

**Case
Report**

Efficacy of Glutaraldehyde-Treated Leaflets for Mitral Valve Repair to Treat Active Infective Endocarditis: A Case Report

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We report the use of glutaraldehyde (GA) in a case of valve repair for mitral valve prolapse associated with active infective endocarditis. GA scrubbed at the site of infection decontaminates and reinforces infected fragile tissue, avoids excessive debridement, and strengthens the edges of valve leaflets to facilitate suturing.

Keywords: mitral valve, active infective endocarditis, glutaraldehyde, valve repair

Introduction

Mitral valve repair is of greater value than valve replacement in young patients, particularly young women, presenting with active infective endocarditis.¹⁾ We introduce a patient whose infected mitral valve leaflet was treated with glutaraldehyde (GA) solution during surgery to overcome the technical limitations of repair, such as destruction of the valve structure, presence of fragile infected tissue, and appearance of large tissue defects secondary to thorough debridement performed intraoperatively to prevent residual infections.^{2,3)}

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Case Report

The patient presented to our hospital in 2017 with complaints of left maxillary and left wrist pain following intermittent fever and arthralgia occurring at multiple sites over the preceding 6 months. The left wrist showed local swelling and erythema. Body temperature was 39.4°C. A pan-systolic heart murmur was heard at the apex. Laboratory tests revealed elevated white blood cell levels at 14300/ μ L, and a C-reactive protein level of 13.8 mg/dL. Transthoracic echocardiography revealed severe mitral regurgitation, anterior leaflet prolapse, and a mobile vegetation >10 mm at the A3 scallop of the mitral valve, as well as a dilated left atrium. Magnetic resonance imaging showed a small area of brain infarction in the left cerebellar hemisphere. Blood cultures were positive for *Streptococcus parasanguinis*. Urgent mitral valve repair surgery was planned due to the risks of recurrent embolization and possible progression to heart failure. The patient underwent surgery after written informed consent was obtained. Intraoperative use of GA was approved by the institutional review board of Fujisawa City Hospital.

Under extracorporeal circulation, an incision of the right side of the left atrium was made to approach the mitral valve. The mitral valve showed A3 prolapse due to ruptured chordae with a vegetation measuring 11 mm \times 13 mm, attached to the free edge of the leaflet, A2-A3 erosion at the left ventricle side with the vegetation, and

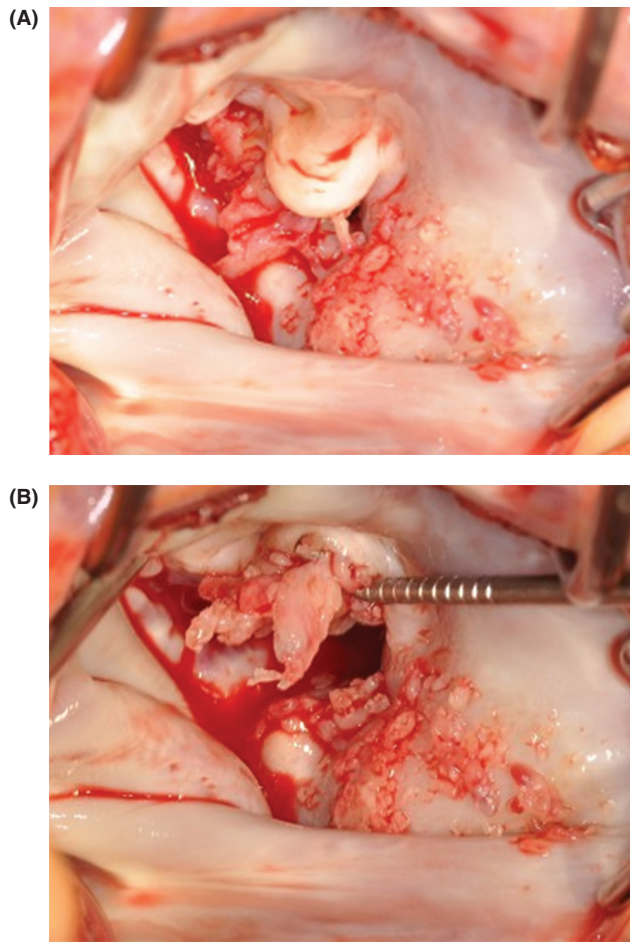


Fig. 1 Mitral valve showing A3 prolapse (A); rupture of the chordae with vegetation attached to the free edge of the leaflet (B); A2-A3 erosion on the side of the left ventricle with vegetation (B); multiple granular vegetations at P2-P3 and the nearby left atrial wall (A, B).

multiple granular vegetations attached to P2-P3 and the adjacent region of the left atrial wall (Figs. 1A and 1B). Large vegetations were removed, and debridement and decontamination were performed by scrubbing the tissue with a GA (0.6% with phosphate buffer, pH: 7.4)-soaked cotton swab and with the use of sharp curettes (Fig. 2A). Strut chordae at A2-A3 were reserved. Following this treatment, A3-P3 coaptation could not be achieved because of shrinkage and hardening of the edematous leaflet, owing to the prior scrubbing with GA (Fig. 2B). Notably, scrubbing with GA strengthened the edges of A3 and P3, which could then withstand stitch suturing. Thus, the posterior commissure was closed with 5-0 polypropylene sutures using an edge-to-edge suturing technique, between the A3 and P3 leaflets (Fig. 2C).

A leak test revealed a minor leak at the P2-P3 transitional zone; thus, the cleft between the P2 and P3 leaflets

was sutured using a single mattress suture with 5-0 polypropylene suture material, and an annuloplasty was performed at P2-P3 using a 2-0 braided polypropylene mattress suture with pledgets. The leak was diminished, and a 25-mm valve sizer could pass through the mitral valve. A semi-rigid mitral ring measuring 30 mm (Carpentier-Edwards Physio II Annuloplasty Ring; Edwards Lifesciences, Irvine, CA, USA) was used, and an ink test revealed a coaptation height of 5 mm at A1 and A2 and of 3 mm at the A2-A3 transitional zone (Fig. 2D). Intraoperative transesophageal echocardiography showed a trivial mitral leak.

The patient's postoperative course was uneventful. Extubation was performed on postoperative day 1, and the patient was discharged from the intensive care unit on postoperative day 2. Postoperative transthoracic ultrasonography revealed trivial mitral regurgitation, and a mitral valve area of 2.04 cm² using the pressure half-time measurement method. The mean pressure gradient across the mitral valve was 5 mmHg. By this time, the patient's left maxillary and left wrist pain had nearly disappeared. Antibiotics were discontinued on postoperative day 25, and the patient was discharged from the hospital on postoperative day 28 without any complications.

Discussion

Although mitral valve repair provides better outcomes than mitral valve replacement does in patients presenting with active infective endocarditis,¹ the surgery can be challenging. This is due to a host of technical limitations of repair, such as the destruction of the valve structure, the presence of fragile infected tissue, and the appearance of large tissue defects secondary to thorough debridement performed intraoperatively to prevent residual infections.^{2,3}

GA, a chemical agent that cross-links proteins, has demonstrated its use in a wide range of applications, including as a disinfectant, a fixative prior to perform an electron microscopy examination, a medication to remove cutaneous warts, a hardener for surgical glue, and a xeno/auto pericardial conditioner for prosthetic valve or aortic valve repair.⁴⁻⁸

Typically, a 0.2% to 2% solution of GA is used as a disinfectant and can inactivate common microbacteria within 2 minutes of use.⁴ In this case, the infected lesion was scrubbed with a cotton swab soaked in a 0.6% solution of GA for approximately 5 minutes, followed by saline rinsing. The total amount of 0.6% GA solution used

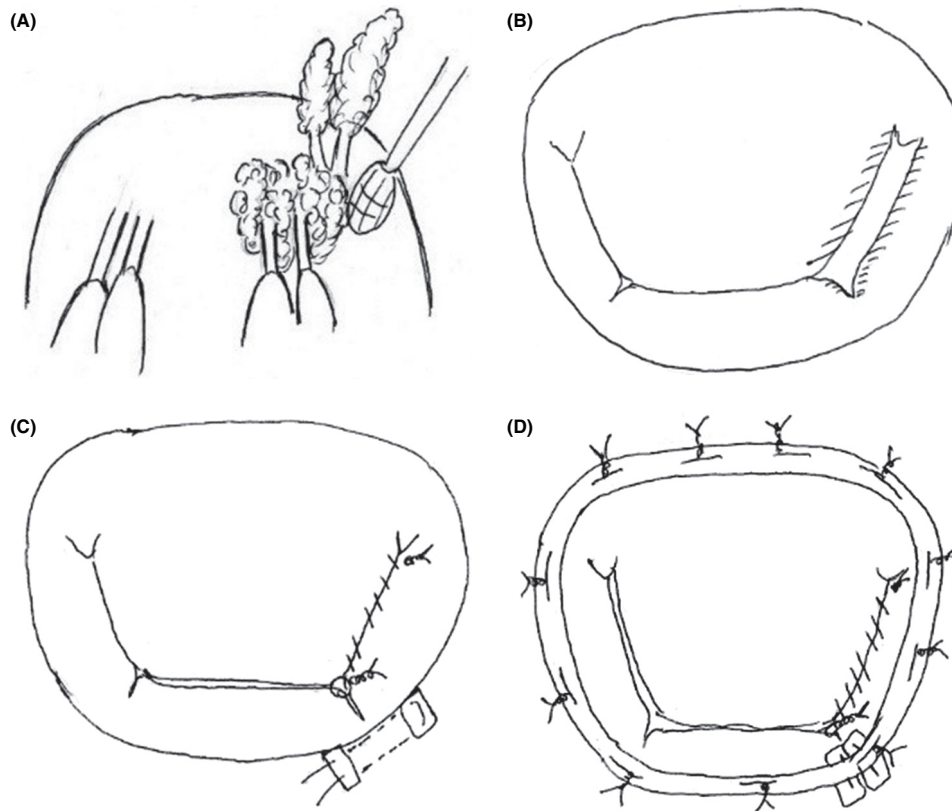


Fig. 2 After decontamination was performed following scrubbing with GA-soaked cotton swab (A), a coaptation of A3 and P3 was not obtained (B). The A3 and P3 leaflets were sutured using an edge-to-edge technique, the P2 and P3 leaflets were attached, and annuloplasty was performed at P2-P3 (C). A semi-rigid mitral ring was applied (D). GA: glutaraldehyde

in the operating field was approximately 1 mL. As such, this disinfection facilitated adequate debridement to minimize the size of the defect that needed to be repaired.

GA strengthens the valve tissue edges that may be damaged, that have become fragile because of the presence of vegetations and/or the occurrence of debridement, or that may have weakened owing to edema associated with inflammation and infection. Strengthening of the leaflets facilitates easier suturing during valve repair.⁹⁾

However, GA use might be associated with drawbacks: 1) shortening of the valve leaflet and 2) hardening of the tissue. In this case, valve leaflets A3 and P3 seemed to be infected, showing edematous appearance, and could not have been used for valve repair if left untreated. GA treatment facilitated convergence of valve leaflet edema and the repair became possible. Ozaki et al.⁸⁾ reported GA (0.6% solution) treatment of autologous pericardium using a buffer for 10 minutes for aortic valve repair. Currently, the technique of scrubbing with a GA solution-soaked cotton swab for approximately

5 minutes is used. Additionally, GA use can be associated with 3) damage to the conduction pathways. Furthermore, 4) residual effects of GA could lead to the formation of pseudoaneurysms as a delayed effect, leading to morbidity. Reportedly, surgical glue containing formaldehyde as a hardener resulted in an aneurysm as an effect of the residual formaldehyde because the ratio of formaldehyde could not be accurately controlled by surgeons.^{10,11)} However, surgical glue containing GA as a hardener (Bioglue; Cryolife, Inc., Kennesaw, GA, USA) seems to provide acceptable results.⁶⁾ Biologic valves treated with a 0.2%–0.625% GA solution have reportedly shown long durability, which indicates the long-term safety of using 0.6% GA solution.⁷⁾

We commenced the use of GA after Hashimoto¹²⁾ reported their experience in cases of active infective endocarditis. We recently successfully treated four consecutive cases of mitral regurgitation with active infective endocarditis with valve repair without associated residual leak. This patient group, not including the case

in this report, comprised a patient with P2 prolapse treated with triangular resection, a patient with A2 prolapse with wedge resection, and a patient with an A3-P3 prolapse treated using commissure closure. All patients presented no abnormal laboratory data in their clinical courses. It is thought that most patients with mitral regurgitation with active infective endocarditis can be treated with GA, but patients with wide and severe lesions may require pericardial patches or valve replacements.

Only a small number of patients were examined, including those with limited etiology and organisms; therefore, these results may not be adequately conclusive. Further studies involving a greater number of patients who can be followed up over a longer period as well as case-control studies should be conducted to conclusively determine the efficacy of GA use in mitral valve repair in patients with active infective endocarditis. In the current case, approximately 1 mL of 0.6% GA solution was used, followed by thorough saline washing to ensure that the toxic environment may not differ very much after a tissue valve replacement procedure involving washing with 0.2%–0.625% GA prior to implantation. According to results of an animal toxicity study involving rats, oral intake of approximately 1000 mL of 0.6% GA for 50 kg body weight is a lethal dose.¹³⁾ We believe that the cautious use of a minimal amount of 0.6% GA is not harmful to the body. However, health-care workers, scrub nurses, and surgeons need to protect their eyes and avoid inhalation, by storing GA in its container with the cap secured, when it is not in active use.

Conclusion

We report intraoperative GA use in a case of valve repair for mitral valve prolapse associated with active infective endocarditis. GA scrubbed at the site of infection resulted in decontamination and reinforcement of infected fragile tissue, prevention of excessive debridement, and strengthening of the edges of valve leaflets to facilitate suturing.

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Disclosure Statement

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