# Myocardial Protection Using HTK Solution in Minimally Invasive Mitral Valve Surgery

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# ABSTRACT

**Background:** Minimally invasive cardiac surgery (MICS) is a safe and satisfactory approach used mainly in mitral valve surgery with excellent results in many centers. Cardioplegia administration can be still a problem, especially when an endoaortic clamp is used. We retrospectively analyzed our early results with histidine-triptophane-ketoglutarate (HTK) solution used for myocardial protection in MICS.

**Methods:** Between February 2003 and February 2004, 8 patients underwent mitral valve surgery using an endocardiopulmonary bypass (CPB) system and HTK solution as myocardial protection. The mean patient age was  $67.7 \pm 9.2$ years, and the preoperative ejection fraction was normal in all patients. Three patients had valve repair and 5 had valve replacement. Mean CPB time was  $129.2 \pm 19.4$  minutes, and aortic cross-clamp duration was  $88.5 \pm 15.4$  minutes.

**Results:** In every case HTK solution was used for only a single dose for cardioplegia at the beginning of the procedure, without any recalls. The heart restarted spontaneously at reperfusion in 6 of 8 cases (75%), and there were no significant modifications in electrocardiogram results or myocardial cytonecrosis enzymes (creatine kinase and its MB fraction) during the postoperative period.

**Conclusions:** HTK solution is a cold crystalloid cardioplegia solution that has demonstrated its utility in MICS because it provides a safe long cardioplegic arrest time and it reduces the risk of inadequate coronary perfusion due to dislodgement of the endoaortic clamp.

# INTRODUCTION

During recent years, minimally invasive cardiac surgery (MICS) has evolved to a point at which it may offer benefits over conventional procedures. New materials and techniques are enabling surgeons to overcome initial difficulties related to surgical exposure, approach, perfusion systems, and instru-

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Address correspondence and reprint requests to: Carlo Savini, Cardiac Surgery Department, Az. Ospedaliera S. Orsola-Malpighi, Via Massarenti 9, 40100 Bologna, Italy; 39-051-6363361; fax: 39-051-345990 (e-mail: c\_savini@yaboo.com). ments. An accurate learning curve is necessary in any case, because technical differences with respect to conventional surgery still remain. For this reason, any means to simplify the approach should be considered in order to improve reproducibility and feasibility. The endoaortic clamp [Peters 1993] (EndoClamp; Heart Port, Redwood City, CA, USA) is commonly used in the port-access surgical approach. This device allows performance of both coronary artery bypass and intracardiac procedures using cardiopulmonary bypass (CPB) and cardioplegic arrest. It is mandatory to assure proper placement of the catheter, because misplacement can result in aortic valve incompetence, arch vessel occlusion, and inability to achieve cardioplegic arrest.

In our center, in the last few years we began using histidinetriptophane-ketoglutarate (HTK) solution (Custodiol; Koehler Chemie, Alsbach-Haenlein, Germany) in conventional cardiac surgery that requires more than 90 minutes of aortic cross-clamp time (eg, complex thoracic aorta procedures, multivalvular disease, redo procedures), thus enjoying the practical advantage of a longer "safe" time of ischemia (180 minutes) obtained with a single dose of HTK solution. Last year we decided to extend its use to include port-access procedures, which we perform routinely in mitral valve surgery. The aim of this report is to present our preliminary experience with this type of solution in MICS and to give some practical suggestions for its administration.

#### MATERIALS AND METHODS

From February 2003 to February 2004, 8 patients underwent mitral valve surgery performed using the HeartPort system. There were 4 men (50%) and 4 women (50%) with a mean age of  $67.7 \pm 9.2$  years (range, 48-77 years). In all of these patients HTK solution was used for myocardial protection.

All patients were preoperatively evaluated with transthoracic/ transesophageal echocardiography (TTE/TEE) and angiography of the coronary vessels and aorta. In 3 cases (37.5%) mitral valve repair was performed (posterior leaflet quadrangular resection and associated annuloplasty); in 5 cases (62.5%) mitral valve replacement was performed (3 mechanical prostheses and 2 bioprostheses).

#### Technique

Every procedure was performed through an anterolateral small right thoracotomy using port-access technology as previously described [Schroeyers 2001]. The EndoClamp was adequately positioned using TEE, and the balloon was inflated. Adenosine (0.25 mg/kg) was injected at the tip of the balloon to achieve a brief cardiac arrest before complete balloon inflation and to prevent balloon dislodgement during inflation. After aortic occlusion, HTK solution was delivered at the balloon tip via a roller pump into the aortic root with a perfusion pressure (aortic root pressure) of 40 to 60 mm Hg. The solution was infused only at the beginning of ischemia for a period of 6 to 8 minutes (20-25 mL/kg); no further cardioplegic perfusion was necessary. The left atrium was opened parallel to the interatrial septum, and then the mitral valve surgery was performed.

# **Biochemical Analysis**

Serial venous blood samples were collected. Laboratory measurements of serum enzymes indicative of myocardial cell damage were creatine kinase (CK) and its MB fraction. Diagnostic criteria for perioperative myocardial infarction or ischemia were CK-MB levels >10% of total CK.

### Electrocardiogram

A 12-lead electrocardiogram (ECG) was recorded prior to surgery, at 1 and 6 hours postoperatively and on the first, second, and seventh day after the operation. Diagnostic criteria for perioperative myocardial infarction or ischemia were new Q waves of 0.04 mm or more, a reduction of R waves of more than 25% in at least 2 leads, ST segment changes of at least 1 mm and lasting more than 15 minutes, T-wave abnormalities, and bundle branch blocks.

#### **Statistical Analysis**

Descriptive statistics are reported as mean  $\pm$  SD for continuous variables and as frequencies and percentages for categorical variables, unless otherwise noted.

### RESULTS

There were no operative deaths and no major postoperative complications. The mean duration of CPB was  $129.2 \pm 19.4$  minutes (range, 101-162 minutes) and the mean cross-clamp time was  $88.5 \pm 15.4$  minutes (range, 66-112 minutes). Cardioplegia reinfusion after the first dose has never been repeated. After cross clamping cardiac rhythm restarted spontaneously in 6 cases (75%), and in 2 cases (25%) it was necessary to defibrillate the heart.

The mean assisted ventilation time was  $6.8 \pm 3.2$  hours (range, 4-13 hours), and mean intensive care unit stay was  $2 \pm 1.0$  days (range, 1-4 days).

The levels of serum enzymes and the ECG results never showed significant alterations.

# DISCUSSION

Since the mid-1990s, together with the development of less invasive techniques for cardiac surgery and the evolution of newer methods and visualization devices for laparoscopic surgery, many centers became interested in expanding MICS. Now, in the treatment of some diseases such as mitral valve pathology, safety and efficacy standards for MICS have been reached that are equivalent to those of conventional surgery [Chitwood 1997, Mohr 1999, Chitwood 2000]. Ideally, every surgical technique should allow a practicing surgeon to continue to use familiar tools and approaches to cardiac operations. Of course, such continuity is not always possible in MICS: a learning curve is still necessary because different instruments and approaches are often used. For this reason, every single thing that simplifies a less invasive procedure may help the surgeon to obtain the best result.

Most centers where MICS is performed protect the myocardium through standard intermittent blood or crystalloid cardioplegia [Schwartz 1996, Chitwood 1997, Mohr 1999, Chitwood 2000, Schroeyers 2001]. This kind of myocardial protection generally requires a new administration of cardioplegia every 20 to 40 minutes depending on the solution. This readministration is not a problem in conventional surgery, but in MICS, in particular when the EndoClamp is used, readministration can be an additional factor contributing to an increase in the difficulties of an already demanding approach. The EndoClamp, the use of which is standard in HeartPort procedures, has several wellknown advantages, but its main disadvantage is that during the cross-clamp time, TEE visualization is very poor and cardioplegia administration can be ineffective because of occlusion of the coronary ostia or remodeling of the balloon itself around the tip of the EndoClamp.

In our institution, HTK solution is routinely applied in conventional cardiac surgery. The effectiveness of this solution, which has low sodium and low calcium buffered with histidine and mannitol, has been clearly demonstrated by a number of studies [Bretschneider 1980, Preusse 1985, Gallandat 1988, Sunderdiek 2000]. The main characteristics of this solution is that it allows a *safe* cardioplegic arrest time of 180 minutes, a time period during which almost every type of cardiac operation can be completed. It has been consequential to extend this kind of protection also to the Heart Port procedures, where we reproduced the same satisfactory results we had in conventional approaches. The only technical detail we would like to stress is the utility of the adenosine infusion at beginning of the cross clamping: the HTK solution, in fact, does not have the same fast plegic power of other hyperpotassic solutions, and it may take a little more time to stop the heart. Adenosine can be helpful in the correct administration of the solution. In our hands, we have never detected problems with solution-dependent myocardial protection, and now, in our center, HTK solution is routinely applied in all HeartPort procedures.

#### REFERENCES

Bretschneider HJ, Gebhard MM, Preusse CJ. 1980. Optimization of myocardial protection. In: Heiss EW, editor. Advances in clinical cardiology. Volume 1. New York: G. Witzstrock. p 581-591.

Chitwood WR Jr. 2000. Video-assisted mitral valve surgery: using the Chitwood clamp. Oper Techn Thorac Cardiovasc Surg 5:190-202.

Chitwood WR Jr, Elbeery JR, Moran JM. 1997. Minimally invasive mitral valve repair: using a mini-thoracotomy and transthoracic aortic occlusion. Ann Thorac Surg 63:1477-9.

Gallandat Huet RCG, Karliczek GF, Homan von der Heide JN, et al. 1988. Clinical effect of Bretschneider—HTK and St. Thomas cardioplegia on hemodynamic performance after bypass measured using an automatic datalogging database system. J Thorac Cardiovasc Surg 36:151-6.

Mohr FW, Onnasch JF, Falk V, et al. 1999. The evolution of minimally invasive valve surgery—2-year experience. Eur J Cardiothorac Surg 15:233-8.

Peters WS. 1993. Minimally invasive cardiac surgery by cardioscopy. Australas J Card Thorac Surg 2:152-4.

Preusse CL, Winter J, Shulte HB, Bircks W. 1985. Energy demand of cardioplegically perfused hearts. J Cardiovasc Surg 26:558-63.

Schroeyers P, Wellens F, De Geest R, et al. 2001. Minimally invasive video assisted mitral valve surgery: our lessons after a 4-year experience. Ann Thorac Surg 72:S1050-4.

Schwartz DS, Ribakove GH, Grossi EA, et al. 1996. Minimally invasive cardiopulmonary bypass with cardioplegic arrest: a closed chest technique with equivalent myocardial protection. J Thorac Cardiovasc Surg 111:556-66.

Sunderdiek U, Feindt P, Gams E. 2000. Aorto-coronary bypass grafting: a comparison of HTK cardioplegia vs. intermittent aortic cross-clamping. Eur J Cardiothor Surg 18:393-9.