level of adjustment, for the association of elevated troponin I level with all-cause mortality among patients receiving dialysis.

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Follow-up, y</th>
<th>Troponin Cutoff, μg/L</th>
<th>Prevalence, %</th>
<th>Patients, n</th>
<th>HR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Adjusted for age and CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apple et al, 2002 (88)*</td>
<td>3</td>
<td>&gt;0.1</td>
<td>6</td>
<td>733</td>
<td>2.10 (1.30–3.30)</td>
</tr>
<tr>
<td>Farkouh et al, 2003 (86)*</td>
<td>1.3</td>
<td>&gt;1</td>
<td>7</td>
<td>137</td>
<td>9.60 (2.80–33.00)</td>
</tr>
<tr>
<td>Helleskov Madsen et al, 2008 (47)†</td>
<td>2.7</td>
<td>&gt;0.06</td>
<td>11</td>
<td>109</td>
<td>1.90 (0.60–6.40)</td>
</tr>
<tr>
<td>Alam et al, 2013 (118)†</td>
<td>3</td>
<td>&gt;0.06</td>
<td>27</td>
<td>133</td>
<td>2.57 (1.30–5.09)</td>
</tr>
<tr>
<td>Kang et al, 2009 (43)†</td>
<td>1</td>
<td>&gt;0.2</td>
<td>30</td>
<td>66</td>
<td>5.90 (2.06–16.87)</td>
</tr>
<tr>
<td>Kalaji and Albital, 2012 (21)†</td>
<td>1.5</td>
<td>&gt;0.2</td>
<td>35</td>
<td>145</td>
<td>1.60 (0.80–3.00)</td>
</tr>
<tr>
<td>Boulier et al, 2004 (74)†</td>
<td>1.3</td>
<td>&gt;0.03</td>
<td>NR</td>
<td>191</td>
<td>3.90 (1.70–8.60)</td>
</tr>
<tr>
<td>Overall (I² = 27%)</td>
<td></td>
<td></td>
<td></td>
<td>1514</td>
<td>2.70 (1.90–4.57)</td>
</tr>
<tr>
<td>Adjusted for age but not CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geese et al, 2013 (19)†</td>
<td>2.3</td>
<td>&gt;0.1</td>
<td>12</td>
<td>206</td>
<td>6.35 (2.43–16.49)</td>
</tr>
<tr>
<td>Iliou et al, 2003 (12)*</td>
<td>2</td>
<td>&gt;0.1</td>
<td>27</td>
<td>258</td>
<td>1.83 (1.10–3.10)</td>
</tr>
<tr>
<td>Overall (I² = 58%)</td>
<td></td>
<td></td>
<td></td>
<td>464</td>
<td>2.97 (0.76–14.67)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artunc et al, 2012 (20)#</td>
<td>1.9</td>
<td>&gt;0.022</td>
<td>NR</td>
<td>239</td>
<td>2.87 (1.27–6.51)</td>
</tr>
</tbody>
</table>

Boxes indicate individual study point estimates. Horizontal lines represent the 95% CI for each study. CAD = coronary artery disease; HR = hazard ratio; NR = not reported.
* Used a troponin assay manufactured by Dade Behring.
† Used a troponin assay manufactured by Beckman Coulter.
‡ Used a troponin assay manufactured by Siemens.

included 2 studies because they had qualitatively different definitions of elevated troponin level (48, 84) and 2 because they had insufficient data or zero events (83, 96). The pooled OR was 6.3 (CI, 3.5 to 13.2).

SOE Grading

The overall summary of SOE grading is shown in Figure 2. Strength of evidence was generally moderate for all outcomes except the association between troponin I level and MACE because no pooled HR could be generated for that outcome. More details about how the SOE grades were assigned can be found in Supplement 1.

Patients With CKD Not Receiving Dialysis

Twenty-six studies included patients with CKD who were not receiving dialysis (10, 22, 24, 26, 28, 33, 34, 37, 39, 45, 49, 54, 55, 60, 63, 70, 76, 80, 87, 102, 103, 110, 112, 115–117).

Troponin I Level and All-Cause Mortality

Four studies (54, 63, 103, 110) examined the association between troponin I level and all-cause mortality, and 2 were used to perform a meta-analysis of HRs adjusted for age and CAD or a risk equivalent. The pooled HR was 1.7 (CI, 1.2 to 2.7) (Supplement 15, available at www.annals.org) with no heterogeneity. No studies presented ORs for this outcome.

Troponin T Level and MACE

Four studies (22, 24, 28, 55) that addressed the association between troponin T level and MACE were included in a meta-analysis of HRs adjusted for age and CAD or a risk equivalent (Supplement 16, available at www.annals.org). The pooled HR was 2.7 (CI, 1.1 to 7.6), and heterogeneity was significant (I² = 85%). Two studies (102, 103) were not included in this meta-analysis because they also included patients receiving dialysis. Cardiovascular mortality was analyzed in 2 studies, but these results are difficult to compare because one study included patients receiving dialysis as well as those who were not (37) and...
the other included predialysis patients, many of whom began receiving dialysis during follow-up (80).

One study of high-sensitivity troponin T level (112) that used a sensitive cut point (0.01 ng/L) found a 2-fold increased risk for MACE (unadjusted OR, 2.1 [CI, 1.0 to 4.2]).

Troponin I Level and MACE

Two studies of the association between troponin I level and MACE included patients who received dialysis and those who did not (102, 103), and ORs were not statistically significant. No studies examined high-sensitivity troponin I levels in asymptomatic patients with CKD who were not receiving dialysis.

Post–Kidney Transplant Patients

The findings for post–kidney transplant patients generally supported similar associations among troponin level and cardiovascular risk and mortality (Supplements 17 and 18, available at www.annals.org).

SOE Grading

Further details on SOE grading for studies of patients with CKD who were not receiving dialysis are presented in Supplement 2.

DISCUSSION

We found that a baseline elevated troponin level was associated with a higher risk (approximately 2- to 4-fold) for all-cause mortality, cardiovascular mortality, and MACE among patients without suspected ACS who were receiving dialysis (moderate SOE). Thus, elevated troponin levels among these patients are not spurious but portend a worse prognosis. Similar associations were generally found for patients with CKD who were not receiving dialysis, but fewer studies were identified for this subgroup. The association of elevated troponin level with adverse outcomes among patients receiving dialysis was generally similar for troponin T and troponin I. Few studies reported results for high-sensitivity troponin T and troponin I assays.

A previous meta-analysis by Khan and colleagues (11) of the use of troponin measurement for risk prediction of all-cause mortality among patients receiving dialysis reviewed studies through 2004. We have updated the literature by performing a comprehensive review through May 2014. We were able to perform meta-analyses of HRs (time to event) stratified separately by levels of adjustment and ORs (relative risk) as available, whereas Khan and colleagues only performed analyses of relative risk. We also performed meta-analyses for the outcomes of cardiovascular mortality and MACE and for patients with CKD who were not receiving dialysis.

Further work is needed to determine the mechanism for the association between elevated troponin levels and adverse outcomes. Is an elevated troponin level a marker of more extensive underlying CAD, silent ischemia, or volume overload? Is the excess mortality associated with elevated troponin levels due to myocardial infarction, heart failure, arrhythmia, or other causes? The identification, testing, and implementation of potential interventions depend on answers to these questions.

An elevated troponin level may simply be a marker of underlying CAD and its associated risk. Although it reflects injury rather than an “exposure” subject to confounding, the issue of whether troponin measurement adds value over known clinical covariates is critical. Many studies did not present adjusted results, but in the pooled analyses of the most adjusted studies, elevated troponin levels were still associated with adverse outcomes.

Yet, when one critically examines the utility of a biomarker for prediction, the more clinically relevant question is how the marker performs in metrics of discrimination and reclassification. The studies found in this review predominantly used traditional regression models to show that the associations persisted after adjustment for clinical factors but generally did not use rigorous methods of comparing troponin testing against clinical models.

One study (59) examined whether troponin testing improves discrimination and found that troponin T level did not change the area under the curve when it was added to a survival model containing routine clinical and laboratory markers. Another study found that troponin level combined with brain natriuretic peptide level improved risk classification by 18% (28). Thus, further research is needed on whether troponin level alone or in conjunction with other biomarkers can better reclassify patients with CKD into higher and lower risk groups compared with existing clinical models.

We were unable to answer the question of how patients with CKD whose risk is stratified by troponin level might be clinically treated. Although this was one of our original objectives, we did not find any intervention studies that compared treatment strategies stratified by troponin level for patients receiving dialysis without suspected ACS in our literature review. Our work highlights a significant knowledge gap in the existing literature. Thus, the risk–benefit balance of additional screening tests (such as stress testing) or intensified prevention strategies among such patients identified as higher-risk is unknown. For example, the National Kidney Foundation already recommends that CKD should be considered a CAD risk equivalent (121). Therefore, what is the additive role (if any) of troponin testing?

Our review found that studies varied widely by prevalence of elevated troponin level and by follow-up. They were also heterogeneous in the troponin assay manufacturers and platforms. New assays can detect ever lower troponin concentrations. Many studies did not report which generation of assay was used or details of the cut point for the assay, including the manufacturer-reported 99th per-
centile threshold or what reference population was used for that threshold. Therefore, we were unable to perform meta-analyses using the 99th percentile cut point. Selective reporting bias in the literature may have influenced our findings.

Our review further emphasizes the need for harmonization so that results can be compared across studies. Future studies should focus on using guideline-established cut points (such as the 99th percentile) for consistency in the literature and relevance to clinical practice. Standardization of the assays is currently one of the goals of the International Federation of Clinical Chemistry Working Group.

To keep the scope of our review specific to the topic at hand, we did not review all studies relevant to troponin testing and did not report results for general populations that were not stratified by CKD subgroups. No studies directly compared troponin testing for patients with CKD and those without it in the same sample.

In conclusion, for patients with CKD without suspected ACS, elevated troponin T and troponin I levels are potent predictors of mortality. Our findings lend support to the current U.S. Food and Drug Administration stance that measuring troponin levels may be reasonable for additional risk stratification. However, the risk—benefit balance of routine measurement of cardiac troponin levels in clinical practice is unclear because how such information should change clinical management is unknown. New research should focus on testing patient treatment strategies that incorporate troponin assays in their algorithms, especially for patients at highest risk.

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References
Cardiac troponin T elevation is independent of renal function and clinical findings in heart failure patients. Cardiol J. 2010;17:42-8. [PMID: 2014456]


111. Le Goff C, Boyv C, Alenodoff MC, Krzesinski JM, Chapelle JP. Three-year prognostic interest of cardiac troponin T (cTnT) and amino-terminal pro-B-natriuretic peptide (NT-proBNP) in hemodialyzed patients. Immuno-Analyse & Biologie Spécialisée. 2008;23:12-8.


120. Vestergaard P, Moskilde L. Cohort study on effects of parathyroid surgery on multiple outcomes in primary hyperparathyroidism. BMJ. 2003;327:530-4. [PMID: 12958111]

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Obtaining of funding: E.B. Bass.
Administrative, technical, or logistic support: E.D. Michos, L.M. Wilson, E.B. Bass.

Appendix Table. MEDLINE Search Strategy

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<td>Hemodialysis[tiab]</td>
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<td>#6</td>
<td>Haemodialysis[tiab]</td>
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<tr>
<td>#11</td>
<td>“unstable angina”[tiab]</td>
</tr>
<tr>
<td>#12</td>
<td>“myocardial infarction”[tiab]</td>
</tr>
<tr>
<td>#14</td>
<td>Acute[tiab]</td>
</tr>
<tr>
<td>#15</td>
<td>#12 AND (#13 OR #14)</td>
</tr>
<tr>
<td>#16</td>
<td>#8 OR #9 OR #10 OR #11 OR #15</td>
</tr>
<tr>
<td>#17</td>
<td>Troponin I[mh] OR “Troponin T”[mh]</td>
</tr>
<tr>
<td>#18</td>
<td>Troponin*[tiab]</td>
</tr>
<tr>
<td>#19</td>
<td>#17 OR #18</td>
</tr>
<tr>
<td>#20</td>
<td>(#7 AND #16) OR (#7 AND #19)</td>
</tr>
<tr>
<td>#21</td>
<td>(animal[mh] NOT human[mh])</td>
</tr>
<tr>
<td>#23</td>
<td>#20 NOT #21 NOT #22</td>
</tr>
</tbody>
</table>

– Publication date from 1990/01/01