



Research Article

Natriuretic Peptide Levels and Early Respiratory Adverse Outcome in Cardiac Surgery: A Short Review of the Literature

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Abstract

Background: B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide are significant biomarkers for predicting outcome among cardiac surgery patients. Their elevated levels have been strongly associated with increased mortality, prolonged intensive care unit stay and postoperative onset of atrial fibrillation. However, early respiratory morbidity indexes have not been long studied.

Aim: To review the association between high natriuretic peptide levels and early adverse respiratory outcome in cardiac surgery patients.

Methods: The Medline electronic database was searched in January 2014 for articles which have been published in the English language, between 1 January 2004 and 31 December 2013, and investigated the association between preoperative natriuretic peptides levels and early postoperative respiratory adverse outcome among adult cardiac surgery patients. Nine articles constituted our final study material.

Results: The current literature reveals studies with small sample sizes, which underline the association between preoperative increased natriuretic peptide levels and postoperative respiratory outcomes, such as prolonged mechanical ventilation and ventilatory weaning failure.

Conclusions: It seems that B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide levels are valuable, effective and inexpensive predictors of the early respiratory outcome in cardiac operated patients. Further research, including multicenter studies with large patient series, is needed to allow more accurate and reliable findings.

Key-words:

B-type natriuretic peptide; Cardiac surgery; Natriuretic peptide; N-terminal pro-B-type natriuretic peptide; Outcome; Respiratory complications

Abbreviations

BNP- B-type Natriuretic Peptide; ICU- Intensive Care Unit; NT pro-BNP- N-Terminal Pro-B-type Natriuretic Peptide

Introduction

B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT pro-BNP) are synthesized and released by ventricular cardiomyocytes in response to ventricular dysfunction and increased wall-stress. [1] BNP promotes natriuresis, diuresis and vasodilatation, whereas NT pro-BNP is biologically inactive. [2] These peptides are well-demonstrated biomarkers for the diagnosis and prognosis of heart failure and their elevation indicates the systolic and diastolic left ventricular dysfunction. [3] However, natriuretic peptide concentration is increased in several cardiovascular disorders, including acute coronary syndromes, valvular heart disease, acute and chronic right ventricular failure and right ventricular hypertrophy secondary to arterial or pulmonary hypertension. [4]

Over the last decade, the interest for perioperative natriuretic peptide levels in the cardiac surgery setting has increased dramatically, as researchers have investigated the value of BNP and NT pro-BNP on predicting cardiac surgery outcomes, such as mortality, postoperative atrial fibrillation, intensive care unit (ICU) and hospital length of stay, requirement for inotropic support or/and intra aortic balloon pump, renal impairment, cardiac arrhythmias and other postoperative complications. [2,5,6,7] It is notable that high natriuretic peptide levels have strong correlated with widely used risk stratification models in cardiac surgery, such as EuroSCORE and Parsonnet score [6,8] and their ability to predict postoperative complications is more accurate than levels of inflammatory markers, such as interleukine-6 and 8, P-selectin, intercellular adhesion molecule and C-reactive protein. [9]

Prolonged mechanical ventilation and ventilatory weaning failure after cardiac surgery indicate the early respiratory adverse postoperative patient outcome. Although, these respiratory parameters are among the most commonly investigated morbidity indexes in patients who underwent cardiac surgery [10] the clinical value of perioperative BNP and NT pro-BNP concentrations in providing powerful predictive information for early respiratory adverse outcome has only been assessed in a small number of studies with small sample sizes. [2,4,8,9,11-14]

The aim of this study was to review the association between high natriuretic peptide levels and early respiratory adverse outcome in cardiac surgery patients. The limited literature data were the main reason for the present short review

Methods

The Medline electronic database was searched in January 2014. Eligible articles must have been published in the English language, between 1 January 2004 and 31 December 2013, and investigated the association between perioperative natriuretic peptides levels and early postoperative respiratory adverse outcome among adult cardiac surgery patients. The following key-words were used: B-type natriuretic peptide, cardiac surgery, natriuretic peptides, N-terminal pro B-type natriuretic peptide, mechanical ventilation, outcome, respiratory complications and weaning failure.

We defined as early postoperative adverse outcome the prolonged mechanical ventilation and/or the patient ventilator weaning failure during the early postoperative period. Nine articles [2,4,8,9,11-15] met the inclusion criteria and constituted our final study material.

single-centre series with observational prospective design and small sample sizes, exclusive of the studies conducted by Nozohoor et al. [4] and Cuthbertson et al. [2], respectively.

Results

Table 1 describes and presents summary data from the studies that were eligible for our review [2,4,8,9,11-15]. All these studies were

Study	Country	Design	Sample	Elective, urgent or emergency status	Natriuretic peptide	Natriuretic peptide measurement period	Respiratory outcome	Major findings
Attaran et al, 2009	UK	Prospective single-centre cohort study	141 cardiac surgery patients (CABG, valve surgery)	95 elective & 45 urgent surgical procedures	BNP	Preoperatively	Mechanical ventilation time	High BNP levels predicted longer ventilation time
Cuthbertson et al, 2009	UK	Prospective single-centre cohort study	1010 cardiac surgery patients (CABG, valve surgery)	Elective surgical procedures	NT pro-BNP	Perioperatively (pro, intra and postoperatively)	Mechanical ventilation time	Preoperative NT pro-BNP were 3% higher in patients with requirement for ventilation > 24 hours
Ganem et al, 2011	Brazil	Prospective single-centre cohort study	62 cardiac surgery patients (CABG, valve surgery, aneurysmectomy)	Elective surgical procedures	BNP	Preoperatively and postoperatively	Mechanical ventilation time	High preoperative and postoperative (6 hours after CPB) were associated with longer mechanical ventilation
Hutfless et al, 2004	USA	Prospective single-centre cohort study	98 male, cardiac surgery patients (CABG, valve surgery, ASD repair, VSD repair, Re-do sternotomy)	Elective surgical procedures	BNP	Preoperatively and postoperatively	Mechanical ventilation time	No association between high pre and postoperative BNP levels and ventilator support > 48 hours
Jogia et al, 2007	New Zealand	Prospective single-centre cohort study	118 cardiac surgery patients (CABG, valve surgery)	Elective surgical procedures	NT pro-BNP	Preoperatively and postoperatively	Mechanical ventilation time	Preoperative NT pro-BNP levels were associated with longer ventilation time
Lara et al, 2013	Brazil	Prospective single-centre cohort study	101 CABG patients	Elective surgical procedures	BNP	Postoperatively	Weaning from mechanical ventilation	A high BNP concentration at the end of a spontaneous breathing trial was the only independent predictor of weaning failure
Nozohoor et al, 2011	Sweden	Retrospective single-centre cohort study	407 cardiac surgery patients (CABG, valve surgery)	374 elective & 33 emergency surgical procedures	BNP	Postoperatively	Mechanical ventilation time	Higher BNP levels on patient admittance to the ICU were associated with prolonged ventilatory support
Sodeck et al, 2008	Austria	Prospective single-centre cohort study	104 patients undergoing surgery for acute type A aortic dissection	Emergency surgical procedures	NT pro-BNP	Preoperatively	Weaning from mechanical ventilation	Increased NT pro-BNP levels were associated with the occurrence of lung failure postoperatively

Wang et al, 2010	China	Prospective single-centre cohort study	112 primary off-pump CABG patients	Elective surgical procedures	BNP	Preoperatively and postoperatively	Mechanical ventilation time	A preoperative BNP levels >100pg/ml was an independent risk factor for ventilation >24 hours postoperatively
ASD: Atrial septal defect, BNP: B-type natriuretic peptide, CABG: Coronary artery bypass grafting, CPB: Cardio-pulmonary bypass, ICU: Intensive care unit, NT pro-BNP: N-terminal pro-B-type natriuretic peptide, UK: United Kingdom, VSD: Ventricular septal defect								

Table 1: Characteristics of the included studies in the literature review (n=9)

BNP levels and respiratory adverse outcome

Elevated preoperative and postoperative BNP levels have been associated with early respiratory adverse outcome after heart surgery. Attaran et al. [8] and Ganem et al. [9] in their studies highlighted the significant association between high preoperative BNP levels and longer mechanical ventilation time among cardiac surgery patients. In addition, Wang et al. [11] investigating 112 off-pump coronary artery bypass grafting patients prospectively, stated by using multivariate analysis that preoperative BNP levels greater than 100 pg/ml was an independent risk factor for mechanical ventilation more than 24 hours after surgery.

Regarding the ability of postoperative BNP concentrations to predict the early respiratory adverse outcome in the setting of cardiac surgery Ganem et al. [9] concluded that BNP levels at 6 hours after cardiopulmonary bypass are strongly associated with longer need of mechanical ventilation. In addition, Nozohoor et al, [4] conducting a retrospective study of 407 patients who underwent cardiac surgery reported higher BNP levels on patient admittance to the ICU among patients who required significantly longer ventilation. Finally, in promising findings concluded Lara et al. [12] in their recent study, indicating BNP as predictive factor for the failure to wean from mechanical ventilation after cardiac surgery? Specifically, a high BNP level at the end of a spontaneous breathing trial was found as the only independent predictor of weaning failure.

Finally and contrary to the above mentioned studies, Hutfless et al. [15] in their study of 98 male open-heart surgery patients found no significantly higher perioperative (pre- and postoperative) BNP levels in patients requiring mechanical ventilator support dependence longer than 48 hours postoperatively.

NT pro-BNP levels and respiratory adverse outcome

Perioperative NT pro-BNP levels have examined as predictors of the early respiratory adverse outcome in some studies [2,13,14] but only the preoperative concentrations were found to have a prognostic value. According the study of Cuthbertson et al [2] preoperative NT pro-BNP levels were significantly higher [468 ng/lit vs 274 ng/lit, Odds Ratio 1.03 (Confidence Interval 1.01-1.05), p = 0.001] in patients with requirement for ventilation more than 24 hours after surgery compared with those with shorter mechanical ventilatory support. In addition, Jogia et al [13] in a prospective study of 118 cardiac surgery patients had similar results, while Sodeck et al, [14] investigating 104 patients who underwent emergency surgery for acute Stanford type A aortic dissection, revealed that increased preoperative levels of NT pro-BNP were strongly associated with the occurrence of major adverse events postoperatively, including lung failure.

Discussion

The ability of natriuretic peptide levels to predict effectively postoperative outcomes and complications in cardiac surgery have long been studied and strongly associated with outcomes such as atrial fibrillation, ICU and hospital length of stay and mortality [6,7,16,17,18]. In addition, two recent meta-analyses with large sample sizes [5,19] examined the predictive ability of preoperayive BNP and NT Pro-BNP on postoperative atrial fibrillation, mortality, and intra-aortic balloon pump requirement. Nevertheless, there is a limited body of knowledge regarding the potential association between these biomarkers and early postoperative adverse respiratory outcome.

As aforementioned, recent literature provides some promising findings, which underline the significant association between elevated perioperative natriuretic peptide levels and prolonged postoperative ventilator dependence and respiratory weaning failure among cardiac surgical patients [2,4,8,9,11-14]. This association may be interpreted by excess fluid and stunning of myocardium. [4] Natriuretic peptides are synthesized and secreted from cardiomyocytes in response to atrial or ventricular wall stretch. The main entities that elevate ventricular or atrial wall stretch after cardiac surgery are acute heart failure and atrial fibrillation. In addition natriuretic peptides increase with age, due to the reduction in their clearance with aging. These three parameters are themselves powerful determinant of poor postoperative outcome, including respiratory complications due to poor myocardial recovery and postoperative function. [20] In addition, several of the factors that influence and elevated natriuretic peptide levels, such as left ventricular filling pressure and diastolic function, as well as chronic ventricular dysfunction and renal impairment are themselves powerful determinants of poor postoperative outcome, including respiratory complications. [2,21,22]

It is worth mentioning that fluid overloading can influence the levels of postoperative natriuretic peptides and consequently can adequately interpret the association between elevated natriuretic peptide levels and adverse respiratory outcome after open-heart surgery. Several studies have highlighted the negative impact of fluid overloading based on its responsibility for the increased natriuretic peptide levels, [23,24] which are indexes for poor outcome, including respiratory complications. Fluid overloading is a not an uncommon scenario regarding the cardiac surgery setting due to infusion of large amounts of products (blood, colloids, crystalloids) trying to manage the severely depleted intravascular volume and hypovolaemia of patients during the immediate postoperative phase. [25]

Natriuretic peptides are described as valuable, inexpensive, and reliable predictors of the early respiratory adverse outcome post cardiac surgery. Elevated perioperative BNP and NT pro-BNP levels

may indicate a tool for the early identification of patients at risk, allowing the application of appropriate therapeutic management. [4] This early identification of high-risk patients for prolonged ventilation and early respiratory complications in general could facilitate both the more effective use of the limited healthcare resources and better planning of the operative list, a fact of great importance for centers with decreased ICU beds availability. [26] In addition, patients who have increased levels of BNP and NT pro-BNP may benefit from increased vasodilatation, diuresis or both aiming to reduce the risk of postoperative respiratory and other complications. [2]

On the other hand, it should be noted, that the predictive value of natriuretic peptides for the early respiratory adverse outcome in cardiac surgery patients remains uncertain, due to the relatively few single-centre studies, with small sample sizes, which have tried to examine this topic.

Conclusions

In conclusion, it seems promising that perioperative BNP and NT pro-BNP levels may have the ability to accurately predict the hazard for early respiratory adverse outcome after cardiac surgery. A simple biochemical test that could improve the accuracy of postoperative respiratory outcome prediction would be of considerable value. However, further research is needed, based on multicentre studies with larger sample sizes, to address if natriuretic peptides either alone or in combination with existing clinical tools could help clinicians to identify earlier the high risk patients and quantify with accuracy the risk of individuals for respiratory adverse outcome.

References

1. Maisel A, Mueller C, Adams K Jr, Anker SD, Aspromonte N, et al. (2008) State of the art: using natriuretic peptide levels in clinical practice. *Eur J Heart Fail* 10: 824-839.
2. Cuthbertson BH, Croal BL, Rae D, Gibson PH, McNeilly JD, et al. (2009) N-terminal pro-B-type natriuretic peptide levels and early outcome after cardiac surgery: a prospective cohort study. *Br J Anaesth* 103: 647-653.
3. Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, et al. (2002) Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 347: 161-167.
4. Nozohoor S, Nilsson J, Algotsson L, Sjögren J. (2011) Postoperative increase in B-type natriuretic peptide levels predicts adverse outcome after cardiac surgery. *J Cardiothorac Vasc Anesth* 25: 469-475.
5. Litton E, Ho KM. (2012) The use of pre-operative brain natriuretic peptides as a predictor of adverse outcomes after cardiac surgery: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 41: 525-534.
6. Eliasdóttir SB, Klemenzson G, Torfason B, Valsson F. (2008) Brain natriuretic peptide is a good predictor for outcome in cardiac surgery. *Acta Anaesthesiol Scand* 52: 182-187.
7. Fellahi JL, Daccache G, Rubes D, Massetti M, Gérard, et al. (2011) Does preoperative B-type natriuretic peptide better predict adverse outcome and prolonged length of stay than the standard European System for Cardiac Operative Risk Evaluation after cardiac surgery? *J Cardiothorac Vasc Anesth* 25: 256-262.
8. Attaran S, Sherwood R, Desai J, Langworthy R, Mhandu P, et al. (2009) Brain natriuretic peptide a predictive marker in cardiac surgery. *Interact Cardiovasc Thorac Surg* 9: 662-666.
9. Ganem F, Serrano CV Jr, Fernandes JL, Blotta MH, Souza JA, et al. (2011) Preoperative B-type natriuretic peptide, and not the inflammation status, predicts an adverse outcome for patients undergoing heart surgery. *Interact Cardiovasc Thorac Surg* 12: 778-783.
10. Serrano N, García C, Villegas J, Huidobro S, Henry CC, et al. (2005) Epidemiological Project for ICU Research and Evaluation (EPICURE). Prolonged intubation rates after coronary artery bypass surgery and ICU risk stratification score. *Chest* 128: 595-601.
11. Wang Z, Liang D, Fu Q, Jia L, Men J, et al. (2010) Perioperative brain natriuretic peptide in off-pump coronary artery bypass. *Acta Cardiol* 65: 297-301.
12. Lara TM, Hajjar LA, de Almeida JP, Fukushima JT, Barbas CS, et al. (2013) High levels of B-type natriuretic peptide predict weaning failure from mechanical ventilation in adult patients after cardiac surgery. *Clinics (Sao Paulo, Brazil)* 68: 33-38.
13. Jogia PM, Kalkoff M, Sleigh JW, Bertinelli A, La Pine M, et al. (2007) NT-pro BNP secretion and clinical endpoints in cardiac surgery intensive care patients. *Anaesth Intensive Care* 35: 363-369.
14. Sodeck G, Domanovits H, Schillinger M, Janata K, Thalmann M, et al. (2008) Pre-operative N-terminal pro-brain natriuretic peptide predicts outcome in type A aortic dissection. *J Am Coll Cardiol* 51: 1092-1097.
15. Hutfless R, Kazanegra R, Madani M, Bhalla MA, Tulu-Tata A, et al. (2004) Utility of B-type natriuretic peptide in predicting postoperative complications and outcomes in patients undergoing heart surgery. *J Am Coll Cardiol* 43: 1873-1879.
16. Chen TH, Lin CL, Shih JJ, Shih JY, Chen CH, et al. (2013) Plasma B-type natriuretic peptide in predicting outcomes of elective coronary artery bypass surgery. *Kaohsiung J Med Sci* 29: 254-258.
17. Tavakol M, Hassan KZ, Abdula RK, Briggs W, Oribabor CE, et al. (2009) Utility of brain natriuretic peptide as a predictor of atrial fibrillation after cardiac operations. *Ann Thorac Surg* 88: 802-807.
18. Hernández-Leiva E, Dennis R, Isaza D, Umaña JP. (2013) Hemoglobin and B-type natriuretic peptide preoperative values but not inflammatory markers, are associated with postoperative morbidity in cardiac surgery: a prospective cohort analytic study. *J Cardiothorac Surg* 8: 170.
19. Cai GL, Chen J, Hu CB, Yan ML, Xu QH, et al. (2014) Value of plasma brain natriuretic peptide levels for predicting postoperative atrial fibrillation: a systemic review and meta-analysis. *World J Surg* 38: 51-59.
20. Liang Y, Gu M, Wang S. (2012) Reasons elevated B-type natriuretic peptide levels are associated with adverse outcome in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 26: e6.
21. Provenchère S, Berroeta C, Reynaud C, Baron G, Poirier I, et al. (2006) Plasma brain natriuretic peptide and cardiac troponin I concentrations after adult cardiac surgery: association with postoperative cardiac dysfunction and 1-year mortality. *Crit Care Med* 34: 995-1000.
22. Cerrahoglu M, Iskesen I, Tekin C, Onur E, Yildirim F, et al. (2007) N-terminal ProBNP levels can predict cardiac failure after cardiac surgery. *Circ J* 71: 79-83.

23. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, et al. (2006) Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 354: 2564-2575
24. Zhang Z, Zhang Z, Xue Y, Xu X, Ni H. (2012) Prognostic value of B-type natriuretic peptide (BNP) and its potential role in guiding fluid therapy in critically ill septic patients. *Scand J Trauma Resusc Emerg Med* 20:86
25. Mariscalco G, Musumeci F. (2014) Fluid management in the cardiothoracic intensive care unit: diuresis--diuretics and hemofiltration. *Curr Opin Anaesthesiol* 27:133-139
26. Giakoumidakis K, Eltheni R, Brokalaki H, Galanis P, Nenekidis I, et al. (2011) Preoperative and intraoperative risk factors for prolonged mechanical ventilation among cardiac surgery patients. *Health Science Journal* 5: 297-305.