

Chemical demineralization of the aortic valve: a potential application and preliminary clinical experience

Experiência clínica inicial na desmineralização química da valva aórtica: potencial aplicação como procedimento minimamente invasivo

Ricardo Carvalho LIMA¹, Gerhard WIMMER-GREINECKER², Mário Gesteira COSTA³, Mozart Augusto Soares de ESCOBAR⁴, Roberto DINIZ⁵, Antônio CÉSIO⁵, Frederico VASCONCELOS⁶, Alexandre MENEZES⁶, Robert POSER⁷, Jerry RIEBMAN⁸

RBCCV 44205-816

Abstract

Objective: To discuss the use of new technology in the chemical demineralization of the aortic valve in coronary artery bypass surgery, together with its hemodynamic changes and to report events related to the technique.

Method: Five patients with mild to moderate aortic stenosis submitted to myocardial revascularization underwent chemical treatment of the aortic valve. The patients' ages ranged from 65 to 81 years, with a mean of 73 years. All were men. One patient had the involvement of a single artery and four multiple arteries (four vessels). The gradient ranged from 13 to 49 mmHg, with a mean of 25 mmHg. The size of the aortic orifice ranged from 0.8 to 1.3 cm², with a mean of 1.1 cm². The following comorbidities were observed: arterial hypertension, hypercholesterolemia, diabetes mellitus and smoking.

Results: The aorta clamping time ranged from 94 to 126 minutes, with a mean of 107 minutes and the bypass time was from 134 to 171 minutes, with a mean of 152 minutes. The time of surgery was from 13 to 33 minutes with a mean of 28 minutes. No deaths were recorded. The only postoperative complication noted was a total AV block in three patients. No events were observed that might impair the integrity of the aortic valve or cause aortic insufficiency following treatment. Likewise, no neurologic, systemic, metabolic or hematologic events were seen. The postoperative transvalvular gradient identified by echocardiography showed an improvement in the systolic gradient and in the mean gradient.

Conclusions: The treatment proved to be effective and safe, causing no lesions of the valve or any systemic event.

1 - Professor of UPE. Head of Cardiovascular Surgery Department HUOC

2 - Professor of Cardiovascular Surgery. Head of Cardiovascular Surgery Department Klinikum der Johann Wolfgang – Frankfurt, German

3 - Adjunct professor of UPE. Assistant head of Cardiovascular Surgery Department of HUOC

4 - Adjunct professor of UFPE. Head of Surgery Department of Unitórax

5 - Cardiovascular surgeon. Surgeon of Unitórax

6 - Cardiovascular surgeon. Preceptor de Cardiothoracic surgery of UPE.

7 - Surgeon. Researcher of Corazón Inc.

8 - Cardiovascular surgeon. Consultant of Corazón Inc.

Work carried out in the Medical Sciences School of the University in Pernambuco; Klinikum der Johann Wolfgang – Frankfurt, Germany and Corazón Technologies - Melon Park / California / USA.

Correspondence address:

Ricardo C. Lima. Rua dos Navegantes, 1515 / 101. Recife, PE, Brazil. CEP 51021-010.

E-mail: rclima@elogica.com.br

Article received in January, 2006

Article accepted in May, 2006

The changes in the conduction system appear to be related to the equipment and its system of releasing the lavage solution. The use of this technology may, in the future, be an important adjuvant in aorta valve replacement using percutaneous techniques.

Descriptors: Aortic valve, surgery. Aortic valve stenosis. Decalcification technique. Calcinosis. Demineralization.

Resumo

Objetivo: Utilização de nova tecnologia na desmineralização química da valva aórtica, em cirurgia cardíaca com circulação extracorpórea, avaliação de suas alterações hemodinâmicas e reportar eventos relacionados à técnica.

Método: Cinco pacientes, submetidos à revascularização miocárdica e portadores de estenose aórtica leve a moderada, receberam tratamento químico na valva aórtica. A idade dos pacientes variou de 65 a 81 anos, com média de 73 anos; sendo todos do sexo masculino. Um paciente tinha doença uniarterial e quatro, multiarterial (quatro vasos). O gradiente médio variou de 13 a 49 mmHg, com média de 25 mmHg. A área média do orifício aórtico variou de 0,8 a 1,3 cm², com média de 1,1cm². Os antecedentes observados foram: hipertensão arterial, hipercolesterolemia, diabetes melito e fumo.

Resultados: O período de pinçamento aórtico variou de 94 a 126 minutos, com média de 107 minutos. O tempo de "bypass" variou de 134 a 171 minutos, com média de 152 minutos. O tempo de tratamento variou de 13 a 33 minutos, com média de 28 minutos. Não foi observado nenhum óbito. Complicações pós-operatórias observadas foram: bloqueio atrioventricular total em três pacientes. Não foram observados eventos que comprometessem a integridade da valva aórtica ou provocassem insuficiência aórtica pós-tratamento. Também não se observaram eventos neurológicos, sistêmicos, metabólicos ou hematológicos. O gradiente transvalvar pós-operatório, determinado pelo ecocardiograma, demonstrou melhora no gradiente sistólico e médio.

Conclusões: O tratamento demonstrou ser efetivo e seguro, não causando lesão à valva ou algum evento sistêmico. As alterações do sistema de condução parecem relacionadas com o equipamento e seu sistema de liberação da substância de lavagem. A utilização desta tecnologia poderá ser, no futuro, um importante coadjuvante na substituição da valva aórtica por via transcutânea.

Descritores: Valva aórtica, cirurgia. Estenose da valva aórtica. Técnica de descalcificação. Calcinose. Demineralização.

INTRODUCTION

In the United States of America approximately 1.2 millions of over 54-years-olds have some degree of aortic stenosis (AoS). Around 23% of these individuals are diagnosed as having differing degrees of aortic valve degeneration and dysfunction. Symptomatic AoS is associated with angina, dizziness and dyspnea. The current forms of treatment consist of valve replacement using a prosthesis, valve repair, balloon valvuloplasty and more recently transcatheter replacement [1-3].

Attempts of AoS correction preserving the valve utilizing ultrasound and other surgical ablation techniques, present problems with the long-term clinical results including mechanical trauma of the surrounding tissues resulting in fibrosis, restenosis and perforation of the cusps [4,5].

The present treatment aims at chemical demineralization of the aortic valve, enabling *in situ* correction of the native valve as an alternative to the current clinical practice of its replacement using a prosthesis.

METHOD

Five patients suffering from mild to moderate AoS associated with coronary insufficiency were submitted to surgeries. The ages ranged from 65 to 81 years old with a

mean of 73 years old. All the patients were men. Four patients presented with coronary artery disease of four vessels and one patient with involvement of a single vessel. The gradient through the aortic valve varied from 13 to 49 mmHg with a mean of 25 mmHg. The mean area of the aortic valve orifice was 1.1 cm², ranging from 0.8 to 1.3 cm². The following comorbidities were present: hypertension in four patients, hypercholesterolemia in four, diabetes mellitus in two and two were smokers. The time of cardiopulmonary bypass was 134 to 171 minutes with a mean of 152 minutes. The time of aortic clamping varied from 94 to 126 minutes with a mean of 107 minutes.

Surgical technique

Longitudinal median sternotomy was performed with dissection of the left internal thoracic artery and the saphenous vein. Cardiopulmonary bypass was established with an arterial cannula at the root of the aorta and simple cannulation of the right atrium. Hypothermia at 28 °C, clamping of the aorta and infusion of isothermal sanguineous cardioplegia solution were utilized. Aortotomy was performed in the usual way for aortic valve replacement and access to the valve. Coronary ostium the lavage system *Corazon Technologies, Inc - CA, USA* with specific protectors was introduced (Figure 1).



Fig. 1 – Catheter utilized during decalcification of the aortic valve with the heart arrested

After setting up the system, intermittent lavage of the aortic valve was initiated with saline solution at pH = 1. At the end of the 30 minutes session established by the protocol, the system was removed and coronary artery bypass grafting was initiated. The aorta was sutured in the normal manner, removing the air from the left chambers and clamping the ascending aorta and reanimating the heart. The project was approved by the Ethics Research Committee of the Oswaldo Cruz Teaching Hospital.

RESULTS

No deaths occurred whatsoever. The postoperative complications observed were total atrioventricular block in the first three patients. No events were seen that might compromise the integrity of the aortic valve or cause post-treatment aortic insufficiency. Moreover no neurological, systemic, metabolic or hematologic events were observed.

The postoperative transvalvar gradient, determined by echocardiography demonstrated an improvement in the mean and systolic gradients (Table 1).

Table 1. Percentage reduction of the pressure gradients as seen by echocardiography in the pre- and post-operative periods of chemical decalcification of the aortic valve

	Gradient		30 days PO (n=3) % mean PR	180 days PO (n=3) % mean PR
	Pre-op (n=4) Minimum	Maximum		
Systolic	21	81	16%	13%
Mean	16	49	14%	10%

PR: Percentage reduction of the pressure gradients; Pre-op: pre-operative; PO: post-operative

DISCUSSION

Current recommendations do not include the treatment of valves during open surgery for AoS as patients are in the initial stages of the disease. However, aortic valve replacement with a prosthesis has been indicated in patients with moderate AoS, mainly in cases of concomitant coronary artery bypass grafting [6-8]. Patients submitted to coronary artery bypass grafting in isolation and that, after a few years, were re-operated for aortic valve replacement due to AoS, frequently present with some evidence of calcification and valve dysfunction [9]. There is up to a sevenfold reduction in the mortality rate comparing patients with calcified AoS in the initial stages of the disease treated pro-actively during coronary artery bypass grafting and patients initially submitted to coronary artery bypass grafting and subsequently aortic valve replacement [7].

There are reports that there are changes in the mean gradient of AoS of 6.0 to 10.0 mmHg/year and that this progression quickens as the disease evolves [6,10]. In a study of 25 patients with calcified AoS, the evolution of the disease was faster when cardiac catheterism was used. Those with calcification presented with a mean increase in the gradient of 9.7 mmHg/year versus a rate of 4.4 mmHg/year in individuals without calcification giving a p-value < 0.02 [6]. The low death rates are associated with an early intervention impeding the evolution of the disease to a severe stage. Patients with calcified AoS

have less favorable prognoses and only about 20% will survive more than four years after diagnosis [10]. It seems to be logical that survival can be increased for some patients if an efficacious treatment were available for early interventions.

This treatment of mild and moderate AoS in patients submitted to concomitant coronary artery bypass grafting enables an early intervention. The system was designed taking into account the fibrotic and calcified tissue that affects normal functioning of the valve. Over the short term, the expected result was confirmed with a reduction in the valve gradient and an increase in the cross-sectional area of the valve seen by echocardiography. We believe that the consolidation of this early technique enables, over the long term, substantial delay in the progression of the disease, removing minerals from the valve which are responsible for the need of aortic valve replacement.

In the current pilot study, there was no evidence of alterations in the integrity of the ventriculo-arterial junction, the appearance of or progression of a preexisting aortic insufficiency, appearance of cerebral injury or adverse effects to the hematologic, metabolic or hemodynamic systems. The first three patients presented with total atrioventricular blocks which were attributed to the type of balloon utilized on the internal face of the left ventricle. After starting to use a different design of balloon, the total atrioventricular blocks were not evidenced. This seems to demonstrate that not only the design of the balloon is important, but also the pressure and the length of time using the balloon in the left ventricle outflow tract during demineralization treatment of the aortic valve.

The next stages of this study will include a continuation of the evaluation of the demineralization technique, in order to try to better understand the acute and chronic impact on hemodynamic parameters of the aortic valve, to refine the inclusion and exclusion criteria of patients who might potentially benefit from this treatment and to expand the clinical research aiming at evaluating the endovascular utilization of this technique on the beating heart.

CONCLUSIONS

The utilization of the technique in this pilot study demonstrated it to be effective at improving the parameters analyzed by echocardiogram, in respect to the transvalvar gradient and valve area. The treatment did not cause any valvular injury or systemic alterations. The alterations observed in the conduction system were not related to the treatment itself, but to the lavage release system. The possibility of using the current treatment as an endovascular technique may allow a less invasive *in situ* treatment of the aortic valve.

ACKNOWLEDGEMENTS

The authors wish to convey their special thanks to Shelby Young and Denise Gottfried for preparing the clinical protocol and giving support during the trial.

REFERENCES

1. Bahler RC, Desser DR, Finkelhor RS, Brener SJ, Youssefi M. Factors leading to progression of valvular aortic stenosis. *Am J Cardiol.* 1999;84(9):1044-8.
2. King RM, Pluth JR, Giuliani ER, Piehler JM. Mechanical decalcification of the aortic valve. *Ann Thorac Surg.* 1986;42(3):269-72.
3. Otto CM, Kuusisto J, Reichenbach DD, Gown AM, O'Brien KD. Characterization of the early lesion of 'degenerative' valvular aortic stenosis: histological and immunohistochemical studies. *Circulation.* 1994;90(2):844-53.
4. Cosgrove DM, Ratliff NB, Schaff HV, Edwards WD. Aortic valve decalcification: history repeated with a new result. *Ann Thorac Surg.* 1990;49(5):689-90.
5. Humphries B, Triplett-McBride T, Newton RU, Marshall S, Bronks R, McBride J et al. The relation between dynamic, isokinetic and isometric strength and bone mineral density in a population of 45 to 65 year old women. *J Sci Med Sport.* 1999;2(4):364-74.
6. Davis SW, Gershlick AH, Balcon R. Progression of valvar aortic stenosis: a long-term retrospective study. *Eur Heart J.* 1991;12(1):10-4.
7. Hilton TC. Aortic valve replacement for patients with mild to moderate aortic stenosis undergoing coronary artery bypass surgery. *Clin Cardiol.* 2000;23(3):141-7.
8. Carabello BA. Progress in mitral and aortic regurgitation. *Prog Cardiovasc Dis.* 2001;43(6):457-75.
9. Eitz T, Kleikamp G, Minami K, Gleichmann U, Korfer R. Aortic valve surgery following previous coronary artery bypass grafting: impact of calcification and leaflet movement. *Int J Cardiol.* 1998;64(2):125-30.
10. Horstkotte D, Piper C, Wiemer M, Schultheiss HP. Diagnostic approach and optimal treatment of aortic valve stenosis. *Herz.* 1998;23(7):434-40.