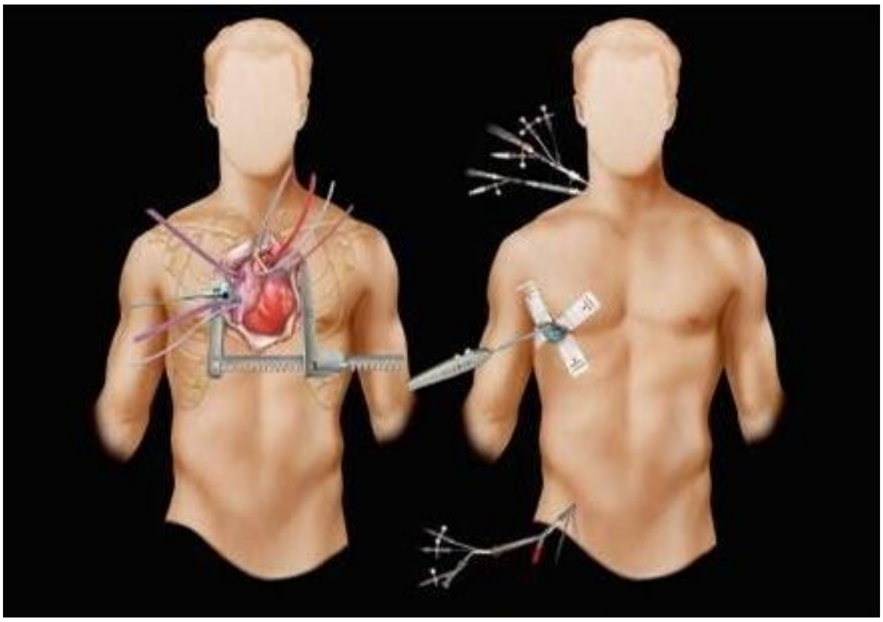
Influence of different perfusion and aortic clamping techniques in minimally invasive mitral valve surgery.

Brief introduction and rationale of the work

Minimally invasive cardiac surgery (MICS) has become a widely adapted approach as it minimizes many of the inconvenient side effects associated with the median sternotomy (wound infection, respiratory disfunction and an unpleasant - looking scar) [10]. The vast majority of larger clinical studies demonstrates, that minimally invasive mitral valve surgery (MIMVS) using the port-access approach after an initial learning curve, is a safe and effective approach in terms of short and long-term results [2,3,12], mainly for redo operations and even for elderly patients with moderately elevated perioperative risk [6].



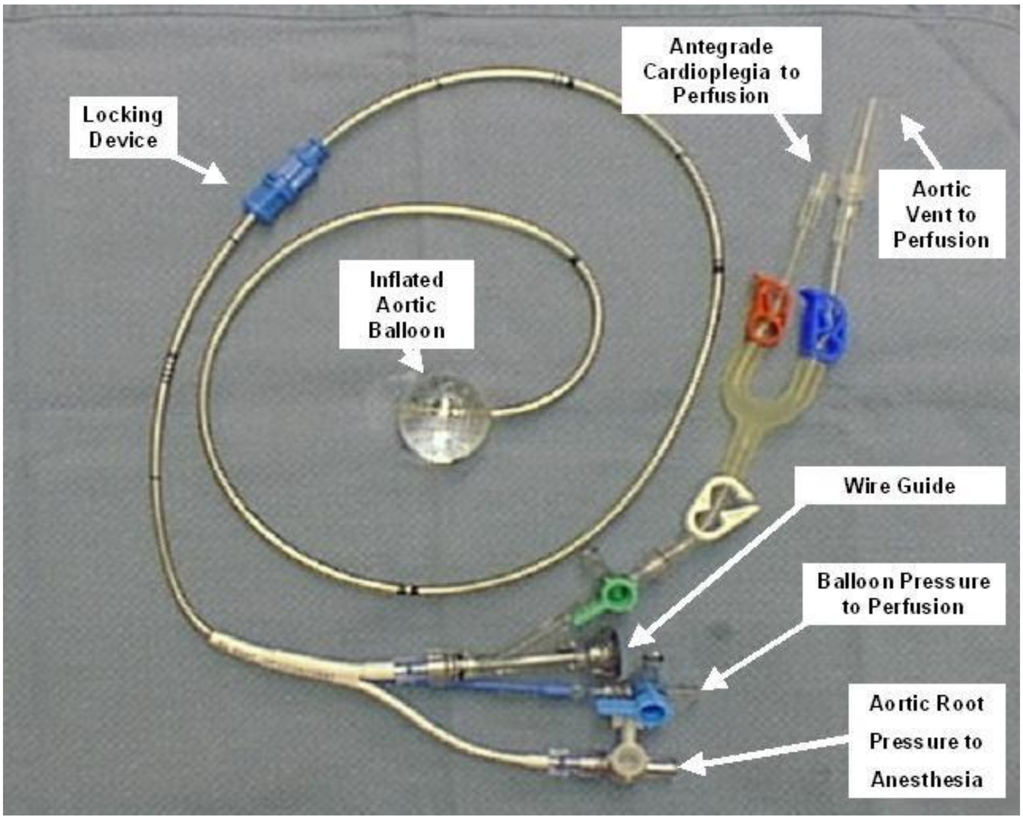
Median sternotomy and right mini-thoracotomy

Furthermore, this technique has shown a low morbidity and mortality achieving functional and echocardiographic outcomes comparable to those obtained with conventional surgery [11,12,18]. Measurable patient's benefits include less pain, less blood transfusions, fewer wound infections and pulmonary complications, and faster recovery as well as a better cosmetic result [5].

Dimensions of the surgical incision post mini-thoracotomic approach

Port Access surgical technique requires the supine position of the patient, with slight elevation (30°) of the right hemithorax. All candidates for mini-thoracotomic video-assisted or video-guided port-access approach are ventilated with a double-lumen endotracheal tube in order to exclude, when needed, right lung ventilation. Monitoring includes double side arterial lines and use of TEE (Transesophageal Echocardiography). Surgical approach is a right mini-thoracotomy in the 4th intercostal space (4-6 cm) without ribs' retraction [6,20]. Using a soft-tissue retractor, the surgical port is exposed [13]. To improve the vision, an endoscope is usually inserted in an accessory port created below the working port.

To date, different perfusion and aortic clamping techniques have been reviewed: retrograde arterial perfusion through the femoral artery with Endoreturn/Intraclude system (Edwards Lifesciences, Irvine, California) [21,22], retrograde arterial perfusion through the femoral artery with trans-thoracic clamp [16], antegrade arterial perfusion with trans-thoracic clamp [14].



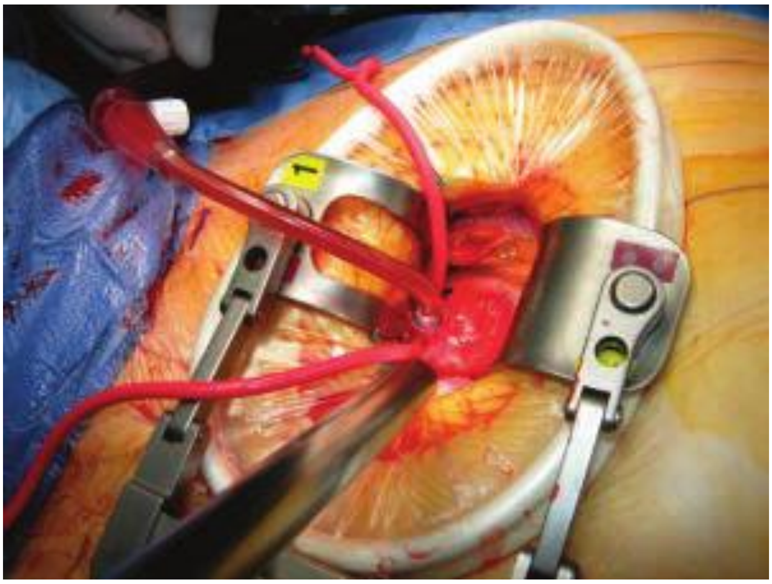
Endoreturn/Intraclude system (Edwards Lifesciences, Irvine, California)

This study analyses an experience in MIMVS from right thoracotomy with different arterial perfusion and aortic clamping strategies to determine if different techniques may impact on early outcomes.

Approach of the work

Minimally invasive mitral valve surgery (MIMVS) requires the use of novel perfusion strategies, especially in patients who hold the highest potential for postoperative morbidity [12]. Cannulation techniques are a fundamental element in minimally invasive cardiac surgery.

Options for arterial cannulation in MICS are the ascending aorta, femoral artery or axillary artery. Central aortic and axillary cannulation have the advantage of antegrade flow, while femoral cannulation is convenient but carries a small risk of retrograde dissection, embolization and ipsilateral limb ischemia. Preoperative computed tomography angiography (CTA) provides valuable information regarding arterial stenosis, tortuosity and the presence of aneurysmal disease that can be useful in choosing a cannulation site.



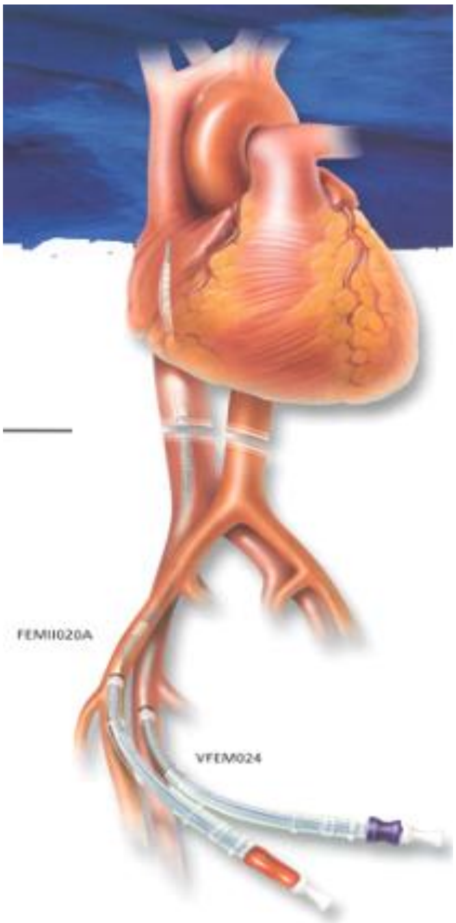
Central aortic cannulation

Central aortic cannulation mimics the approach used in sternotomy methods, and its use in MICS is limited by the degree of access to the ascending aorta. In addition, placing the cannula through a small incision can limit visibility.

The more lateral right chest incision that is required for MIMVS places the aorta slightly father away, and most surgeons would opt for an alternative site for cannulation. One of the most feared complications of central aortic cannulation is dissection, which occurs in 0.01% to 0.09% of patients [4,5]. As a routine, the intraoperative transesophageal echocardiography (TEE) protocol should include examination for aortic dissection after cannulation and after instituting cardiopulmonary bypass [3,10]. If TEE confirms the diagnosis of aortic dissection, CPB should be terminated immediately and alternative arterial cannulation performed, usually in the groin.

In the absence of significant aortoiliac disease, femoral arterial cannulation is the preferred choice of many surgeons for MIMVS. It offers convenience and improved exposure through a limited chest incision [4,6].

Exposure of the femoral artery and direct cannulation is probably the most common approach. The cannula is usually placed over a wire that is positioned in the true lumen of the aorta [4,5].



Both arterial and venous cannulation using Seldinger technique

Groin complications such as infection, hematoma, and lymphocele occur in a few cases and are more likely in obese patients. Femoral artery cannulation carries a small risk of retrograde aortic dissection, embolization and ipsilateral limb ischemia.

Axillary artery cannulation offers the advantage of antegrade perfusion without crowding the operative field in MICS [9,14,15].

Edwards cannula for axillary artery cannulation

While this site tends to be relatively disease free, its use is contraindicated in the presence of subclavian or innominate artery stenosis.

Venous return is routinely obtained with a double cannulation: jugular cannulation is always achieved percutaneously using a 17-21Fr Medtronic cannula or using a 18-20Fr Edwards; femoral cannulation is performed percutaneously in all the cases of simultaneous central aortic cannulation.

It is possible to use also modern three-stage cannulas provide good drainage and decompression of the right heart with the aid of kinetic drainage assist device [17,19]. The latter is an important element of myocardial protection during cardioplegic arrest. The right femoral vein is favored because of the straighter alignment with the inferior vena cava, which is important for optimal drainage. In the case of retrograde arterial perfusion through the femoral artery with Endoreturn/Intraclude system or standard femoral artery cannulation a minimal groin incision is necessary and both arterial and femoral cannulation are directly performed using Seldinger technique [21].

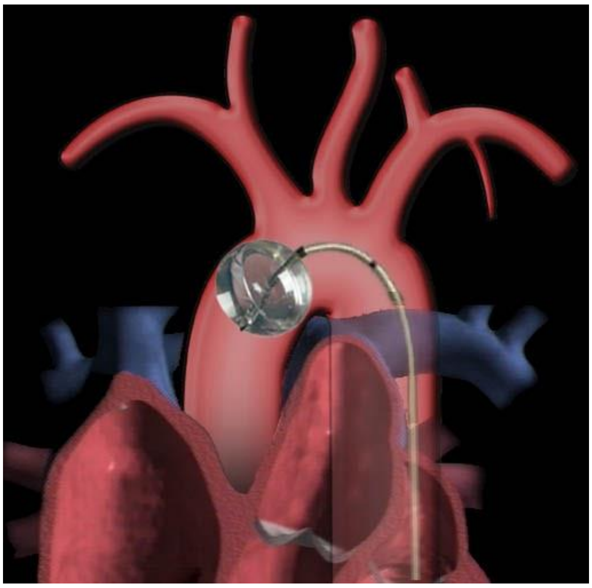
Edwards cannula for using Endoreturn/Intraclude system

Although most of studies showed the feasibility and safety of minimally invasive mitral valve surgery using the endoaortic clamping technique [6], several specific issues emerged from data reported in literature. Particularly in first series, multiple severe complications have been described, such as aortic dissection or iliac artery injury, probably due to first generation stiffer catheters, worse monitoring techniques, and learning curve of the operator. Nowadays severe vascular complications are very rare and cannot be considered a specific burden of endoluminal clamping technique itself.

Compared with conventional surgery, MIMVS is associated with optimum outcomes, even if concerns still remain about neurological complications. The incidence of neurologic events in MIMVS compared with that of conventional surgery is a controversial issue [8,15,17]. In a meta-analysis published by Modi [7], equal occurrence of neurologic events between patients who underwent MIMVS and those who underwent a median sternotomy was found. Conversely, the Thoracic Surgeons Adult Cardiac database and the Cleveland Clinic group concluded that the risk of stroke is significantly higher in the less invasive group [8]. Moreover, recent data have suggested that retrograde arterial perfusion, particularly in patients with severe aortic atherosclerosis, could be the source of the significant increase in the incidence of cerebral complications. The risk of stroke in consequence of MIMVS, varies from 2 to 10% as reported by various studies. Concerning generic complications some authors and especially the ISMICS (International Society for

Minimally Invasive Cardiothoracic Surgery) summit claimed an augmented risk for cerebrovascular events, hypothetically due to greater use of femoral arterial cannulation for CPB [23].

Plaque embolization during catheter introduction into the femoral artery or related to retrograde perfusion as well as traumatic injuries with consequent artery dissection or pseudoaneurysms formation and epiaortic vessel obstruction caused by balloon migration are well known complications limited in more recent practice by the adoption of a more careful monitoring and dedicated catheter and devices.

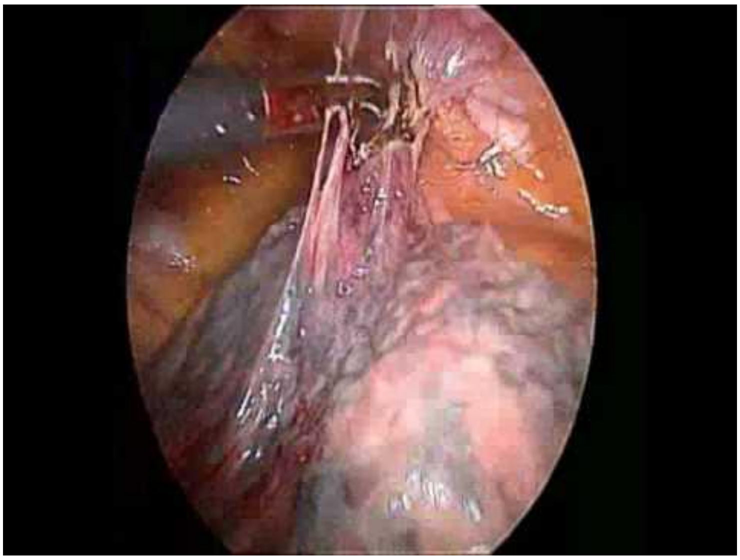


Inflated aortic ballon and aortic clamping with Endoreturn/Intraclude system

The aim of study is to determine if different techniques of perfusion and aortic clamping may impact on early outcomes including neurologic impairment.

Methods and main results

Between March 2014 and March 2019 665 consecutive patients underwent MIMVS from right mini-thoracotomy. It was systematically introduced a preoperative screening regarding arterial stenosis, tortuosity and the presence of aneurismal disease for patients who underwent MIMVS. During the period of study it was routinely introduced, in the surgical practice, the delivering of CO2 and all the arterial perfusion and aortic clamping settings available in the trade: P+EB (retrograde arterial perfusion through the femoral artery with Endoreturn/Intraclude system) , P+XC (retrograde arterial perfusion through the femoral artery with transthoracic clamp) and C+XC (antegrade arterial perfusion through the axillary artery with transthoracic clamp). Moderate aortic regurgitation, severe lung adhesions, urgent or emergent status with hemodynamic instability that precludes preoperative work-up were considered major contraindications to MIMVS.



In the same period 60 patients underwent MVS through standard sternotomy. All patients were screened preoperatively for adequate vascular access at the time of cardiac catheterization or by computed tomography angiography scan; an antero-posterior and lateral chest x-ray were obtained to better evaluate the relationship among chest wall, sternum, and aorta; in addition, an ascending aorta evaluation during echocardiographic examination was requested to obtain diameter measurements.

After a full preoperative work-up based on clinical history and anatomy, each patient was allocated to the most appropriate out of the 3 MIMVS approaches. In case of previous cardiac surgery procedures the P+EB setting was used mostly; in case of dilated ascending aorta (diameter >40 mm) or moderate-tortuous aortoiliac-femoral vessels, the P+XC setting was predominantly used; in case of severe tortuous and/or atheromatous aortoiliac-femoral vessels, the C+XC setting was preferred. The selection of one setting in respect to the others was patient orientated and independent from the learning curve.

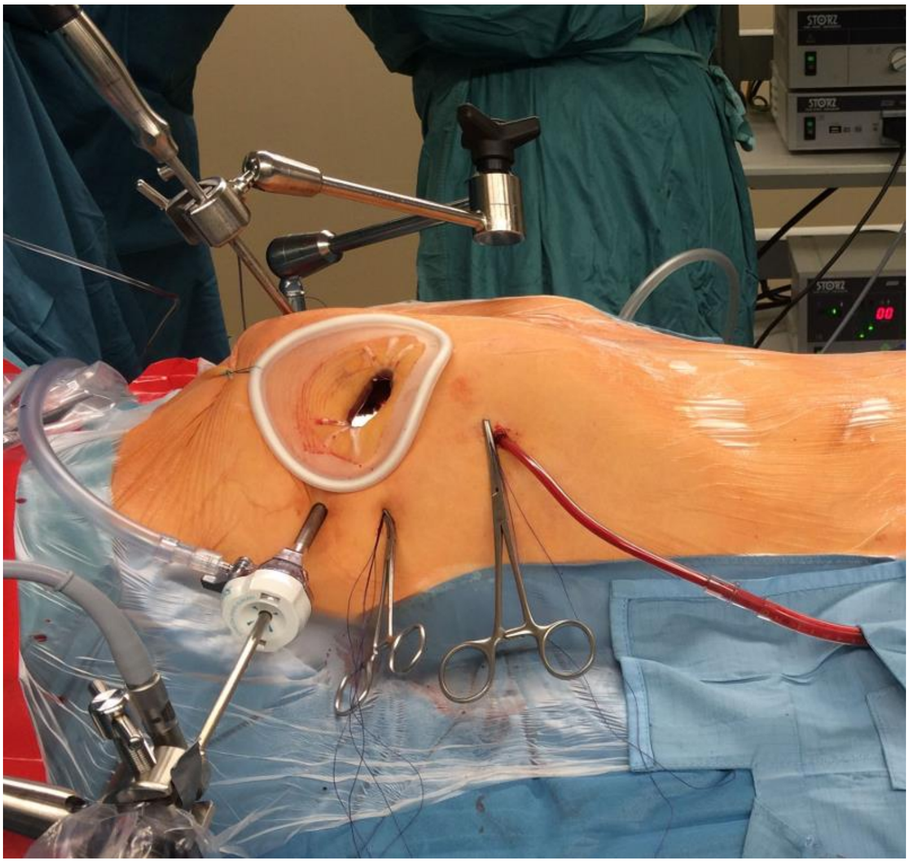
Immediate intraoperative conversion to median sternotomy was required in 14 cases because of extensive lung adhesions. Moreover, 18 redo patients underwent fibrillating heart MVS for patent grafts. In 8 patients (1.2%) due to preoperative features with large pericardial adhesions, central cannulation (axillary artery) with endoclamp was occasionally used. These patients were not considered in the main statistical analysis. The reference population thus obtained is 625 patients on which were conducted subsequent analyzes.

The P+EB group collected 319 patients (51.0%), the P+XC group collected 262 patients (41.9%), and C+XC group collected 44 patients (7.0%). Subgroup patients' characteristics are reported in Table 1.

Variable	**P + EB (n=319)**	**P + XC (n=262)**	**C + XC (n=44)**	***p*Value**
Age, years	**61.0 ± 12.9 (63)**	**67.9 ± 10.9 (70)**	**74.0 ± 8.9 (77)**	**0.00086**
Male	**162 (50.8%)**	**137 (52.3%)**	**24 (54.5%)**	**0.86603**
BMI	**24.3 ± 4.5 (23.6)**	**24.2 ± 4.0 (23.9)**	**26.1 ± 5.2 (25.7)**	**0.02618**
Logistic EuroSCORE	**7.5 ± 9.6 (3.7)**	**6.9 ± 6.9 (4.5)**	**11.4 ± 12.9 (7.2)**	**0.008085**
EuroSCORE II	**3.1 ± 4.3 (1.2)**	**3.2 ± 4.3 (1.8)**	**5.4 ± 5.1 (4.0)**	**0.004255**
Renal failure	**29 (9.0%)**	**23 (8.8%)**	**8 (18.2%)**	**0.133126**
Creatinine, mg/dL	**1.07 ±0.70 (0.91)**	**1.04 ± 0.56 (0.95)**	**1.16 ± 0.35 (1.13)**	**0.483786**
COPD	**27 (8.5%)**	**23 (8.8%)**	**10 (22.3%)**	**0.009027**
IDDM	**26 (8.2%)**	**29 (11.0%)**	**4 (9.1%)**	**0.486813**
Peripheral vasculopaty	**6 (1.9%)**	**11 (4.2%)**	**43 (97.8%)**	**0.00001**
Atrial fibrillation	**105 (32.9%)**	**97 (37.0%)**	**27 (61.4%)**	**0.001166**
Neuro	**16 (5.0%)**	**11 (4.2%)**	**0**	**0.204692**
Previous cardiac surgery	**90 (28.2%)**	**8 (3.1%)**	**2 (4.5%)**	**0.00001**
Ejection fraction, %	**60.0 ± 9.7 (60)**	**58.7 ± 11.2 (60)**	**58.7 ± 10.9 (60)**	**0.298516**
PAPS, mmHg	**46.0 ±16.4 (42.5)**	**46.5 ± 15.4 (45)**	**51.4 ± 15.5 (50)**	**0.108396**

P+EB (retrograde arterial perfusion through the femoral artery with Endoreturn/Intraclude system); P+XC (retrograde arterial perfusion through the femoral artery with transthoracic clamp; C+XC (antegrade arterial perfusion through the axillary artery with transthoracic clamp); COPD – chronic obstructive pulmonary disease; IDDM – insulin-dependent diabetes mellitus

Surgical Technique



MIMVS from right mini-thoracotomy technique used during the period of study have been previously described. Double lumen endotracheal tube was positioned to allow 1-lung ventilation and bilateral radial arterial lines was used for monitoring blood pressure.

The bilateral monitoring of blood pressure is particularly important in case of P+EB technique so that migration of the endoaortic balloon can be appreciated. All patients underwent operation through a right mini-thoracotomy in the fourth intercostal space (4 to 6 cm). Using a soft-tissue retractor, the surgical port was exposed. To improve the vision, an Olympus endoscope (Olympus Corporation, Tokyo, Japan) was inserted in an accessory port created below the working port.

Intraoperative transesophageal echo was performed in all the patients to evaluate valve pathophysiology and function and to guide cannulas positioning.

Arterial perfusion was obtained with the P+EB cannula (21F to 23F Edwards) through the femoral artery or with Edwards cannula for axillary artery cannulation in case of C+XC, or with a standard femoral artery cannulation. In the first case clamping and cardioplegia delivery were gained through a balloon catheter (Intraclude, Edwards Lifesciences) inserted through the sidearm of the arterial cannula; in the case of standard femoral artery cannulation or axillary artery cannulation a Chitwood transthoracic clamp (Scanlan International, Inc, St Paul, MN) was used and the cardioplegia was delivered through a 7F cardioplegia needle (CalMed Technologies, CA) placed into the ascending aorta at its highest point.

Chitwood transthoracic clamp (Scanlan International, Inc, St Paul, MN)

Venous return was routinely obtained with a double cannulation: jugular cannulation was always achieved percutaneously using a 17F to 21F Medtronic cannula (Medtronic, Inc, Minneapolis, MN) or using a 18F to 20F Edwards cannula

(OptiSite) (Edwards Lifesciences, Irvine, CA). In the case of P+EB or standard femoral artery cannulation a minimal groin incision was necessary and both arterial and venous cannulation were directly performed using Seldinger technique. In the case of concomitant operations (tricuspid valve surgery or atrial septal defect closure), superior and inferior vena cava snaring was obtained by placing tourniquets around the vessels. Patients with symptomatic drug resistant atrial fibrillation underwent concomitant cryoablation. The pleural and pericardial cavities were flooded continuously with CO_2.

Results

Subgroup patients' operative data and postoperative outcomes are reported in Table 2.

Variable	**P + EB (n=319)**	**P + XC (n=262)**	**C + XC(n=44)**	***p*Value**
MV repair	**184 (57.7%)**	**146 (55.7%)**	**16 (36.4%)**	**0.028239**
MV/MP replacement	**135 (42.3%)**	**116 (44.7%)**	**28 (63.6%)**	**0.028239**
TV procedure	**33 (10.3%)**	**26 (9.9%)**	**2 (4.5%)**	**0.474669**
ASD/PFO closure	**30 (9.4%)**	**20 (7.6%)**	**5 (11.4%)**	**0.62199**
AF cryoablation	**32 (10.0%)**	**25 (9.5%)**	**2 (4.5%)**	**0.504925**
Cardiopulmonary bypass, min	**137.9 ± 37.8 (132)**	**133.5 ± 36.0 (127)**	**144.8 ± 70.7 (121.5)**	**0.157144**
X-Clamp, min	**102.0 ± 26.5 (100)**	**93.5 ± 28.0 (90)**	**92.6 ± 28.1 (86.5)**	**0.000429**
Aortic dissection	**0**	**1 (0.4%)**	**1 (2.3%)**	**0.202053**
Conversion to sternotomy	**2 (0.6%)**	**4 (1.5%)**	**2 (4.5%)**	**0.085614**
Ventilation time, hours	**19.4 ±53.4 (11)**	**20.7 ± 57.9 (12)**	**23.9 ± 47.0 (12)**	**0.865823**
ICU Stay, days	**2.0 ± 4.8 (1)**	**2.1 ± 3.2 (1)**	**2.7 ± 5.0 (1)**	**0.587076**
Re-exploration for bleeding	**8 (2.5%)**	**7 (2.7%)**	**2 (4.5%)**	**0.736869**
Minor neurological events	**8 (2.5%)**	**1 (0.4%)**	**1 (2.3%)**	**0.118455**
Major neurological events	**4 (1.3%)**	**4 (1.5%)**	**0**	**0.857835**
Hemodyalisis	**10 (3.1%)**	**10(3.8%)**	**1 (2.3%)**	**0.827631**
PM implantation	**10 (3.1%)**	**10 (3.8%)**	**1 (2.3%)**	**0.827631**
Hospital stay, days	**9.2 ± 14.9 (7)**	**8.2 ± 4.7 (7)**	**8.3 ± 4.7 (7)**	**0.542686**
30-day mortality	**2 (0.6%)**	**2 (0.8%)**	**1 (4.9%)**	**0.632564**

P+EB (retrograde arterial perfusion through the femoral artery with Endoreturn/Intraclude system); P+XC (retrograde arterial perfusion through the femoral artery with transthoracic clamp; C+XC (antegrade arterial perfusion through the axillary artery with transthoracic clamp); MV – mitral valve; MP – mitral prosthesis; TV – tricuspide valve; ASD – atrial septal defect; PFO – patent foramen ovale; AF – atrial fibrillation.

Discussion

In the analysis of pre-operative data, some significant differences were observed between the groups. In P+EB group was observed a higher frequency of previus cardiac surgery (p< 0.00001). In the C+XC group was observed a higher age (p=0.00086), BMI (p=0.02618), prevalence of COPD (p=0.009027) and a higher incidence of peripheral vasculopathy (p=0.00001) and AF (p=0.001166). These differences justify the higher predicted mortality in the C + XC group: Logistic EuroSCORE (p=0.008085) and EuroSCORE II (p=0.0042559).

All the statistically significant differences reported are to be correlated to the choice of the type of cannulation / perfusion and clamping technique that was chosen based on patient characteristics. In fact, in patients with history of previous cardiac surgery the retrograde arterial perfusion through the femoral artery with endoclamp was preferentially chosen while antegrade arterial perfusion through the axillary artery was chosen in patients with severe peripheral vasculopathy

As regards intra-operative results, a higher incidence of miltral valve replacement in group C + XC was observed (p=0.028239). This fact we believe is to be associated to the type of population of the group in object that as we have previously reported has a more advanced age with different comorbidities. There were not significant differences in cardiopulmonary bypass time (P=0.157144). On the contrary, a significant reduction in clamping times has been reported in favor of group C + XC (p=0.000429). This difference is mainly due to fewer mitral repairs performed in this group. In the major peri-operative complications (conversion to sternotomy and aortic dissection) no significant differences were reported.

In the post-operative period there were no differences in the timing of ventilation (P=0.865823), ICU stay (p=0.587076) and hospital stay (0.542686). Furthermore, no significant differences were observed between the three groups regarding the main complications: re-exploration for bleeding (p=0.736869), Hemodyalisis (p=0.827631) and PM implantation (p=0.827631).

Also, with regard to both minor and major neurologic complications, in contrast to what is reported in some publications, no statistically significant differences were reported (minor p=0.118455, major p=0.857835).

Finally, even in 30-day mortality, no differences were found (p=0.632564)

Conclusions

The three techniques studied have reported good results with reduced complications and therefore can be considered safe, feasible and reproducible.

The availability of different perfusion and clamping techniques allows the minimally invasive method to be adapted to the different characteristics of the patients. This tailored approach gives the possibility to obtain a better result by reducing complications both intra and post operatively.

References

1. Bailey C. P., O'Neill T. J., Glover R. P., Jamison W. L., Redondo-Ramirez H. P. Surgical repair of mitral insufficiency (preliminary report) *Diseases of the Chest*. 1951;19(2):125–137. doi: 10.1378/chest.19.2.125. [PubMed] [Cross Ref]

2. Lillehei C. W., Gott V. L., Dewall R. A., Varco R. L. Surgical correction of pure mitral insufficiency by annuloplasty under direct vision. *The Journal-lancet*. 1957;77(11):446–449. [PubMed]

3. Mongero LB, Beck JR, editors. On bypass: advanced perfusion techniques. New York: Springer Science & Business Media; c2008. p. 576. p.

4. Grossi EA, Loulmet DF, Schwartz CF et al. Evolution of operative techniques and perfusion strategies for minimally invasive mitral valve repair. J Thorac Cardiovasc Surg. 2012 Apr;143(4 Suppl):S68–70. [PubMed]

5. Murzi M, Glauber M. Central versus femoral cannulation during minimally invasive aortic valve replacement. Ann Cardiothorac Surg. 2015 Jan;4(1):59–61. [PMC free article] [PubMed]

6. Ricci D, Pellegrini C, Aiello M, et al. Port-access surgery as elective approach for mitral valve operatione in re-do procedures. Eur J Cardiothorac Surg 2010;37:920-7.

7. Modi P, Hassan A, Chitwood WR Jr. Minimally invasive mitral valve surgery: a systematic review and meta-analysis. Eur J Cardiothorac Surg 2008;34:943-52.

8. Gammie JS, Zhao Y, Peterson ED, O'Brien SM, Rankin JS, Griffith BP. Maxwell Chamberlain Memorial Paper for adult cardiac surgery. Less-invasive mitral valve

operations: trends and outcomes from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Ann Thorac Surg 2010;90:1401-8.

9. Sinclair MC, Singer RL, Manley NJ, Montesano RM. Cannulation of the axillary artery for cardiopulmonary bypass: safeguards and pitfalls. Ann Thorac Surg. 2003 Mar;75(3):931–4. [PubMed]

10. Reser D, Holubec T, Scherman J, Yilmaz M, Guidotti A, Maisano F. Upper ministernotomy. Multimed Man Cardiothorac Surg. 2015 Nov 2;2015

11. Mohr FW, Falk V, Diegeler A, et al. Minimally invasive port-access mitral valve surgery. J Thorac Cardiovasc Surg 1998;115:567-74; discussion 574-6. [PubMed]

12. Spencer FC, Galloway AC, Grossi EA, et al. Recent developments and evolving techniques of mitral valve reconstruction. Ann Thorac Surg 1998;65:307-13. [PubMed]

13. Glower DD, Siegel LC, Frischmeyer KJ, et al. Predictors of outcome in a multicenter port-access valve registry. Ann Thorac Surg 2000;70:1054-9. [PubMed]

14. Sabik JF, Nemeh H, Lytle BW et al. Cannulation of the axillary artery with a side graft reduces morbidity. Ann Thorac Surg. 2004 Apr;77(4):1315–20. [PubMed]

15. Etz CD, Plestis KA, Kari FA et al. Axillary cannulation significantly improves survival and neurologic outcome after atherosclerotic aneurysm repair of the aortic root and ascending aorta. Ann Thorac Surg. 2008 Aug;86(2):441–6. [PubMed]

16. Navia JL, Cosgrove DM 3rd. Minimally invasive mitral valve operations. Ann Thorac Surg 1996;62:1542-4. [PubMed]

17. Colangelo N, Torracca L, Lapenna E, Moriggia S, Crescenzi G, Alfieri O. Vacuum-assisted venous drainage in extrathoracic cardiopulmonary bypass management during minimally invasive cardiac surgery. Perfusion. 2006 Nov;21(6):361–5. [PubMed]

18. Cohn LH, Adams DH, Couper GS, et al. Minimally invasive cardiac valve surgery improves patient satisfaction while reducing costs of cardiac valve replacement and repair. Ann Surg 1997;226:421-6; discussion 427-8. [PubMed]

19. De Somer F. Venous drainage--gravity or assisted? Perfusion. 2011 Sep;26(Suppl1):15–9. [PubMed]

20. Colvin SB, Galloway AC, Ribakove G, et al. Port-Access mitral valve surgery: summary of results. J Card Surg 1998;13:286-9. [PubMed]

21. Fann JI, Pompili MF, Stevens JH, et al. Port-access cardiac operations with cardioplegic arrest. Ann Thorac Surg 1997;63:S35-9. [PubMed]

22. Saito N, Matsumoto H, Yagi T et al. Evaluation of the safety and feasibility of resuscitative endovascular balloon occlusion of the aorta. J Trauma Acute Care Surg. 2015 May;78(5):897–903. [PubMed]

23. Bentala M, Heuts S, Vos R et al. Comparing the endo-aortic balloon and the external aortic clamp in minimally invasive mitral valve surgery. Interact Cardiovasc Thorac Surg. 2015 Sep;21(3):359–65. [PubMed]