

died. An alternative method of repair was therefore attempted with BioGlue surgical adhesive (Cryolife International Inc, Kenesaw, GA), which is a polymer of bovine serum albumin and glutaraldehyde that reaches bonding strength within 2 minutes of mixing and application.

The patient was placed back onto bypass and cooled, and the heart was perfused with cardioplegic solution. BioGlue was then applied to the external surface of the dehisced margins of the atrioventricular groove, and a patch of bovine pericardium was placed over the glue before it set, with a total circulatory arrest time of 2 minutes to ensure a dry field.

The circulation was then restarted, but further bleeding complicated attempted weaning from cardiopulmonary bypass. Therefore, the pericardium was removed, and 2-0 Ticon polytetrafluoroethylene (Teflon) -bolstered sutures were used to attempt to close the defect. However, the sutures themselves caused additional bleeding from the damaged tissues. Consequently, a further attempt to achieve hemostasis with the BioGlue surgical adhesive was performed with the heart arrested and perfused with cardioplegic solution again.

The BioGlue was applied under and over the Teflon-pledgeted sutures, and another patch of Teflon felt was glued on top of the Teflon-pledgeted sutures. It was held firmly in place for 2 minutes to achieve good adhesion, and then the aortic cross-clamp was released. Fortunately this second attempt resulted in a dry operative field with complete control of the bleeding. The patient spontaneously went into sinus rhythm after the cross-clamp was released, and bypass was withdrawn without inotropic support. The patient was deliberately kept hypotensive overnight with a mean blood pressure less than 70 mm Hg. She then made an uneventful recovery. Before discharge an echocardiograph showed no perivalvular leak from either the mitral or aortic valve.

### Comment

Atrioventricular disruption, injury to the left circumflex artery, and thromboembolic events are complications associated with a heavily calcified mitral annulus in mitral valve replacement [4]. Various predisposing and intraoperative factors have been suggested as to the cause of atrioventricular disruption [5]. Dark and Bain [6] have suggested that the possible cause of the rupture at the atrioventricular groove occurs after damage to the thin myocardium that has lost the internal buttress of the subvalvular apparatus. With the rise in intraventricular pressure at the end of bypass, blood dissects into the myocardium, resulting in a large hematoma and eventual rupture.

This case report involved debridement of calcium from the heavily calcified posterior mitral annulus. This calcium removal may produce severe thinning of the atrioventricular junction and thus predispose to rupture. It was an interesting observation that the pericardial patch did not adhere very well to the glue but that the Teflon seemed to have a better binding capacity.

Although this complication is uncommon, it is frequently fatal, and this new application for BioGlue as an

adjunct to the conventional repair of atrioventricular disruption may be of benefit to others who are unfortunate enough to be in this dilemma.

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## Nesiritide (BNP) in the Management of Postoperative Cardiac Patients

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Recombinant human B-type natriuretic peptide (BNP) is a promising new agent in the management of heart failure. The pharmacologic properties of BNP make it desirable to use in a subset of patients after cardiac surgical operations. Among these therapeutic potentials is the effect on markedly reducing pulmonary vascular resistance and central venous pressure with mild systemic vasodilatation. In addition, BNP directly effects the kidneys to promote natriuresis. We believe this agent to be useful in the treatment of the postcardiac surgery patients with left ventricular dysfunction and mild to moderate renal insufficiency. This report summarizes our experience in 2 patients.

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Recombinant human B-type natriuretic peptide (BNP) is a promising new agent in the management of heart failure. A previous study in patients with acute

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decompensated heart failure with associated dyspnea has shown improved hemodynamics with intravenous administration related to reduction in pulmonary capillary wedge pressure, pulmonary vascular resistance, and right atrial pressure [1]. The efficacy of BNP administration in patients with poor left ventricular (LV) function undergoing cardiac operations has not been evaluated. We present our experience with 2 patients with preoperative LV dysfunction and renal insufficiency.

## Case Reports

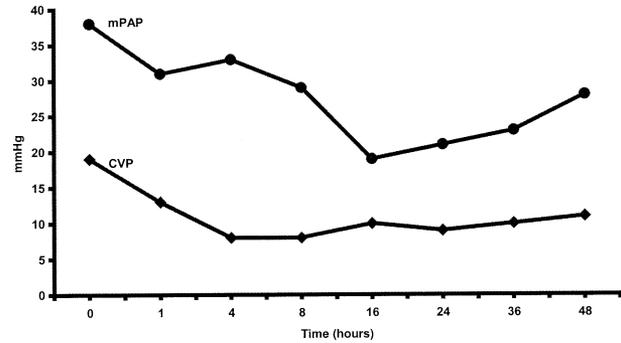
### Patient 1

An 87-year-old woman with acute myocardial infarction and moderate left ventricular dysfunction (ejection fraction 30%) underwent emergent coronary artery bypass surgery for unstable angina. Preoperative serum creatinine was 2.1 mg/dL. She required placement of intraaortic balloon pump (IABP) and subsequently had three-vessel coronary artery bypass grafting. Milrinone, dobutamine, and IABP were needed to wean her from cardiopulmonary bypass. Initial hemodynamics included blood pressure (BP) 148/52 mm Hg, pulmonary artery pressure (PAP) 65/24 mm Hg (mean 38), central venous pressure (CVP) 19 mm Hg, and cardiac index (CI)  $2.7 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ . Despite inotropic therapy, filling pressures remained high and she was oliguric.

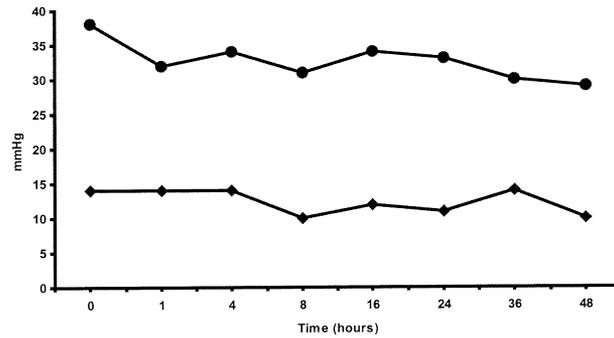
Nesiritide infusion was started at  $0.01 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . Within 4 hours the hemodynamics were as follows: BP 129/46, CVP 13, PA 54/26 (mean 33), and CI 2.8 (Fig 1, A). Sixteen hours after initiation of nesiritide, IABP had been removed, milrinone had been weaned off, and dobutamine infusion reduced to  $2 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . The following hemodynamics were obtained BP 131/86, CVP 10, PAP 37/10 (mean 19), and CI 2.9. Concomitant with the above improvements in filling pressures there was a significant increase in urine output from less than 200 mL per 8 hours to more than 800 mL per 8 hours, which was sustained over the ensuing days (Fig 2). Serum sodium and creatinine remained stable at 138 mEq/L and 2.7 mg/dL, respectively.

### Patient 2

A 65-year-old man with a history of repeated percutaneous transluminal coronary angioplasty and stents in the past presented with recurrent in-stent restenosis and myocardial infarction. He required preoperative placement of an IABP, had ejection fraction of 15% and serum creatinine of 2.9 mg/dL. He underwent urgent three-vessel coronary bypass surgery. Postoperatively he continued to require dobutamine and milrinone with the following hemodynamics: BP 144/57, PAP 64/25 (mean 38), CVP 14, CI 2.8. Nesiritide infusion was started at  $0.01 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . Four hours later hemodynamics were as follows: BP 139/56, PAP 54/19 (mean 33), CVP 10, and CI 2.5 (Fig 1, B). Sixteen hours after starting the infusion, IABP had been removed, milrinone was discontinued, and dobutamine was infusing at  $3 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . Hemodynamics were BP 118/51, PAP 42/23 (mean



A



B

Fig 1. Mean pulmonary arterial pressures (mPAP) and central venous pressures (CVP) for patient 1 (A) and patient 2 (B). Circles = mPAP; diamonds = CVP.

31), CVP 11, CI 2.8. The hemodynamics remained unchanged over a 2-day infusion period. With initiation of treatment, urine output increased from 200 mL per 8 hours to more than 500 mL per 8 hours and remained high throughout the infusion period (Fig 2). Serum sodium and creatinine remained stable at 137 mEq/L and 2.7 mg/dL, respectively.

## Comment

The recombinant B-type natriuretic peptide, nesiritide, has been recently approved for use in patients with decompensated heart failure and associated dyspnea at rest or with minimal activity. The Vasodilation in Acute Congestive Heart Failure (VMAC) trial [1] evaluated the efficacy of this treatment in a prospective randomized trial involving 489 patients. The trial involved a comparison between intravenous nesiritide compared to nitroglycerin or placebo and demonstrated significant reduction in pulmonary capillary wedge pressure, pulmonary vascular resistance, and central venous pressure.

To date the use of BNP has not been evaluated as a pharmacologic adjunct for the management of critically ill patients postcardiac operations. This new agent has many therapeutic properties that are desirable in a subset of cardiac surgical patients. We have reported on the

effect of BNP in 2 patients who were recently treated at our institution.

Recombinant human B-type natriuretic peptide is a peptide that is normally secreted by ventricular myocardium in response to hemodynamic overload. Elevated levels have been found in conditions of increased preload, afterload, myocardial hypertrophy, myocardial infarction and most cardiomyopathies [2]. Hemodynamic overload induces the expression of BNP from the ventricular myocardium at the transcriptional level. It has been suggested that despite increased circulating levels of BNP in patients with heart failure, there may be a relative deficiency due to inability to upregulate transcription or due to receptor down regulation.

Nesiritide mimics the actions of endogenous BNP by binding to vascular smooth receptors. Activation of the receptors leads to increased synthesis of cyclic guanine monophosphate (cGMP) which mediates the vasodilator actions of this peptide. Clinically this is manifested by decrease in CVP and PVR and systemic arterial vasodilation. In both cases presented here, we observed a reduction in central venous and pulmonary pressures without any clinically significant systemic hypotension. In the VMAC trial [1] the incidence of systemic hypotension was not significantly different between nesiritide and nitroglycerin (4% and .5%, respectively). The drug has a rapid onset of action, with most of its effect seen in the initial 30 minutes of infusion. The drug remains effective throughout the duration of therapy and does not need dose adjustment in patients with renal insufficiency. In addition to its effect on the vascular system BNP also promotes natriuresis [3]. This effect may be ideal in the fluid overloaded post surgical patient with renal insufficiency. In both of our patients there was a dramatic and sustained increase in urine output without any significant change in serum sodium or creatinine.

Finally, other properties of the natriuretic peptides that are theoretically beneficial include attenuation of the sympathetic outflow [4] and inhibition of endothelin, renin and aldosterone production [5]. These neurohormonal pathways clearly play a central role in the pathogenesis of heart failure and down regulation may also be beneficial in the perioperative period.

In conclusion BNP exhibits pharmacologic properties that may be desirable in the post surgical cardiac patient. The exact profile of surgical patients who may benefit from nesiritide has not been clearly defined. Based on knowledge of its pharmacologic action patients who have

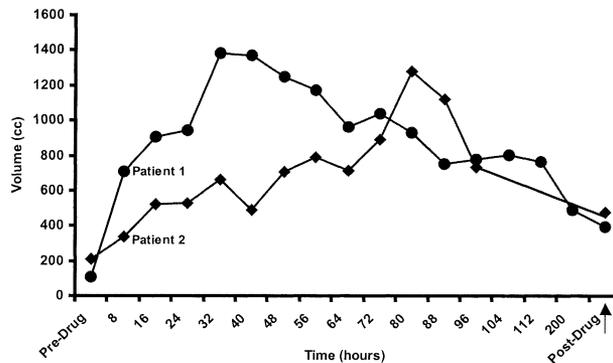


Fig 2. Urine output at 8-hour intervals after initiation of nesiritide infusion.

moderate to severe LV dysfunction, with or without elevated pulmonary artery pressures, may benefit from its vasodilatory properties. In patients with renal insufficiency, unresponsive to standard diuretic therapy, the natriuretic effects may also be beneficial. Whether the counter regulatory neurohormonal effects will also be beneficial remains to be seen. In our brief experience we did not encounter any significant side effects. Ultimately the true potential of this new therapy in the cardiac surgical arena needs to be defined by a well-designed randomized prospective trial. The initial patients for this study can be those with preexisting ventricular dysfunction or the group of heart failure patients after ventricular assist device placement or cardiac transplantation.

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