

Mechanism of Hemolysis after Mitral Valve Repair and New Surgical Management: Prosthetic Annuloplasty Ring Covered with Autologous Pericardium

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Background and aims of the study: Hemolysis after mitral valve repair is a rare occurrence, but is one of the complications leading to reoperation. Since 1999, mitral valve repair at the authors' institution has been performed using a prosthetic annuloplasty ring covered with autologous pericardium to prevent this complication. The study aims were to investigate the mechanism of hemolysis after mitral valve repair and to describe the surgical management of this complication.

Methods: This retrospective study comprised 204 consecutive patients who underwent mitral valve repair using an annuloplasty ring between October 1991 and April 2000 at the authors' institution. Patients were allocated to the non-covered ring group (n = 174) and the covered ring group (n = 30), and compared for the degree of mitral regurgitation (MR), serum levels of lactate dehydrogenase (LDH), and occurrence of hemolysis. The degree and flow pattern of MR, and patient prognoses were described for hemolytic patients.

Hemolysis is a well-recognized complication of heart valve prostheses, but it occurs only rarely after mitral valve repair (1-5). Although the importance of hemolysis has been underemphasized, this is one of the reasons for reoperation after mitral valve repair (6,7). Based on their personal experience, the present authors hypothesized that a prosthetic annuloplasty ring covered with autologous pericardium would prevent this complication, and consequently have utilized this technique at their institution since 1999. The study aims were to investigate the mechanism of hemolysis after mitral valve repair and to describe the surgical management of this complication.

Results: Postoperative MR and serum LDH were not significantly high in either group. A total of seven patients presented with hemolysis; postoperative echocardiography revealed MR to be mild in two patients, moderate in three and severe in two. Collision of the regurgitant jet into the artificial ring was evident in all seven patients. A beta-blocker proved effective in treating hemolysis in three patients, mitral re-repair was performed in three, and a prosthetic mitral valve was inserted in one patient. None of the patients in the covered ring group presented with hemolysis.

Conclusion: The major cause of hemolysis after mitral repair was collision of the regurgitant jet into the artificial ring. The simple technique used herein prevented contact of the regurgitant jet with the rough surface of the ring, and may in turn have prevented hemolysis. In selected patients, hemolysis was improved by beta-blocker administration.

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Clinical material and methods

Patients

The study group comprised 218 consecutive patients who underwent mitral valve repair using a prosthetic annuloplasty ring, between October 1991 and April 2000, at the present authors' institution. Fourteen patients who underwent concomitant mechanical aortic valve replacement and tricuspid valve repair using a prosthetic annuloplasty ring were excluded. The 204 patients included in the study (mean age 53.9 ± 14.6 years) were allocated to either the non-covered ring group (174 patients, in whom the conventional prosthetic annuloplasty ring was used, until April 1999) or the covered ring group (30 patients in whom a prosthetic annuloplasty ring covered with autologous pericardium was used, from May 1999), and compared for the degree of mitral valve regurgitation, serum levels of lactate dehydrogenase (LDH), and occurrence of hemolysis. Hemolysis was defined by the presence of

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the following three conditions: progressive anemia (hematocrit <33%), re-elevated serum LDH (>750 IU/ml) and the presence of urinary hemosiderin.

Among the hemolytic patients, the methods used for the initial repair, the type of annuloplasty ring, the degree and flow pattern of mitral regurgitation, as well as the patients' prognoses were obtained retrospectively from the clinical chart, hospital progress notes and the operation records (Table I).

Surgical procedure and patient management

For reconstruction of the mitral annulus, between July 1991 and September 1996, total ring annuloplasty was performed in 96 patients using a Carpentier-Edwards ring (Baxter Healthcare Corporation, Santa Ana, CA, USA). From October 1996 onwards, in order to retain the natural shape of the anterior leaflet, physiological remodeling annuloplasty was performed in 78 patients using part of a flexible Duran ring (Medtronic Inc. Minneapolis, MN, USA) and an adjustable obturator (8). From May 1999 onwards, physiological remodeling annuloplasty was performed to prevent hemolysis using part of a flexible Duran ring covered with fresh autologous pericardium and Prolene sutures. At the present authors' institute, artificial chordae replacement using expanded polytetrafluoroethylene sutures and small tourniquets was performed for anterior leaflet prolapse (9), and sliding plasty with leaflet resection was performed for posterior leaflet prolapse.

From April 1993 onwards, intraoperative trans-

esophageal echocardiography was performed after completion of cardiopulmonary bypass (CPB) and, if a mitral valve regurgitation >2.0 cm² in area or >1.0 cm in length was revealed, reperfusion of the CPB and re-repair were performed, irrespective of the completion test during cardiac arrest (10). This intraoperative management remarkably improved the results (10). Transthoracic echocardiography was performed to evaluate mitral valve regurgitation at the time of the patients' discharge from hospital and again at six months after surgery. As initial therapy, patients presenting with hemolysis were treated with a beta-blocker to reduce the heart rate and thereby the velocity of the regurgitant jet.

Statistical analysis

Continuous variables were expressed as mean ± SD. Continuous variables were compared using an unpaired *t*-test, while non-continuous variables with rank were compared using the Kruskal-Wallis test employing a statistical analysis software package (StatView 5.0; SAS Institute, Inc., Cary, NC, USA).

Results

Mortality and morbidity

The overall survival rate was 94%. Early death occurred in three patients, and late death in nine; all 12 deaths occurred in patients with a non-covered ring. The causes of early death were heart failure due to chronic ischemic cardiomyopathy, pneumonia and

Table I: Details of the hemolytic patients.

Patient no.	Age (years)	Gender	Ring	Initial repair	Post-MR	Flow pattern	Prognosis (reoperative technique)
1	48	F	Duran	Chordae replacement	Mild	Collision of jet into the ring	Improvement by beta-blocker
2	54	F	Duran	Chordae replacement	Moderate	Collision of jet into the ring	Improvement by beta-blocker
3	14	F	CE	Leaflet resection	Moderate	Collision of jet into the ring	Improvement by beta-blocker
4	49	M	CE	Chordae replacement	Severe	Collision of jet into the ring and pledget	Re-repair at 7 months after operation (chordal replacement)
5	5	M	Duran	Chordae replacement; leaflet resection	Moderate	Collision of jet into the ring	Re-repair at 11 days after operation (chordal replacement, leaflet resection. Annuloplasty using autologous pericardium)
6	57	F	Duran	Leaflet resection	Mild	Collision of jet into the ring	Re-repair at 3 months after operation (dehisced leaflet repair, annuloplasty using ring covered with autologous pericardium)
7	14	F	Duran	Chordae replacement; mobilization	Severe	Collision of jet into the ring	Mitral replacement at 8 months after operation (SJM prosthetic valve 27 mm)

CE: Carpentier-Edwards ring; Duran: Flexible Duran ring; MR: Mitral regurgitation; SJM: St. Jude Medical.

septic shock in one patient each. The causes of late death were sudden death in two patients, pneumonia in two, and heart failure after mitral valve replacement and pulmonary lung cancer in one patient each. The cause of late death in the other three patients was unknown. The overall freedom from reoperation was 96.5%. One patient required early reoperation due to hemolysis. Six patients required later reoperation; of these reoperations, three were due to hemolysis and three to residual mitral regurgitation.

Hemolysis

In total, seven patients (three of whom were aged <15 years) presented with hemolysis. For the initial repair, a Carpentier-Edwards ring had been used in two patients and a flexible Duran ring in five. Two patients presented with hemolysis despite only mild regurgitation, while collision of the regurgitant jet into the ring was detected in all seven cases (Table I).

In three patients, treatment with a beta-blocker proved effective against hemolysis, and serum levels of LDH decreased (#1 - 3,370 IU/ml at 4 weeks after surgery, 2,470 IU/ml at 6 months, and 1,470 IU/ml at 12 months; #2 - 4,630 IU/ml at 4 weeks, 1,211 IU/ml at 6 months, and 648 IU/ml at 12 months; #3, 2,010 IU/ml at 4 weeks and 1,356 IU/ml at 6 months). The beta-blocker treatment was withdrawn after hemolysis had disappeared.

Four patients required continuous transfusions and subsequently underwent reoperation. The cause of residual regurgitation was incomplete coaptation of the mitral leaflets in two patients, and prolapse of the anterior leaflet or a dehiscence of the posterior leaflet in one patient each. The techniques utilized for re-repair are summarized in Table I. In case #7, mitral valve replacement was performed because of severe deformation. All surgical interventions resulted in a disappearance of hemolysis.

Hemolysis did not occur in the covered ring group. The serum LDH level at four weeks after surgery was not significantly high (mean 479 ± 152 IU/ml versus 547 ± 452 IU/ml in the non-covered group).

At six months after surgery, moderate mitral regurgitation was observed in 10 patients (nine non-covered ring, one covered ring), and severe regurgitation in five patients of the non-covered ring group. At the time of hospital discharge, and at six months after surgery, residual mitral regurgitation was not statistically significant as assessed by the Kruskal-Wallis test.

Discussion

The results of the present study led to three major findings: First, that the major cause of hemolysis after mitral valve repair was collision of the regurgitant jet

into the annuloplasty ring; second, that patients receiving an annuloplasty ring covered with autologous pericardium did not present with hemolysis; and third, that in selected patients the administration of a beta-blocker improved hemolysis.

On the basis of the mechanisms of mitral valve repair-related hemolysis, Carpentier identified three conditions inherent to the regurgitant jet, namely high velocity, eccentricity, and contact with a rough surface (6). With regard to the causes of hemolysis, collision of the regurgitant jet into the ring, fragmentation of the regurgitant jet by a dehiscence of the annuloplasty ring, and rapid acceleration of the regurgitant jet through a small para-ring channel have been suggested (11-13). In all of the present patients with hemolysis, collision of the jet into the ring was detected, and this was considered to be the major cause of mitral valve repair-related hemolysis. Consequently, since 1999 the present authors have used annuloplasty rings covered with autologous pericardium for mitral valve repair, and hemolysis has not been identified. The main preventive measure is to avoid residual mitral regurgitation, though this complication is not related solely to the degree of residual regurgitation (6,7). Indeed, in the present series two patients presented with hemolysis despite having only mild residual regurgitation. With regard to the occurrence of hemolysis, the hydrodynamic pattern of the jet appears to be more important than the degree of hemolysis. Therefore, if the regurgitant jet is characterized by high velocity and is eccentric, the simple technique reported herein will prevent the jet from making contact with the rough surface of the prosthesis, thereby reducing the risk of hemolysis.

The incidence of hemolysis after mitral valve repair has been reported as between 0.55% and 5.6% (6,11). In the present series - which included pediatric patients - hemolysis occurred in only seven cases (3.4%), and three of these were aged <15 years. In pediatric patients, if the regurgitant jet contacts a rough surface, the frequency of contact will be high due to the high heart rate, while the velocity of the jet may be high due to a better ventricular function compared to older patients. Thus, pediatric patients may be at a greater risk of presenting with hemolysis.

Among the seven patients with hemolysis, three showed an improvement of hemolysis and a lowering of serum LDH levels after treatment with a beta-blocker. This improvement was considered to be due to a lower heart rate and therefore a lower velocity of the jet as a result of a reduction in after-load. Although initially the beta-blocker was administered to treat hemolysis, all patients who showed improvement of hemolysis had mild or moderate residual mitral regurgitation. Therefore, severe residual regurgitation, pro-

gressive hemolytic anemia and the need for continuous transfusion are clear indications for an early reoperation.

Although the present study was retrospective and non-randomized in nature, the authors believe that an evaluation of the mechanisms of hemolysis and its surgical management are important.

In conclusion, the major cause of hemolysis after mitral valve repair was collision of the regurgitant jet into the annuloplasty ring. The simple technique described herein, using an annuloplasty ring covered with autologous pericardium, may prevent hemolysis in patients with mild to moderate regurgitation and thereby reduce the risk of subsequent reoperation.

References

1. Yeo TC, Freeman WK, Schaff HV, Orszulak TA. Mechanisms of hemolysis after mitral valve repair: Assessment by serial echocardiography. *J Am Coll Cardiol* 1998;32:717-723
2. Mestres CA, Soo CS, Sim EK, Adebo OA, Yan P, Lee CN. Intravascular hemolysis after mitral valve repair: A word of caution. *Eur J Cardiothorac Surg* 1992;6:103-105
3. Kihara S, Kasegawa H, Kobayashi N, et al. Severe hemolysis due to artificial chordae displacement. *J Heart Valve Dis* 1997;6:69-70
4. Wilson JH, Rath R, Glaser R, Panke T. Severe hemolysis after incomplete mitral valve repair. *Ann Thorac Surg* 1990;50:136-137
5. Brandon Bravo Bruinsma GJ, Bredee JJ, de Mol BA. Mitral valve repair-related hemolysis: A report of two cases. *Int J Cardiol* 1997;60:317-320
6. Cerfolio RJ, Orszulak TA, Daly RC, Schaff HV. Reoperation for hemolytic, anaemia complicating mitral valve repair. *Eur J Cardiothorac Surg* 1997;11:479-484
7. Lam BK, Cosgrove DM, Bhudia SK, Gillinov AM. Hemolysis after mitral valve repair: Mechanisms and treatment. *Ann Thorac Surg* 2004;77:191-195
8. Kasegawa H, Kamata S, Ida T, Kawase M, Fujimoto T, Umezu M. Physiologic remodeling annuloplasty to retain the shape of the anterior leaflet: A new concept in mitral valve repair. *J Heart Valve Dis* 1997;6:604-607
9. Kasegawa H, Kamata S, Hirata S, et al. Simple method for determining proper length of artificial chordae in mitral valve repair. *Ann Thorac Surg* 1994;57:237-239
10. Kasegawa H, Furusawa T, Okada Y, et al. Mitral valve plasty for better long-term results. *Kyobu-Geka* 1995;48:638-641
11. Yamaura Y, Yoshikawa J, Yoshida K, et al. Mechanism of intravascular hemolysis after mitral valve repair: Assessment by transesophageal echocardiography. *J Cardiol* 1994;24(Suppl.38):91-94
12. Garcia MJ, Vandervoort P, Stewart WJ, et al. Mechanisms of hemolysis with mitral prosthetic regurgitation: Study using transesophageal echocardiography and fluid dynamic simulation. *J Am Coll Cardiol* 1996;27:399-406
13. Ward RP, Sugeng L, Weinert L, et al. Images in cardiovascular medicine. Hemolysis after mitral valve repair. *Circulation* 2000;101:695-696