Operative Myocardial Protection in Patients with Left Ventricular Hypertrophy: The Role of Systemic Hypothermia

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Abstract:
Objectives: Myocardial hypertrophy represents a great challenge in cardiac surgery. Several strategies have been described to protect the hypertrophied myocardium during cardiopulmonary bypass, and aortic clamping, yet the ideal strategy has not been identified. This study investigates the use of moderate systemic hypothermia (MSH) as an adjuvant method to protect the hypertrophied myocardium in patients undergoing aortic valve replacement (AVR).

Methods: Twenty eight patients undergoing AVR were divided into two groups, (Group I) received continuous cold 5–8 °C retrograde blood cardioplegia (CRBC) and their body temperature was cooled down to 23–26 °C. (Group II) also received CRBC but their body temperature was kept at 32–34 °C.

Results: No operative mortality (30 days) was noted in both groups. Postoperative reduction in ejection fraction (EF) was seen in nine patients of group I and in twelve patients of group II \((P < 0.05)\). The need for multiple inotropes was more in group II (eight patients) than in group I (two patients) \((P < 0.001)\). IABP was needed in three patients of group II and non in group I \((P < 0.01)\).

Conclusion: Moderate systemic hypothermia might have a role in protecting hypertrophied myocardium in patients undergoing AVR.

Keywords: ventricular hyperatrophy, hypothermia, cardioplegia
Introduction
Myocardial hypertrophy is the physiological myocardial response to the increased cardiac after-load eg, in the state of hypertension, Aortic valve stenosis, etc. The increased cardiac muscle mass is not associated with an adequate and proportional increase in the intra-myocardial vasculature. The physiological oxygen supply demand ratio in hypertrophied myocardium is disturbed and therefore is vulnerable to ischemic damage and myocardial fibrosis.

Various intra-operative myocardial protective methods have been used to protect the structure and therefore the function of the hypertrophied left ventricle. These methods include: Intermittent, continuous, cold or warm cardioplegia delivered either ante-grade or retrograde or both.

The effect of moderate systemic hypothermia 23 °C to 26 °C has not been tested as an additive intraoperative protective method for hypertrophied myocardium. This study with its small patient’s sample is considered as a pilot study based on the following hypothesis: systemic moderate hypothermia has a positive additive protective effect on hypertrophied left ventricle. This is based on the understanding that cooling the body helps in keeping the myocardial temperature down and prevents quick myocardial ischemic re-warming. Patients with severe isolated aortic valve stenosis represent a good practical left ventricular hypertrophied model and therefore were used in this study.

Patients and Methods
Consecutive twenty eight patients with isolated critical aortic stenosis and left ventricular hypertrophy undergoing aortic valve replacement were prospectively included in the study. All patients provided informed consent to be included. To avoid technical differences, all cases were done by one surgeon. The patients were alternatively assigned to MSH as (Group I) or not (Group II). The patients of both groups are demographically well matched (Table 1). The patient’s inclusion criteria includes: 1) Critical aortic valve stenosis defined as “mean Pressure gradient > 30 mmHg and valve area of <0.7 cm² measured by the continuity equation Echocardiographically and by the Gorlin equation during Cardiac catheterization”. 2) Left Ventricular Hypertrophy (LVH) defined as: >15 mm myocardium thickness at the septum and or the inferior wall during diastole by 2D-Echocardiography.

| Table 1. Patient’s characteristics. |
|--------------------------------------|
|                                   | Group (I) | Group (II) |
| Age (years)                        | 55 [34–76] | 59 [39–79] |
| Gender (M/F)                       | 8/6       | 9/5        |
| E. F. (%)                          | 63 ± 8    | 56 ± 7     |
| Valve area (cm²)                   | 0.55 [0.4–0.7] | 0.5 [0.3–0.7] |
| Pressure gradient (mmHg)           | 77.5 [45–110] | 79 [53–105] |
| IVS thickness (mm)                 | 16 [15–18] | 17 [15–19] |

Abbreviation: IVS, intra-ventricular septum.

All patients were operated upon using a median sternotomy incision. After giving heparin, aortic cannula and a double-stage right atrial venous cannula were used, cardiopulmonary bypass started when ACT reaches 400 or higher. Retrograde cardioplegia cannula is inserted in the coronary sinus guided by tans-esophageal echocardiogram (TEE). Antegrade cardioplegia is usually used as an initial dose in patients with no aortic incompetence. In addition to the use of CRBC, the body temperature is lowered to 23–26 °C during aortic cross clamping in the group I (fourteen patients). The other fourteen patients of group II also received CRBC but the body temperature was kept at 32–34 °C. The intra-operative TEE is used to assess the wall motion (WM) and estimates the ejection fraction (EF), postoperative use of inotrops, intra aortic balloon pump (IABP) use, and Troponin leak were compared in the two groups.

Data were expressed as mean ± SEM and were analyzed with analysis of variance (ANOVA) followed by t test. P values of <0.5 were considered statistically significant.

Results
Reduction in EF compared to the pre operative value by TEE was seen in nine patients in group I (13%) and in 12 patients of group II (32%), (P < 0.05). seven patients in group I 50% compared to four patients 29% in group II required single inotrope (P < 0.05) while two patients 14% in group I required multiple inotropes compared to eight patients 60% in group II (P < 0.001). IABP was needed in three patient 21% in group II and non in group I (P < 0.01). No significant difference between the two groups in post pumps Troponin levels. No Myocardial infarctions were reported based on combined ECG changes and rise in Troponin levels. No operative mortality (30 days) was noted in the two groups (Table 2, Fig. 1).
The role of hypothermia in myocardial hyperatrophy protection

Discussion

Cardiac hypertrophy comprises a tenuous balance between adaptive characteristics and potentially deleterious structural, functional, and biochemical/molecular alterations including enlarged muscle mass with alterations in the cardiac configuration, enhanced metabolic requirements, synthesis of abnormal proteins, decreased capillary/myocyte ratio, fibrosis, micro vascular spasm, and impaired contractile mechanisms. Hypertrophy also decreases myocardial compliance and thereby hinders diastolic filling. In addition, LVH is an independent risk factor for cardiac mortality and morbidity, especially for sudden death. Duncan et al concluded that concentric geometries, weather concentric hypertrophy or concentric remodeling, are associated with increased risk for in-hospital mortality after aortic valve replacement. And that postoperative risk stratification should include assessments of LV hypertrophy and LV geometry.

The adequate protection of the hypertrophied myocardium during surgical procedure is still a challenge. It is known that the hypertrophied myocardium already presents ultra structural changes that rend it more susceptible to ischemia and fibrosis. Moreover, these changes and the relative deficiency of microcirculation hinder the delivery of the cardioplegic solution to the sub-endocardium, compromise intra-operative myocardial preservation and render the heart particularly susceptible to ischemic damage and infarction.

Various methods of myocardial protection have been used to protect hypertrophied myocardium. Different delivery routes (antegrade, retrograde and combinations), temperature (cold, tepid or warm), or composition (blood and crystalloid) were compared and different strategies have been tried. Lotto et al showed that myocardial protection with either antegrade or retrograde intermittent delivery of cold blood cardioplegia is suboptimal.

A study done by Ascione et al examined myocardial injury in hypertrophic hearts of patients undergoing aortic valve surgery showed evidence of metabolic derangement and reperfusion injury, indicating suboptimal myocardial protection by both cold and warm blood cardioplegia.

Ovrum et al found that there was no indication that the composition of cardioplegia; whether blood or crystalloid administered retrograde in patients undergoing AVR; had an effect on the immediate postoperative outcome of these patients. It is worth mentioning that their group of patients was identified as low or moderate risk group and that they did not identify patients according to the severity of LVH.

Terminal retrograde “hot shot” reperfusion was studied by Ascione et al in patients with left ventricular hypertrophy undergoing aortic valve replacement. The group concluded that this technique did not add any extra benefit to antegrade cold-blood cardioplegia in preventing myocardial injury in patients with left ventricular hypertrophy undergoing aortic valve replacement.

The use of MSH, to our knowledge, was not used or at least mentioned in the literature as an additive protective method for LVH in patients with severe aortic stenosis.

Despite the small patient sample in the current study, we think that it represents the problem of protecting the hypertrophied myocardium during heart surgery. This has been achieved by selecting patients with isolated severe aortic stenosis and randomizing

Table 2. Summary of the results.

|                          | Group (I) | Group (II) | P-value |
|--------------------------|-----------|------------|---------|
| Post pump E. F. reduction| 9 Pt      | 12 Pt      | <0.05   |
| Single inotrope need     | 7 Pt      | 4 Pt       | <0.05   |
| Multiple inotropes need  | 2 Pt      | 8 Pt       | <0.001  |
| Post pump IABP use       | 0 Pt      | 3 Pt       | <0.01   |
| Troponin release         | 233.6 [146.0 to 321.2] μg/L | 240.25 [179.3 to 301.2] μg/L | <0.15 |

Figure 1. Results comparison.
them alternatively between control and study cases. The results compared important variables and showed difference between the two groups in the immediate post-operative Cardiac performance. This is seen by the significant differences in the use of IABP, EF reduction and the use of inotropes.

Conclusion
The results indicate that combining moderate systemic hypothermia with continuous retrograde cold blood cardioplegia might have a better protective effect on hypertrophied myocardium in patients undergoing aortic valve replacement.

Disclosure
This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

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