

# 'BioGlue' for the Repair of Aortic Insufficiency in Acute Aortic Dissection

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**Background and aim of the study:** Concern has been raised regarding the late effects of tissue glues. Herein is described the authors' experience with a new bioadhesive (BioGlue; Cryolife) for repair of the aortic root in acute dissection.

**Methods:** BioGlue is composed of bovine serum albumin (BSA) and glutaraldehyde. Glutaraldehyde exposure causes the lysine molecules of BSA, extracellular proteins and cell surfaces to bind to each other, creating a strong scaffold. Between January 2001 and January 2003, BioGlue was used to repair the aortic root in 22 patients with acute aortic dissection. Moderate or severe insufficiency was present in 16 cases, and mild insufficiency in six. The mechanism of insufficiency was commissure detachment in 15 cases, penetration of the intimal flap into the valve in three, and dilatation of the sinotubular junction in four. The aortic valve was resuspended to the aortic

wall using pledgeted sutures. BioGlue was used to glue the dissected layers of the aortic root and create stronger tissue for sewing. Two patients required complete resection of the sinuses and aortic root remodeling with a Dacron graft.

**Results:** There were two operative deaths. Postoperative transesophageal echocardiography showed mild or no aortic insufficiency in 18 patients, and moderate insufficiency in two. During follow up (mean 16 months), none of the patients required reoperation for proximal redissection, delayed rupture, or aortic insufficiency.

**Conclusion:** BioGlue is useful for aortic valve repair in aortic dissection. It is less toxic and has a stronger adhesive effect than the older surgical glues, and is expected to have better long-term results.

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Biological glue was first proposed for the treatment of acute aortic dissection more than 20 years ago (1). Gelatin-resorcin-formalin (GRF) glue is currently the most widely used adhesive in this setting (2-6), and is associated with a 7 to 39% rate of proximal aortic redissection (3,5,6). The aim of the present study was to describe the authors' mid-term results with a newly developed biological glue (BioGlue; Cryolife Inc., Kennesaw, GA, USA), for repair of the aortic valve in acute aortic dissection.

## Clinical material and methods

### Patients

Between January 2001 and January 2003, BioGlue was used for aortic root repair in 22 patients with acute type A aortic dissection. The mean ( $\pm$  SD) patient age at surgery was  $64 \pm 9$  years, and 68% were males. Insufficiency was moderate or severe in 16 cases, and mild in six. The mechanism of insufficiency was commissure detachment in 15 cases, penetration of the intimal flap into the valve in three, and dilatation of the sinotubular junction in four.

### Surgical technique

All operations were performed under deep hypothermia (rectal temperature 18°C) and total circulatory arrest. Brain cooling was achieved with retrograde cerebral perfusion via the superior vena cava with flows of up to 500 ml/min or a maximal bulb pressure of 25 mmHg. BioGlue was used to adhere the dissected layers at the distal anastomotic site in order to obliterate the false lumen and to create a stronger

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aortic tissue for sewing (Fig. 1). Before the glue was applied, all tissues surrounding the aortic arch were protected with wet sponges. Care was taken to avoid exposure of structures close to the aortic arch (such as the phrenic and vagus nerves) to the toxic effect of the glutaraldehyde component. As no long-term follow up data are available on the effect of BioGlue on arterial tissue, its use was limited to the local aortic tissue. A simple end-to-end anastomosis between the Dacron graft and the treated aorta was completed. In general, it was not found necessary to use any reinforcement sutures or Teflon felt strips to support the anastomosis. Thereafter, cardiopulmonary bypass was reinstated, rewarming of the patient was started, and the proximal aorta prepared for suturing. The aortic valve was resuspended to the aortic wall using pledgeted sutures. The glue was applied in the same manner as at the distal anastomosis, with protection of the surrounding tissues (Fig. 2). Importantly, a fine flexible plastic cannula was inserted into the ostia before the glue was applied to protect against accidental spillage of the adhesive. In some cases, precise resuspension of the commissures required scalloping of the residual proximal aortic wall and complementary scalloping of

the Dacron graft. The use of BioGlue and avoidance of stiff Teflon felt strips made this reconstruction easier. A simple end-to-end anastomosis between the proximal aorta and the Dacron graft was performed.

### BioGlue composition

BioGlue is composed of purified bovine serum albumin (BSA; 45% w/v) and glutaraldehyde (10%, w/v) in a 4:1 ratio. Glutaraldehyde exposure causes lysine molecules of the BSA, extracellular matrix proteins and cell surfaces to bind to each other, creating a strong scaffold (Fig. 3). The reaction is instantaneous, and maximum bonding strength is reached in 2-3 min. In-vivo bovine studies have demonstrated that aortic bonding with BioGlue produced a tensile strength of  $847 \pm 127$  g/cm and an ex-vivo shear strength (lamina to media) of  $256 \pm 46$  g/cm (7).

### Results

Owing to complete destruction of the aortic root, during surgery, two patients required complete resection of the sinuses of Valsalva with aortic root remodeling using a tailored Dacron graft.

There were two operative deaths, both from complications of heart failure. The mean ( $\pm$  SD) postoperative 24-h blood loss was  $720 \pm 640$  ml; only one patient required reoperation for bleeding.

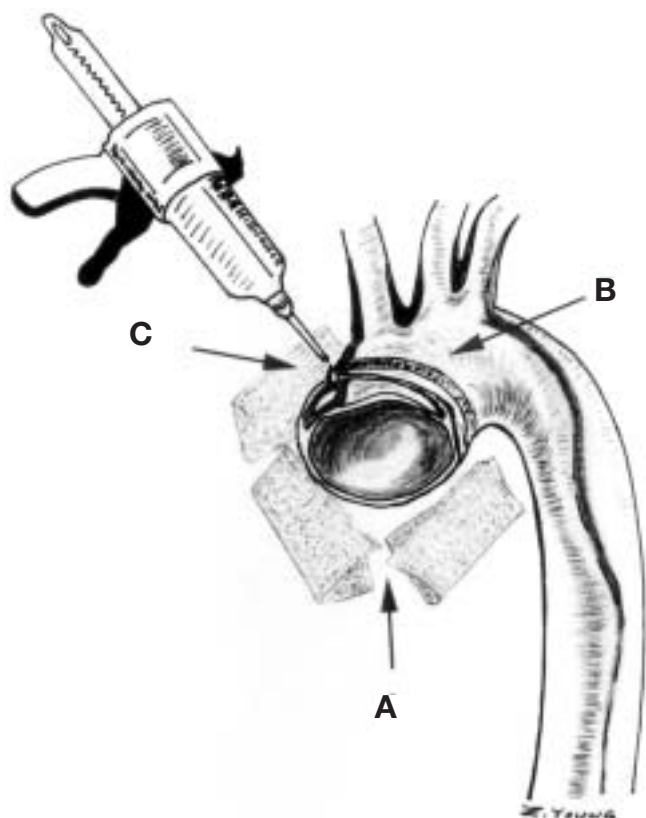


Figure 1: Distal repair using BioGlue. Wet sponges (A) protect surrounding tissues. BioGlue is applied between the layers of the aorta (B) and the adventitial surface of the aorta (C).

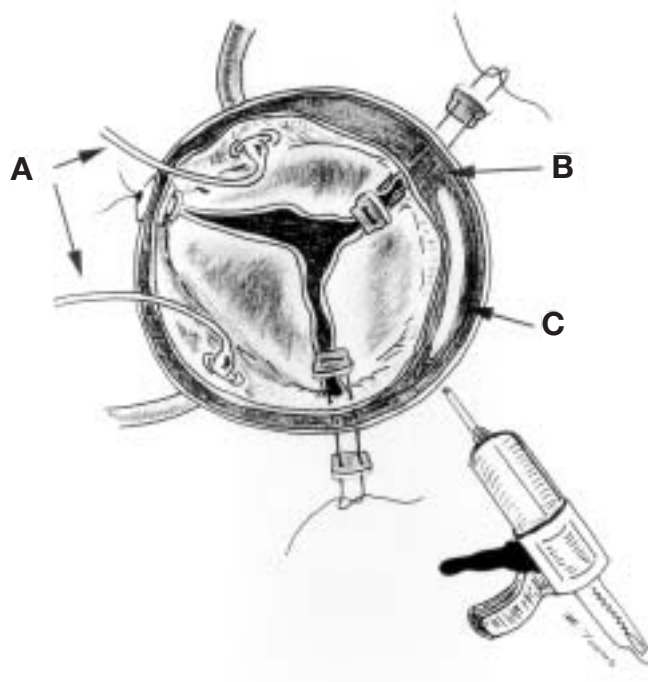


Figure 2: Proximal repair using the glue. (A) A soft cannula protects coronary ostia. (B) Commissures are resuspended. (C) BioGlue is applied between dissected layers.

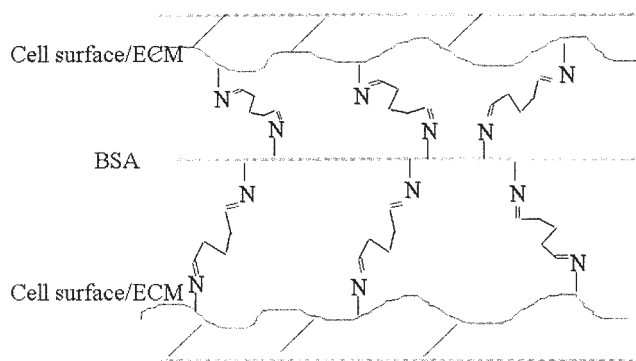


Figure 3: Bonding mechanism. Bovine serum albumin (BSA), extracellular matrix (ECM), and cell membrane proteins contain lysine molecules with an amine group side chain (N). Aldehyde links two amine groups.

There were no new postoperative neurological deficits. Postoperative transesophageal echocardiography showed mild or no aortic insufficiency in 18 patients and moderate insufficiency in two. During the mean follow up of 16 months (range: 5 to 29 months) none of the patients required reoperation for proximal redissection or delayed rupture. In all patients follow up echocardiography revealed a stable aortic repair, with no significant difference from the early postoperative findings. A follow up computed tomography scan was performed in 18 patients (at a mean of 11 months). In nine out of 15 patients in whom the dissection extended beyond the Dacron graft during surgery, the false lumen was found to be thrombosed.

## Discussion

There are several reasons for the development of aortic valve insufficiency in acute type A aortic dissection, including dilatation of the aortic root (especially the sinotubular junction), detachment of one or more aortic commissures, or penetration of the intimal flap into the aortic valve during diastole. When the aortic root itself is not involved, replacement of the ascending aorta from the level of the sinotubular junction is sufficient. When the root is involved, the best surgical technique for aortic root reconstruction remains controversial. Replacing the root with a composite graft has the disadvantage of a prosthetic valve implantation and exposure of the patient with a diseased aorta to long-term warfarin treatment and other prosthetic valve complications. Valve-sparing aortic root replacement using either David's reimplantation (8) or Yacoub's remodeling technique (9), seems to be the most logical approach, as the entire diseased aortic root is resected and the patient retains his or her native aortic valve; moreover, there is no need for long-term anticoagulation. However, these procedures are tech-

nically more demanding, especially in critically ill patients, and long-term follow up is needed to assess any recurrence of aortic regurgitation. The third option is to repair the aortic root by resuspension of the valve commissures back to the aortic wall and obliteration of the proximal dissected layers using Teflon felts, biological glue, or both (Fig. 3).

Gelatin-resorcin-formalin glue ('French glue') was first applied for aortic root reconstruction in acute aortic dissection by Guilmet and colleagues (1) in 1977, and its use has since become popular in this setting. Studies have suggested that the use of GRF glue is associated with a reduced operative mortality and better early outcome (10), in addition to long-term aortic stability with no adverse effects (11-13). However, others have reported a 7 to 39% rate of reoperation in the late postoperative period (3,5,6). Fukunaga and colleagues (3) found that seven of their 148 patients required reoperation due to redissection at the area of GRF glue repair. On the basis of their macroscopic and microscopic findings, these authors speculated that the complications were related to the toxic effect of the glue's high formalin concentration (37%). Similar findings were noted by Bingley, Kazui and their colleagues (5,6). Surgical failure may also be partly due to the limitations of the glue's non-precise delivery system.

BioGlue, a newly developed bioadhesive, is composed of BSA and a relatively low concentration of glutaraldehyde (10%), and has an easy-to-use and precise delivery system. The present authors have been using BioGlue in the repair of acute aortic dissection for several years, and have found that it makes the operation both safer and easier. The operative mortality seems to be acceptable, and postoperative blood loss is low: only one of the present patients required reexploration for bleeding. By using BioGlue, it was possible to repair most of the valves (90%), and mid-term follow up showed no recurrence of either aortic insufficiency or proximal redissection.

Reconstruction of the aortic root in aortic dissection with biological glues has been associated with some risk of late redissection. It is believed that BioGlue, because of its stronger adhesive effect and lower toxicity than the older surgical glues, will also prove to have better long-term results. However, longer-term follow up of patients treated with BioGlue is necessary to verify this hypothesis.

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