



ADMISSION CARDIAC TROPONINS PREDICT HOSPITAL MORTALITY IN TYPE A ACUTE AORTIC DISSECTION: A META-ANALYSIS OF ADJUSTED RISK ESTIMATES

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SUMMARY – Acute aortic dissection (AAD) is a serious medical emergency that requires early diagnosis and rapid treatment. Whether cardiac troponin could be an independent prognostic marker in patients with type A AAD is still unknown. We systematically searched Medline and Scopus to identify all observational cohort studies published before January 2020 that compared outcome (in-hospital mortality) in patients with type A AAD with and without troponin elevation on admission. Four studies with 412 patients were included in final analysis (median age 59 years, 65% of males). A total of 124 (30%) patients died during in-hospital stay, and 73% underwent surgery. Elevated troponins (39.6% of patients) were associated with an increased risk of short-term mortality (adjusted odds ratio 1.26; 95% confidence interval 1.08-1.47), with low heterogeneity among studies ($I^2=29.81\%$). Elevated troponins on admission are independently associated with increased in-hospital mortality in type A AAD.

Key words: *Troponin; Aortic dissection; Mortality; Meta-analysis*

Introduction

Acute aortic dissection (AAD) is a serious medical emergency that requires early diagnosis and rapid treatment¹. There is still lack of data on the role of circulating biomarkers in risk stratification of patients with AAD. Cardiac troponins, the preferred biomarker in diagnosing acute coronary syndromes, provide prognostic information in a broad spectrum of non-cardiac conditions². Troponin elevation among patients with AAD is common, and may be associated

with in-hospital diagnostic delay and misdiagnosis^{3,4}. This becomes even more important after the introduction of high-sensitivity troponins in routine clinical practice². We conducted a systematic review with meta-analysis to evaluate whether admission troponin positivity was associated with an increased risk of hospital mortality in patients with type A AAD.

Material and Methods

This meta-analysis was performed in accordance with the PRISMA statement⁵. We systematically searched Medline and Scopus to identify all observational cohort studies published before January 2020 that compared outcome (in-hospital mortality) in patients with type A AAD (presented within 14 days of

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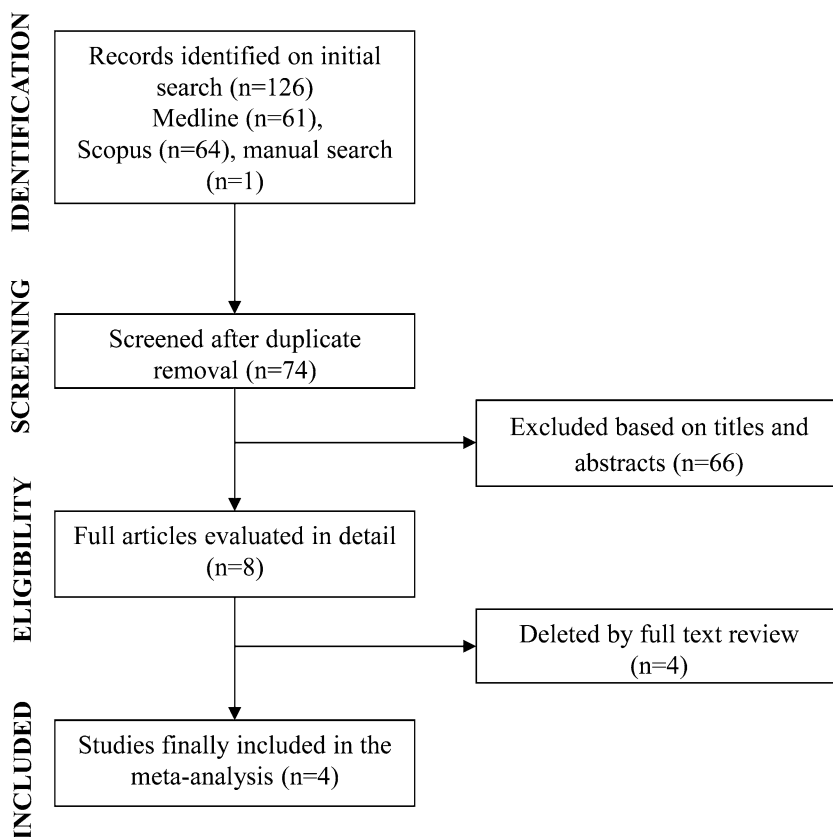


Fig. 1. Study flow diagram for meta-analysis of cardiac troponins and type A acute aortic dissection in-hospital mortality.

symptom onset) with and without troponin elevation on admission, combining terms “troponin” and “aortic dissection”. Study selection and data extraction were conducted independently by two investigators (MV and AVP), and study quality was evaluated using the validated Newcastle-Ottawa Scale⁶. Completed database contained the following data: the name of the first author, year of publication, country of origin, total number of patients in each study, study design, mean age of a population, the percentage of males and patients with hypertension, type of troponin and diagnostic assay, cut-off value, in-hospital mortality, adjusted effect estimates, and confounding factors.

A meta-analysis was conducted using the generic inverse variance method, and pooled odds ratio (OR) was reported with 95% confidence interval (CI). Heterogeneity among studies was investigated using the Cochrane’s *Q* test and *I*² statistic. Statistically significant heterogeneity was considered to be present at $p < 0.10$ and $I^2 > 50\%$. Publication bias was assessed

graphically using a funnel plot. Analyses were conducted using MedCalc Version 19.1.5 statistical software.

Results

A total of 126 citations were obtained by electronic search. After reading titles and abstracts, followed by review of the potentially relevant studies, four studies were included in final analysis, including a total of 412 patients (Fig. 1, Table 1)⁷⁻¹⁰. Median age of the population was 59 (range 54 to 69) years, 65% were males (range 57% to 70%), and 70% had hypertension (range 50% to 93%). Two studies were retrospective^{7,8} and two were prospective by design^{9,10}. Multivariate statistical analysis was performed in all these studies. Using the Newcastle-Ottawa scoring system, scores ranged from 8 to 9 for the included studies.

Overall, 124 (30%) patients with type A AAD died during hospital stay, and 73% underwent surgery. Elevated cardiac troponin was present in 39.6% of pa-

Table 1. Characteristics of studies included in meta-analysis

Author, year	Country	Patients (n)	Age (years)	Male (%)	HTN (%)	Study design	Mortality (%)	Troponin T or I	Troponin positive (%)	Cut-off (ng/L)	Assay	Adjusted OR (95% CI)	Confounders	NOS (0-9)
Bonnefoy, 2005	France	119	63	70	50	R	30	I	24	350	Immunoenzymatic fluorescent assay, Dade International Inc.	2.20 (0.70-7.40)	Age, stroke, ST-segment elevation, tamponade, catecholamine infusion, renal failure	9
Vrsalovic, 2015	Croatia	54	69	63	93	R	44	T	33	10	TnT Elecsys assay, Hoffmann-La Roche Ltd	2.24 (0.48-10.69)	Age, surgery	8
Li, 2016	China	103	55	69	79	P	35	T	61	14	Elecsys 2010 system, Roche Diagnostics	2.20 (1.11-4.37)	Surgery, systolic blood pressure, CRP, D-dimer, platelet count	9
Feng, 2017	China	136	54	57	71	P	21	I	NR	NR	NR	1.20 (0.96-1.33)	Surgery, ascending aorta diameter, WBC, CRP, D-dimer, cysstatin C	9

CI = confidence interval; CRP = C-reactive protein; HTN = hypertension; HTN = hypertensive; NOS = Newcastle-Ottawa scale; NR = not reported; OR = odds ratio; P = prospective; R = retrospective; WBC = white blood cells

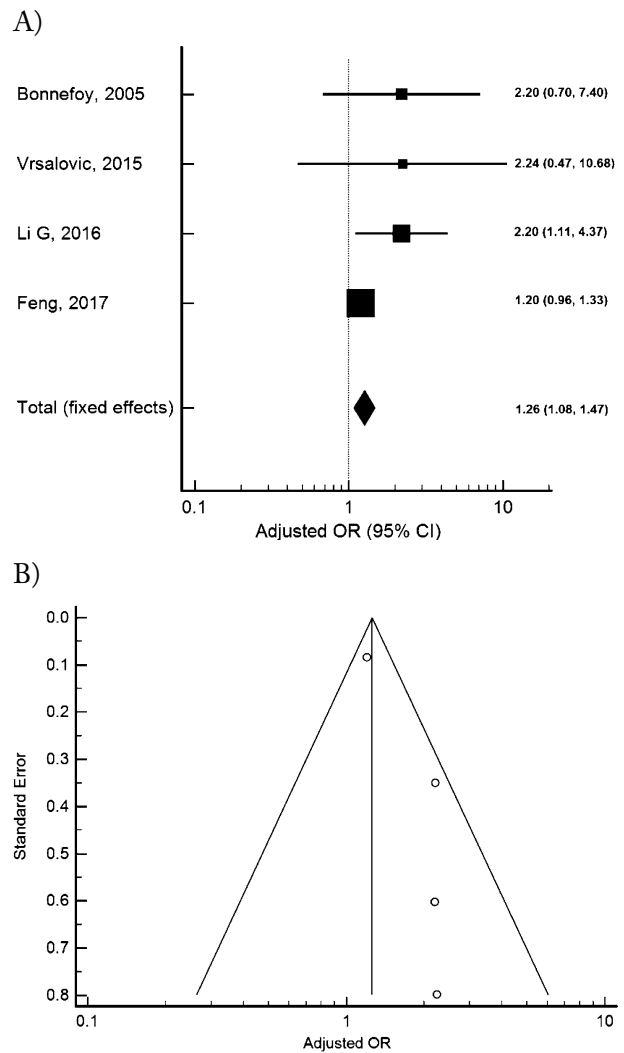


Fig. 2. Meta-analysis of studies testing the association between cardiac troponin elevation on admission and in-hospital mortality in type A AAD (N=412): (A) meta-analysis of studies that reported adjusted ORs (generic inverse variance method, fixed effects model); (B) funnel plot of adjusted ORs of in-hospital mortality.

AAD = acute aortic dissection; CI = confidence interval; OR = odds ratio

tients, ranging between 24% and 61%. Meta-analysis of studies that reported adjusted ORs (fixed effects model)⁷⁻¹⁰ showed a significant association between elevated troponin values and mortality (OR, 1.26; 95% CI, 1.08-1.47) (Fig. 2A). Analysis of pooled studies showed low heterogeneity ($P=29.81\%$, Cochrane $Q=4.27$, $p=0.23$) and funnel plot asymmetry (Fig. 2B).

Discussion

Our meta-analysis showed for the first time that elevated cardiac troponins are independently associated with increased in-hospital mortality in mostly hypertensive patients with type A AAD.

Aortic dissection is a life-threatening condition with various clinical presentations, which requires immediate diagnostic assessment and therapy¹. Troponin positivity is a common finding in patients with AAD, who can easily be misdiagnosed by physicians for other causes of acute chest pain (i.e. myocardial infarction, pulmonary embolism)²⁻⁴. The prognostic role of troponins is already established in cardiovascular conditions such as acute coronary syndrome, pulmonary embolism, and acute ischemic stroke². To date, a few biomarkers demonstrated the potential for risk stratification of patients with AAD^{3,11,12}. According to our previous meta-analysis that included patients with both type A and type B AAD, troponin elevation was associated with an increased risk of in-hospital mortality³. The present study extended the previous findings, analyzing the adjusted effect estimates for outcome and focused exclusively on type A AAD that is treated differently with worse in-hospital outcomes compared to type B AAD. This is of importance in clinical assessment and differential diagnosis, since the risk of death for type A AAD increases by 3-4 percent every hour until the patient undergoes surgery¹. The predictive value of troponin for myocardial damage is the result of several factors, including supply-demand imbalance due to severe drop in blood pressure, demand ischemia from severe aortic regurgitation, an intimal flap covering the coronary ostia, pressure overload from resistant hypertension and left ventricular dysfunction, or associated coronary artery disease^{3,4}.

Along with the data reported in the International Registry of Acute Aortic Dissection, in our meta-analysis aortic dissection was reported predominantly in hypertensive men in the sixth decade of life¹. Troponin positivity on admission was common and provided clear and independent prognostic information in type A AAD. Clinicians should bear it in mind in the evaluation, differential diagnosis, management and follow-up of patients with a history of hypertension and acute chest pain. More research is needed to evaluate the role of troponins in the whole spectrum of patients with acute aortic syndromes.

In conclusion, our meta-analysis clearly showed the independent prognostic value of admission troponin elevation for in-hospital mortality in patients with type A AAD.

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Sažetak

SRČANI TROPONINI PRETKAZUJU BOLNIČKU SMRTNOST
U BOLESNIKA S AKUTNOM DISEKCIJOM AORTE TIPA A:
META-ANALIZA PRILAGOĐENIH OMJERA IZGLEDA*M. Vrsalović i A. Vrsalović Presečki*

Akutna disekcija aorte (AD) predstavlja životno ugrožavajuće hitno stanje koje zahtijeva ranu dijagnozu i liječenje. Do sada nije istraživana uloga srčanog troponina kao nezavisnog prognostičkog biljega u bolesnika s AD tipa A. Sustavno su pretražene baze podataka Medline i Scopus s ciljem pronalaska opservacijskih kohortnih studija objavljenih do siječnja 2020. godine, koje su uspoređivale bolničku smrtnost bolesnika s tipom A AD u ovisnosti o povišenim vrijednostima troponina u trenutku prijma. U istraživanje su uključene četiri studije s ukupno 412 bolesnika (medijan dobi 59 godina, 65% muškaraca). Ukupno su tijekom hospitalizacije umrla 124 (30%) bolesnika, od kojih je 73% podvrgnuto kirurškom liječenju. Povišene vrijednosti srčanih troponina (39,6% bolesnika) bile su nezavisno povezane s povišenim rizikom kratkoročne smrtnosti (prilagođeni omjer izgleda 1,26; 95% interval pouzdanosti 1,08-1,47), uz nisku heterogenost među uključenim istraživanjima ($I^2=29,81\%$). Povišene vrijednosti troponina u trenutku prijma nezavisno su povezane s povišenom bolničkom smrtnošću u bolesnika s AD tipa A.

Ključne riječi: *Troponin; Disekcija aorte; Smrtnost; Meta-analiza*