Title page

Left thoracotomy approach for off-pump coronary artery bypass grafting surgery: fifteen years' experience in 2500 consecutive patients

* Gustavo Antonio Guida[1,2]; Gabriel Alessandro Guida[1]; Vito Domenico Bruno[2]; Mustafa Zakkar[2]; Estefania De Garate[2]; Miriam Terry Pecchinenda[1]; Alfredo Homes[3]; Calogerino Borzellino[3]; Pablo Mendoza[1]; Giuseppina Pecora[1]; Ivan Bonillo[1]; Umberto Benedetto[2]; Antonio Maria Calafiore[4]; Gianni Davide Angelini[2]; and Maximo Cosimo Guida[1].

1. Department of Cardiac Surgery, Fundacardio Foundation, Valencia, Venezuela
2. Bristol Heart Institute, Bristol University, Bristol, United Kingdom
3. Cardiac surgery service, Clinica Acosta Aortiz, Barquisimeto, Venezuela
4. Division of Cardiac Surgery, John Paul II Foundation, Campobasso, Italy

Meeting presentation: An extract from this paper was presented at the 32nd EACTS Annual Meeting, in Milan on the 18th of October Abstract number 000189

Word count: 3520 words

*Corresponding author: Gustavo Antonio Guida

Address: Bristol Heart Institute

Bristol Royal Infirmary
Upper Maudlin Street
BS2 8HW
Bristol – United Kingdom

Phone number: +4401173423523

Email: gustavo.guidi@uhbristol.nhs.uk

Central image and visual abstract

Key question:

What is our experience on off-pump coronary artery bypass grafting via left thoracotomy after 2500 patients?

Key findings:

- Reproducible surgery
- Low mortality and early complications rate
- Good early, mid and long-term results

Take-home message

The left thoracotomy is a safe alternative to median sternotomy for coronary artery bypass grafting on the beating heart, with low early complications and good mid and long-term results.

Abstract and key words

Objectives:

A two-centers experience with off pump coronary artery bypass (OPCAB) grafting using a left thoracotomy approach.

Methods:

From January 2002 to December 2017 a total of 2528 consecutive patients (578 female, mean age 62.3 ± 9.1 years) were operated using this technique. Data was collected prospectively and analyzed retrospectively.

Results:

There was no conversion to median sternotomy in the whole series and 6 patients (0.2%) were converted to on-pump. Mean number of grafts per patient was 2.8 ± 0. 9. 30-day mortality was 1.0% (25 patients).

Most patients were extubated in theatre (97.3%), and 47patients (1.9%) needed re-exploration for bleeding. Seven patients (0.3%) experience a cerebrovascular event, four (0.3%) a post-operative myocardial infarction and 84 (3.4%) a new onset of atrial fibrillation. 1510 patients (61.1%) were discharged from hospital in the first 48 hours post-surgery. Long term survival rates were 98.8%, 93.6% and 69.1% at 1,5 and 10 years respectively. During follow-up sixty patients (2.9%) were reinvestigated for recurrence of angina with a new coronary angiogram, and of those 24 (1.2%) required PCI and 11 (0.5%) redo surgery.

Conclusion:

The left thoracotomy is a safe alternative to median sternotomy for coronary artery bypass grafting on the beating heart, with low early complications and good mid and long-term results.

Keywords: Off-Pump; minimally invasive; coronary; survival.

Introduction

The median sternotomy remains the standard approach for Coronary Artery Bypass Grafting (CABG) [1]. One of the most feared complications related to this approach is sternal dehiscence and potential mediastinitis, which carries an incidence of mortality between 1.4% and 3.6% despite modern and more advanced treatments [2].

To avoid this complication, many alternative approaches to full sternotomy have been proposed such as video assisted coronary by-pass grafting [3], 3rd intercostal space anterior thoracotomy (Dresden technique) [4] and minimally invasive left anterior thoracotomy [5]. Most of these techniques however, do not allow for total revascularization unless combined with percutaneous coronary intervention (PCI) as a hybrid revascularization procedure [6]. However, hybrid revascularization poses challenges of its own such as the difference of post-procedure protocols between CABG and percutaneous coronary intervention (PCI) [7], the increased risk of bleeding associated to higher use of anticoagulation [8] and can be significantly more expensive than a single intervention [7].

While avoiding the Cardiopulmonary Bypass (CPB) has shown some advantages especially in the high-risk patients [9], there remains the problem that the technique has been associated with lower rates of complete revascularization and poor long-term outcome when compared with conventional on pump CABG [10].

This led our group to pursue the development of the left thoracotomy approach a technique that would avoid the complications of sternotomy and allows to perform off-pump multivessel revascularization with minimal displacement of the heart [11,12].

Materials and methods

Patients and Data collection

This is a retrospective analysis of prospectively collected data on a cohort of patients from two different regional cardiac surgical units: Fundacardio Foundation in Hospital Metropolitano del Norte in Valencia – Venezuela (Center A 1404 patients), and Ascardio Foundation in Barquisimeto – Venezuela (Center B 1124

patients). Between May 2002 and December 2017, 2528 consecutive patients underwent elective or urgent/emergency CABG via left thoracotomy.

Data was collected prospectively and retrospectively analyzed. Long term follow-up was obtained with annual outpatient visits and was available for 2067 patients (81.8%).

Operative technique:

The initial operative technique previously reported [11] has undergone changes over the years. At the beginning of our experience, the patient was, positioned in a lateral position, as we approached the heart through a fourth/fifth intercostal space with a full posterolateral thoracotomy; our primary aim was to avoid the median sternotomy and achieve good exposure. The approach to the ascending aorta for the proximal vein graft anastomosis was a challenge as was the use of bilateral internal thoracic arteries.

In our current technique: the patient is positioned 30 degrees laterally with the left arm gently elevated. The upper and lower side of the incision is injected with 20 to 40 milliliters of 0.25% bupivacaine solution to at the beginning and end of the procedure for pain management. An anterior thoracotomy (7 to 12 cm) is carried out and the chest entered in the fifth intercostal space (figure 1). This allows revascularization of both left and right sided territories without excessive displacement of the heart. Access to the ascending aorta is achieved using pericardial suspension sutures, placed on the right side of the pericardium close to the aorta to provide enough traction to perform the anastomosis (figure 2). Harvesting of the left internal thoracic artery (LITA) is performed under direct vision using diathermia with a long tip extension and a special bayonet forceps (CERAMO® PLANO-S Fehlings Instruments), after the LITA is harvested systemic heparin is administered aiming for an activated clotting time above 350 sec, the LITA is then clipped distally, transected and gently sprayed with papaverine solution (figure 3). The right pleura is then opened, and two lap sponges are placed to gentle retract the right lung and improve visualization of the right internal thoracic artery (RITA) which is then harvested in a skeletonized fashion using specially designed forceps (CERAMO® Guida Forceps Fehlings Instruments). The RITA is harvested full length (figure 4) and can be used as an in-situ graft, “y” graft with LITA, or when prolonged with a radial artery or a great saphenous vein graft (SVG) for sequential grafting.

Once both ITAs are harvested, if performing an aorta-touched technique, the proximal anastomoses are done first, access to the aorta is facilitated by partially opening the pericardium and utilizing four pericardial suspension sutures as described above. The distal anastomoses are performed on the beating heart with standard stabilizer, starting from left anterior descending (LAD), diagonal (Diag), intermediate (Interm), obtuse marginal (OM), and lastly posterior descending artery (PDA) or right coronary artery (RCA). After opening the coronary an intracoronary shunt is introduced in the lumen. The distal anastomoses (figure 5) are performed with a single running 7-0 or 8-0 polypropylene suture. Graft quality is routinely checked using transit time flow measurement (Medistim VeriQ™). Heparin is reversed, and two thoracic silicone drains are placed (Blake Ethicon) on the left pleura and the right across the mediastinum with care to avoid the grafts. The thoracic incision is closed in a standard manner.

We aim to routinely extubate patients on the operating table as part of our fast-track protocol prior to transfer them to the intensive care unit (ICU).

Once discharged patients on the first week after surgery are routinely monitored at least twice a day by our team of visiting nurses. Patients are then follow-up in outpatient's clinic at 1 and 2 weeks, 1, 2 and 6 months and then at yearly intervals.

Outcome Measures and definitions

30-day mortality was defined as a death by any cause occurred at any time during the first 30 days after surgery. New neurological impairment was defined as a new post-operative stroke identified clinically and/or by CT scan that happened during the post-operative course and determined a permanent neurological impairment. In addition, we collected generic in-hospital outcome including reopening for bleeding, atrial fibrillation and duration of hospital stay. Major adverse cardiovascular events were defined as death from any cause or repeated revascularization or new major neurological event. Furthermore, we assessed 1, 5 and 10-year survival defined as any cause of death.

Statistical analysis

Data are presented as mean ± one standard deviation for numeric continuous variables and as per total number and percentages for categoric variables. Survival

analysis was conducted using Kaplan–Meier methods. A parsimonious multiple logistic regression model was done to identify the independent predictors for operative mortality: this model was run only on the patients of center A (n= 1404), due to lack of some preoperative variables in center B. The statistical software used was R version 3.5.0, R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

Results

From January 2002 to December 2017 a total of 2528 consecutive patients (578 female, mean age 62.3 ± 9.1 years) underwent coronary artery bypass surgery on the beating heart using the left thoracotomy approach. Baseline characteristics are presented in table 1 and early post-operative outcomes in table 2. Total arterial revascularization was achieved in 373 patients (14.7%) and exclusively venous graft revascularization in 115 patients (4.5%). The remaining patients received a combination of arterial and venous grafts. The average number of grafts was 2.8 ± 0.9: 212 patients received 1 graft (8.3%), 479 patients two grafts (18.9%), 1364 patients 3 grafts (53.9%) and 439 (17.4%) patients more than 3 grafts (data was not available for 40 patients).

There was no conversion to median sternotomy in the whole series and 6 patients (0.2%) were converted to on-pump (two for anaphylactic reaction to protamine, and four for hemodynamic instability). Overall 30-day mortality was 1.0% (25 patients).

After multiple logistic regression modelling (with backward selection) only three variables were identified as independent predictor for short term mortality and these were female gender (OR=9.2, 95% CI:3.2-30.6, p <0.01) reoperation (OR=4.5, 95% CI 0.66-18.3, p = 0.06) and reduced LVEF (OR=6.1, 95% CI 2.1-19.02, p < 0.01).

Most patients had a fast-track protocol and were extubated in theatre (97.3%), with 47 patients (1.9%) requiring re-exploration for bleeding. Seven patients (0.3%) experience a cerebrovascular event, four (0.3%) a post-operative myocardial infarction and 84 (3.4%) had new onset of atrial fibrillation. 1510 patients (61.1%) were discharged from hospital in the first 48 hours post-surgery. Readmission to hospital in the first 30 days from discharge was 0.5%. Long term survival rates were

98.8%, 93.6% and 69.1% at 1,5 and 10 years respectively (central figure). During follow-up, sixty patients (2.9%) required new coronary angiogram, of those 24 patients (1.2%) required PCI and 11 (0.5%) redo surgery (table 3).

Discussion

This study provides evidence that coronary artery bypass on the beating heart via a left thoracotomy is safe, with good early mid and long-term outcome while avoiding the morbidity associated with median sternotomy. Using a relatively small incision it is possible to mobilize both internal thoracic arteries and gain access to the ascending aorta to perform proximal graft anastomosis. The displacement of the heart is minimal for distal coronary grafting, hence reducing hemodynamic and electrical instability. This combined with our fast-track protocol allowed extubating of most patients in the operating theatre. We were also able to discharge most patients in the first 48 post-operatively, by a combination of early extubation, mobilization and pain control, associated with close home visit by our nurses' team.

Our early and mid-term outcomes compare favorably with previous large case reports and prospective randomized trials on patients having conventional sternotomy on-pump or off-pump CABG [13,14,15] and minimally invasive CABG 16,17]

The slightly inferior long-term results of our cohort may be explained in the context of the patients' socioeconomic and health provision status, of a developing country [18].

The left thoracotomy approach has been previously proposed by other groups to reduce the morbidity associated with conventional sternotomy but also in the hope to reduce post-operative pain and facilitate a quicker return to normal life activity [13,14,15]. However, concern remains on the applicability of the technique and the possibility of increased post-operative pain from excessive rib retraction and occasional fracture. In the only randomized clinical trial conducted of median sternotomy versus left lateral thoracotomy the benefits of thoracotomy, reduced inflammatory response, shorter intubation times, and fewer arrhythmias, were offset by longer operations, a greater need for postoperative pain relief, worse lung

function at discharge, and higher costs [19]. Patients' quality of life at 12 months was also similar with the two procedures. These results were at odds with the benefits reported in observational studies. One possible explanation for this and for the main barrier to the implementation of the left thoracotomy technique is the learning curve, a problem that is shared with most minimally invasive techniques on centers that previously used a standard technique.

Of interest, whereas at Fundacardio Foundation the procedures were performed all by the senior surgeon, the second center Ascardio Foundation is a teaching hospital and left thoracotomy is the routine approach for isolated CABG operations. This does not affect juniors' development as they are trained hands-on on this technique.

This study has several limitations. First, its retrospective design (prospectively collected data) might be suggestive of residual bias and unconsidered factors.

Second, our patient's cohort was treated over a long period, thus possibly introducing confounding factors owing to changes in clinical practice over time, like advances on the surgical technique, changes in medical therapy, and on the risk profile of patients referred to cardiac surgery.

Third, due to the long time period of this cohort the variable of completeness of revascularization was not available for the entire cohort, which is a variable that demonstrates feasibility of the technique.

Despite the changes in practice overtime the current technique is in line with the latest ESC/EACTS Guidelines on Myocardial Revascularization keeping with section 15 procedural aspects of coronary artery bypass grafting and subsection 15.1.9 Minimally invasive and hybrid procedures. [20]

In conclusion, the left thoracotomy is a safe alternative to median sternotomy for coronary artery bypass grafting on the beating heart, with low early complications and good mid and long-term results.

Acknowledgement

Fundacardio Foundation in Valencia and Ascardio Foundation in Barquisimeto – Venezuela are charities foundations which provided patients with the means to afford their operations and extensive support both before and after surgery. We wish to thank the medical and surgical staff for their help.

Funding: This study was funded/supported* by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

Conflict of interests

None declared

Figures

Central figure: Kaplan Meier Survival curve (note the rang is from 100%-50% to highlight the changes over time)

Figure 1. Operative incision

Figure 2. Aorta exposure and pericardial suspension

Figure 3. LITA harvesting

Figure 4. LITA and RITA harvested

Figure 5. LITA to intermediate and RITA to LAD anastomoses

Tables

Table 1.

Variables	Center A and B (n=2528)	Center A
Age	63.3 ± 9.1 (range 28-90)	
Sex	Female: 578 (22.9%) Male: 1947 (77.1%)	
Poor EF ≤30%		128 (9.5%)
Hypertension		1249 (91.5%)
DM		571 (41.8%)
CKD		170 (12.4%)
Previous MI		616 (45.1%)
Previous stroke		13 (0.9%)
NYHA class III/IV		281 (20.8%)
Previous PCI		101 (10.3%)
PVD		167 (12.2%)
Left main disease		343 (25.1%)
Redo cardiac surgery		48 (3.5%)
Euroscore	3.73±3.14	
Logistic Euroscore	4.58 ± 7.56	

Table 1. Preoperative characteristics: Data available only from center A (Fundacardio foundation) is specified on the center A column, the rest of the data is available from both centers. Percentage is calculated on the available data without counting missing values

283 Table 2.

Variables	Center A and B (n=2528)	Center A
Re-exploration for bleeding	47 (1.9%)	
Extubated in the OR		1321 (97.3%)
Postoperative MI		4 (0.3%)
New onset of AF	84 (3.4%)	
New neurological impairment	7 (0.3%)	
30-day Mortality	25 (1.0%)	
ICU length of stay		
≤ 24 hours	2387 (95.7%)	
> 24 ≤ 48 hours	92 (3.7%)	
> 48 hours	14 (0.6%)	
Hospital length of stay		
≤ 48 hours	1510 (61.1%)	
> 48 ≤ 72 hours	830 (33.6%)	
>72 hours	132 (5.3%)	

Table 2. Post-operative characteristics: Data available only from center A (Fundacardio foundation) is specified on the center A column, the rest of the data is available from both centers. Percentage is calculated on the available data without counting missing values

284

285 Table 3.

Variables	Patients both Centers (n=2023)
New angiogram	60 (2.9%)
MACCE	63 (3.1%)
Redo-CABG	11 (0.5%)
Redo-PCI	24 (1.2%)
Late mortality	328 (15.8%) †

Table 2. Post-operative characteristics: Data available only from center A (Fundacardio foundation) is specified on the center A column, the rest of the data is available from both centers. Percentage is calculated on the available data without counting missing values.
†: Survival data were available for

286

References

[1] Head SJ, Kieser TM, Falk V, Huysmans HA, Kappetein AP. Coronary artery bypass grafting: Part 1--the evolution over the first 50 years. Eur Heart J. 2013 Oct;34:2862-72.

[2] De Feo M, Della Corte A, Vicchio M, Pirozzi F, Nappi G, Cotrufo M. Is post-sternotomy mediastinitis still devastating after the advent of negative-pressure wound therapy? Tex Heart Inst J. 2011;38:375-80

[3] Benetti FJ, Ballester C, Sani G, Boonstra P, Grandjean J. Video-assisted coronary bypass surgery. J Card Surg 1995;10:620–5.

[4] Gulielmos V, Brandt M, Knaut M, Cichon R, Wagner FM, Kappert U, et al. The Dresden Approach for Complete Multivessel Revascularization. Ann Thorac Surg 1999 Oct;68:1502–5

[5] Calafiore AM, Angelini GD, Bergsland J, Salerno TA. Minimally Invasive Coronary Artery Bypass Grafting. Ann Thorac Surg 1996 Nov;62:1545-8

[6] Angelini GD, Wilde P, Salerno TA, Bosco G, Calafiore AM. Integrated left anterior small thoracotomy and angioplasty for multivessel coronary artery revascularization. Lancet 1996 Mar;347:757-8.

[7] Murphy GJ, Bryan AJ, Angelini GD. Hybrid coronary revascularization in the era of drug-eluting stents. Ann Thorac Surg. 2004 Nov;78:1861-7

[8] Lloyd CT, Calafiore AM, Wilde P, Ascione R, Paloscia L, Monk CR, et al. Integrated left anterior small thoracotomy and angioplasty for coronary artery revascularization. Ann Thorac Surg. 1999 Sep;68:908-11

[9] Guida GA, Chivasso P, Fudulu D, Rapetto F, Sedmakov C, Marsico R, et al. Off-pump coronary artery bypass grafting in high-risk patients: a review. J Thorac Dis. 2016 Nov;8: S795-S798

[10] Nierich AP, Diephuis J, Jansen EW, Borst C, Knape JT. Heart Displacement During Off-Pump CABG: How Well Is It Tolerated? Ann Thorac Surg 2000;70:466-72

[11] Guida MC, Pecora G, Bacalao A, Muñoz G, Mendoza P, Rodríguez L. Multivessel Revascularization on the Beating Heart by Anterolateral Left Thoracotomy. Ann Thorac Surg 2006; 81:2142-6

[12] Srivastava S, Gadasalli S, Agusala M, Kolluru R, Naidu J, Shroff M, et al. Use of bilateral internal thoracic arteries in CABG through lateral thoracotomy with robotic assistance in 150 patients. Ann Thorac Surg. 2006 Mar;81:800-6

[13] Mohr FW, Morice MC, Kappetein AP, Feldman TE, Ståhle E, Colombo A, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet. 2013 Feb 23;381:629-38

[14] Kim JB, Yun SC, Lim JW, Hwang SK, Jung SH, Song H, et al. Long-Term Survival Following Coronary Artery Bypass Grafting Off-Pump Versus On-Pump Strategies. J Am Coll Cardiol. 2014 Jun 3;63:2280-8.

[15] Angelini GD, Taylor FC, Reeves BC, Ascione R. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet. 2002 Apr 6;359:1194-9.

[16] Holzhey DM, Cornely JP, Rastan AJ, Davierwala P, Mohr FW. Review of a 13-year single-center experience with minimally invasive direct coronary artery bypass as the primary surgical treatment of coronary artery disease. Heart Surg Forum. 2012 Apr;15:E61-8.

[17] Sorm Z, Harrer J, Voborník M, Cermáková E, Vojácek J. Early and long-term results of minimally invasive coronary artery bypass grafting in elderly patients. Kardiol Pol. 2011;69:213-8.

[18] Dzayee DA, Ivert T, Beiki O, Alfredsson L, Ljung R, Moradi T. Short and long term mortality after coronary artery bypass grafting (CABG) is influenced by socioeconomic position but not by migration status in Sweden, 1995-2007. PLoS One. 2013 May 22;8:e63877.

[19] Rogers CA, Pike K, Angelini GD, Reeves BC, Glauber M, Ferrarini M, et al. An open randomized controlled trial of median sternotomy versus anterolateral left thoracotomy on morbidity and health care resource use in patients having off-pump coronary artery bypass surgery: the Sternotomy Versus Thoracotomy (STET) trial. J Thorac Cardiovasc Surg. 2013 Aug;146:306-16.e1-9.

[20] Miguel Sousa-Uva, Franz-Josef Neumann, Anders Ahlsson, Fernando Alfonso, Adrian P Banning, Umberto Benedetto, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization, Eur J Cardiothorac Surg. 2019 Jan 1;55:4-90