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# Original article

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#### ABSTRACT

*Background:* The aim of this paper is to describe a newly developed endoscopic coronary artery bypass graft (Endo-CABG) technique to treat patients with single- and multi-vessel disease and discuss the short-term clinical results in a large patient cohort. This technique avoids a median sternotomy by combining a thoracoscopic technique via three  $\sim$ 5 mm thoracic ports and a mini-thoracotomy utility 3–4 cm port through the intercostal space.

*Methods:* From January 2016 to January 2018, data from consecutive patients undergoing an elective Endo-CABG were prospectively entered into a customized database and retrospectively reviewed. Patients scheduled for a combined hybrid intervention were excluded. Conversion rate to sternotomy, incidence of surgical revision and postoperative graft failure, one-month survival, morbidity, and length of stay (LOS) were investigated. Subgroup analyses were performed.

*Results:* A total of 342 patients undergoing an Endo-CABG with one (n=53) or multiple (n=289) bypasses were included. No conversion to sternotomy occurred and incidence of surgical revision, graft failure, and 30-day mortality was 7.3%, 1.5%, and 1.8%, respectively. Adverse neurological outcomes were rare: cerebrovascular accident, transient ischemic attack, epilepsy, and postoperative delirium were observed in 0.6%, 0.3%, 0.3%, and 5.3% of patients, respectively. Median intensive care unit and hospital LOS were 2.75 (IQR 1.8 to 3.8) and 8.0 days (IQR 7.0 to 10.0), respectively. Thirty-day mortality in obese patients, diabetics, and octogenarians was 0%, 3.6%, and 5.6%, respectively. EuroSCORE II > 5% was associated with a high 30-day mortality (25%).

Conclusions: Endo-CABG can be considered a safe and effective procedure to treat single- and multivessel coronary artery disease. Individual patient selection seems not necessary to apply this technique. © 2020 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

#### Introduction

Coronary artery bypass graft (CABG) remains the standard of care for patients with multi-vessel coronary artery disease [1]. Although traditional CABG is performed via median sternotomy, this surgical access route is associated with major disadvantages such as a prolonged recovery time, a poor cosmetic result, and a significant risk of chronic post-sternotomy pain, as well as several potential complications, including sternal instability, delayed bone healing, and wound infections [2]. Diabetes, obesity, and large breast size in females are important risk factors for sternal wound complications and therefore relative contraindications for bilateral internal mammary artery (BIMA) grafting via classic sternotomy. To overcome these restrictions, less invasive access routes to the heart, including mini-thoracotomy or partial opening of the sternum have been investigated since the mid-1990s. During the past decade, these minimally invasive procedures have increased in popularity, are more commonly applied, and have even become the routine method in several centers around the world [3]. They are proven to be safe and feasible [4] with excellent surgical outcomes, including a reduced patient recovery time [5], lower transfusion rates, less wound infections, shorter hospitalization time, and low hospital mortality rate [6].

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 $<sup>\,</sup>$  All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Currently recognized forms of minimally invasive CABG with preservation of sternal integrity, include minimally invasive direct coronary artery bypass (MIDCAB) and video- or robotically assisted techniques [e.g. totally endoscopic coronary artery bypass (TECAB)] [7]. MIDCAB is performed through a left-anterolateral thoracotomy using rib-spread and is restricted to grafting the left internal mammary artery (LIMA) to the left anterior descending artery (LAD) (or side branches of the LAD) without cardiopulmonary bypass [8]. Right internal mammary artery (RIMA) grafting is not possible with this technique without an additional thoracotomy for dissection of the RIMA. In contrast, endoscopic techniques using video-assisted thoracoscopic surgery (VATS) or robotic technology do not require a second thoracotomy and have the advantage of precisely identifying an optimal thoracotomy location via visualization of the thoracic cavity and being less invasive in incision length without use of rib-spread. However, the complexity of these procedures restricts the practical implementation to specialized centers. Also, technical difficulties and complications (e.g. robotic malfunctioning), as well as appropriate patient selection [9] are important factors that determine surgical success rate. Importantly, these techniques are also mainly restricted to single vessel bypass grafting and less complex anatomy [9]. Other limitations of the robotically assisted technique include increased financial cost, heterogeneous clinical outcomes, and prolonged operative duration [10].

Therefore, we have developed and implemented a new minimally invasive CABG (Endo-CABG) technique to treat patients with single- and multi-vessel coronary artery disease regardless of which vessel is involved. With the Endo-CABG technique, all walls of the heart can be easily grafted and no specific patient selection is required, making this a suitable technique to treat all patients, including those with increased risk factors [e.g. morbid obesity, diabetes [11], elderly (>80 years) or patients with thoracic deformations (e.g. scoliosis)]. This technique avoids a median sternotomy by combining a thoracoscopic technique via three  $\sim$ 5 mm thoracic ports and a mini-thoracotomy utility 3–4 cm port through the intercostal space. The aim of this paper is to describe this newly developed technique and discuss the short-term clinical results in a large patient cohort undergoing an Endo-CABG for single- and multi-vessel disease.

#### Methods

From January 2016 to January 2018, data from 423 consecutive patients undergoing an elective Endo-CABG for single- or multivessel disease at the Department of Cardiothoracic Surgery of the Jessa Hospital, Belgium, were prospectively entered into a customized database that included baseline characteristics, perioperative variables, and postoperative outcomes. This database was then merged with data from the Belgian Association for Cardio-Thoracic Surgery and retrospectively reviewed. Perioperative outcomes included conversion rate to sternotomy, total intraoperative and postoperative blood loss, aortic clamping and perfusion time, ventilation time, incidence of surgical revision and postoperative graft failure, one-month survival, morbidity, length of stay (LOS) in the intensive care unit (ICU), and hospital LOS. All surgical procedures were performed by a single surgeon (A. Y.) who was already highly experienced in performing the procedure. Patients scheduled for a combined hybrid intervention, i.e. minimally invasive bypass CABG with subsequently catheterbased coronary intervention, were excluded. Non-elective cases were also excluded. This study was approved by the ethics committee of the JESSA Hospital Hasselt on October 12th 2018 (ethical committee N°: 18.79/carchir18.02, chairperson: Dr K. Magerman). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

#### Endo-CABG: description of operative technique

After induction of general anesthesia, surgery is performed in supine position.  $CO_2$ -induced controlled pneumothorax (6–8 mmHg), to create sufficient working space, is applied to avoid the need for selective lung ventilation. When selective lung ventilation is needed, a bronchus-blocker (Teleflex Medical Europe Ltd, Athlone, Co Westmeath, Ireland) is utilized.

LIMA and/or RIMA are harvested ipsi- or contra-laterally through three  $\sim$ 5 mm endoscopic ports in the 2nd, 3rd, and 4th intercostal space, approximately 2 cm above and below the anterior axillary line in a triangular configuration (Fig. 1). The mammary artery is harvested with its adjacent veins in a typical fashion using "normal" long-shafted VATS instruments, small endoscopic clip-applicator, and a 5 mm zero-degree camera. After completing the dissection, the patient is heparinized, distal parts of the mammary arteries are clipped and transected, taking special care not to twist the pedicle. The pericardium is freed from any additional fat and opened anteriorly to the left phrenic nerve to visualize and identify all target vessels. Typically, a 3-4 cm skin incision is made through the selected intercostal space and a soft tissue retractor (Shanghai International Holding Corporation GmbH, Hamburg, Germany) is placed to enable sufficient view of the heart (Fig. 1). Selection of the exact intercostal space for the mini-thoracotomy is based on the location of the target coronary vessel. This is achieved by simple transthoracic needle insertion through the selected space under VATS-vision. Intercostal space II and III close to the midline are mainly selected. Rarely, it is necessary to relocate the intercostal space through the same skin incision to reach all target vessels.

Cardiopulmonary bypass is achieved using retrograde perfusion via peripheral cannulation of the common femoral artery and vein through a 2 cm oblique skin incision below the inguinal ligament. Care is taken not to damage any adjacent lymph nodes and vessels to minimize postoperative lymphedema. Both common femoral vessels are ventrally exposed, a safe place for the position of the cannulas is identified, and purse string sutures are put in place using 5-0 prolene. Depending on the patient's size and thus on magnitude of extracorporeal circulation (ECC) flow needed, a 17-21 Fr arterial cannula and 21-25 Fr multi-stage drainage venous cannula (Medtronic Inc., Minneapolis, MN, USA) are inserted with Seldinger technique. Cardiopulmonary bypass (CPB) is performed using a minimally invasive ECC system [the mini-Inspire JESSA MiECC (Sorin S.p.A., Mirandola, Italy)]. This technique has been reported in Perfusion [12]. Patients undergoing single vessel LIMA-LAD are also placed on MiECC CPB to decompress the heart but do not receive cardioplegia. This no-touch-aorta technique is an empty beating approach to reduce technical surgical difficulty. All other patients receive cardioplegia. A Pledgeted purse-string suture for antegrade cardioplegia is placed endoscopically through the right-sided port at the ascending aorta. After complete decompression of the right atrium, a transthoracic clamp is placed at the ascending aorta through the 2nd right intercostal space in the anterior axillary line. Direct aortic cross clamping is followed by antegrade cardioplegia through a transthoracic puncture of the ascending aorta. In our experience, 800 ml of mixed blood cardioplegia in a 3:1 ratio (blood:crystalloid) through a 14 gauge Secalon TTM catheter (Argon critical care systems, Singapore, Pte. Ltd., Singapore) is sufficient for cardioplegic arrest and completion of all required anastomoses. This Secalon TTM catheter is kept in position and is used for venting of the aortic root, achieving a total empty heart. Since proximal anastomoses (with venous graft or radial artery) are never constructed, the manipulation of the ascending aorta is limited to transthoracic aortic clamping. All



**Fig. 1.** Picture of three  $\sim$ 5 mm thoracic ports and a mini-thoracotomy utility 3–4 cm port through the intercostal space. An additional  $\sim$ 5 mm subxiphoid port was placed for the placement of a subxyphoid rigid holder.

target coronary vessels, including the right coronary artery, can be visualized and reached by gentle manipulation of the emptied heart by a subxyphoid introduced endoscopic clamp holding a peanut gauze. Additional epicardial stay sutures with prolene 6/0 laterally to the target vessels are used when necessary. To visualize and anastomose target vessels on the lateral wall, the empty heart has to be pushed up and tilted to the midline. When the posterior descending artery needs to be anastomosed, the inferior wall of the empty heart has to be pushed cranially. Anastomoses with LIMA and/or RIMA are performed through the above chosen intercostal space in a typical fashion using normal Castroviejo needle-holders. When necessary, a Y-graft construction is created intrathoracically by performing an end to side anastomosis of free RIMA (and/or rarely venous graft) to in situ LIMA through the mini-thoracotomy utility 3-4 cm port. An intracoronary shunt is used to create a blood-free operative field in case of back bleeding. After completing the anastomosis, the aortic clamp is released and the grafts are checked for possible distention, twists, or leakage before the patient is weaned from cardiopulmonary bypass and an appropriate dose of protamine is administered. The pericardium is always closed by separated sutures, leaving only the entrance space for the LIMA or RIMA. Pericardial drainage is only used when necessary. Chest tubes are placed in both thoracic cavities with negative suction (-15 cm water). Surgical wounds are closed with uninterrupted intradermal sutures and simple stitches (Fig. 2).

# Statistics

Descriptive statistics are presented as mean (SD), median (min.-max), or number (%). To maintain paired samples, data were



Fig. 2. Picture of surgical wound sutures.

excluded from analyses regarding blood chemistry and/or hematology when either pre- or postoperative values were missing. All variables were checked for normality and variables were transformed to satisfy conditions of normality (C-reactive protein, leukocytes, urea, creatinine). Pre- and postoperative blood chemistry and hematology data were analyzed with a paired sample T-test. A *p*-value of <0.05 is considered statistically significant. All analyses were performed using IBM SPSS v.18.0 for Windows (IBM, Chicago, IL, USA).

#### Results

During the study period, 423 patients underwent elective Endo-CABG in our hospital. In total, 81 patients that were scheduled for a hybrid approach, were excluded. This resulted in data of 342 patients that underwent Endo-CABG for single- (15.5%) or multi-vessel (85.5%) disease for the final analysis. Patient characteristics are presented in Table 1.

Details of graft material, target vessels, and graft design are shown in Table 2. In case both mammary arteries were used (n = 254), the construction consisted of BIMA in situ (n = 112) or in a Y-graft construction (n = 142). Y-graft construction was normally required to bypass the posterolateral and/ or inferior wall, especially in cases of more than three anastomoses.

Subgroup analysis of surgery details are presented in Table 3. All patients were successfully treated with this newly developed minimally invasive technique: perioperative mortality was absent, no procedure had to be aborted, and no conversion to sternotomy occurred. On average, three bypasses per patient were performed. All patients received a total arterial revascularization in convenience with perioperative surgical findings. A total of 76 patients (22%) required blood transfusion and 30 patients (8.8%) required thrombocyte transfusion. Blood chemistry and hematology data are shown in Table 4.

Postoperative outcomes are presented in Table 5. Median ICU LOS was 2.75 days (IQR 1.8 to 3.8 days) and median hospital LOS was 8.0 days (IQR 7.0 to 10.0 days). A surgical revision was performed in 25 (7.3%) patients because of excessive postoperative bleeding. All these revisions were performed endoscopically without conversion to sternotomy. Hemorrhage was caused by bleeding of the anastomoses (n = 16) or the thoracic wall (n = 2), pleural hemorrhage (n = 3), bleeding elsewhere (e.g. thymus) (n = 2), or without clear cause (n = 2). Prolonged ventilation, defined as an extubation time of >24 h, >48 h, and >72 h, occurred in 27 (7.9%), 18 (5.3%), and 10 (2.9%) patients, respectively. Seventy patients (20%) had a prolonged stay at the ICU (>4 days) [13], with a maximum ICU stay of 44 days. In 72 patients (21%), overall hospital stay was >10 days (maximum hospital stay was 134 days).

Five patients (1.5%) required a rescue percutaneous transluminal coronary angioplasty (PTCA) due to postoperative graft failure (defined as a complete dysfunctional anastomosis). Three patients (0.8%) required a longer follow-up due to small wound healing problems. Adverse neurological outcomes were rare (Table 5). Thirty-day mortality rate was 1.8% (n = 6). None of the postoperative deaths were due to graft failure. Four patients (75year-old female, 67-year-old male, 78-year-old male, and 83year-old male) suffered from respiratory insufficiency and/or hemodynamic collapse causing multi organ failure. Cardiac mortality risk profile in these 4 patients was very high. Finally, 1 patient (75-year-old female) with pre-existing pleuropericarditis died from severe systemic inflammatory response syndrome and 1 patient (84-year-old male) died suddenly during the first postoperative night without any warning signs after an uncomplicated Endo-CABG.

#### Table 1

Patients' baseline characteristics.

| Variable                                     | (n=342)          |
|--|------------------|
| Age (years)                                  | $66.8 \pm 9.9$   |
| Gender (male), n (%)                         | 268 (78.4%)      |
| BMI $(kg/m^2)$                               | $27.6 \pm 4.3$   |
| <20.0, n (%)                                 | 5 (1.5%)         |
| 20.0–24.9, n (%)                             | 95 (27.8%)       |
| 25.0–29.9, n (%)                             | 154 (45,0%)      |
| 30.0–39.9, n (%)                             | 83 (24.3%)       |
| >40.0, n (%)                                 | 5 (1.5%)         |
| $BSA(m^2)$                                   | $1.93 \pm 4.3$   |
| EuroSCORE II (%)                             | 1.63 (0.49-37.5) |
| NYHA   | 1.5 (1.0-4.0)    |
| NYHA (I–II), n (%)                           | 299 (87.4%)      |
| NYHA (III–IV), n (%)                         | 23 (6.7%)        |
| EF   |                  |
| very poor, n (%)                             | 0 (0%)           |
| poor, n (%)                                  | 7 (2.0%)         |
| moderate. n (%)                              | 54 (15.8%)       |
| good, n (%)                                  | 188 (55.0%)      |
| not determined, n (%)                        | 93 (27.2%)       |
| Comorbidities                                | . ,              |
| Diabetes, n (%)                              | 111 (32.5%)      |
| Smoker, n (%)                                | 97 (28.4%)       |
| Arterial Hypertension, n (%)                 | 225 (65.8%)      |
| Cholesterol, n (%)                           | 291 (85.1%)      |
| COPD, n (%)                                  | 33 (9.6%)        |
| Medical History                              |                  |
| Atrial Fibrillation, n (%)                   | 39 (11.4%)       |
| Peripheral vascular problems, n (%)          | 52 (15,2%)       |
| Carotid artery stenosis                      |                  |
| Unilateral high grade                        | 15 (4.4%)        |
| Bilateral high grade                         | 7 (2.0%)         |
| Carotid endarterectomy                       | 15 (4.4%)        |
| Combined surgery with Carotid endarterectomy | 2 (0.6%)         |
| Atrial Fibrillation, n (%)                   | 39 (11.4%)       |
| Neurological complications                   |                  |
| CVA, n (%)                                   | 20 (5.8%)        |
| TIA, n (%)                                   | 10 (2,9%)        |
| Epilepsy, n (%)                              | 4 (1.2%)         |
| Syncope, n (%)                               | 8 (2.3%)         |

Data are presented as mean  $\pm$  SD or as number (%).

BMI, body mass index; BSA, body surface area; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; EF, ejection fraction category, classified according to the Belgian Association for Cardio-Thoracic Surgery (<20%: very poor; 21–29%: poor; 30–49%: moderate;  $\geq$ 50%: good); EUROSCORE II, European System for Cardiac Operative Risk Evaluation; MI, myocardial infarct; NYHA, New York Heart Association functional classification; TIA, transient ischemic attack.

#### Subgroup analyses

A single bypass surgery was performed in 52 patients [age:  $65.2\pm8.9$  years; male: 39 (75.0%)]. The New York Heart Association classification was  $1.4\pm0.70$  and the EuroSCORE II was

#### Table 2

Details of source of graft material, target vessels, and graft design

 $2.21\pm5.3$ . A revision was performed in one patient due to hemothorax with clinical instability (although no hemorrhage was found) and graft failure in two (3.8%) patients required a rescue PTCA with stenting. Thirty-day mortality and postoperative neurological complications were absent in this subgroup.

In this cohort, 88 patients were obese (body mass index >30,0) [age:  $64.7 \pm 9.2$  years; male: 69 (78.4%)]. Diabetes mellitus was present in 111 patients [age:  $67.0 \pm 9.4$  years; male: 85 (76.6%)] and 36 patients were octogenarians [age:  $83.4 \pm 2.5$  years; male: 27 (75.0\%)]. Postoperative outcomes are presented in Table 4.

Based on the Euroscore II, we stratified our patients according to their cardiac mortality risk profile [low-risk profile (<2.0%), moderate-risk profile (2.0-5.0%), and high-risk profile (>5.0%)] [14]. Postoperative outcomes of these groups are presented in Table 5.

# Discussion

In this retrospective study, we describe a newly developed minimally invasive coronary artery bypass grafting (Endo-CABG) technique to treat single- and multi-vessel coronary artery disease and report the short-term clinical outcomes of this technique in a large non-selected patient cohort.

In our patient cohort, perioperative mortality was absent, no Endo-CABG procedure had to be aborted, and no conversion to sternotomy occurred. Excessive postoperative bleeding required a relook procedure, performed by VATS surgery, in 7.3% of patients. Prolonged stay at the ICU and overall hospital stay was observed in respectively 20% and 21% of all patients. Post-operative graft failure was observed in only 1.5% of patients and 30-day mortality was 1.8%. The incidence of adverse neurological outcomes was low: cerebrovascular accident, transient ischemic attack, epilepsy, and postoperative delirium were observed in 0.6%, 0.3%, 0.3%, and 5.3% of patients, respectively. These results are comparable with the results of a minimally invasive CABG through a small thoracotomy approach (MIDCAB) [6]. Our results regarding conversion to sternotomy are even superior to the 19.4% sternotomy conversion rate reported by West et al. [15] in patients undergoing an endoscopic atraumatic coronary artery bypass (Endo-ACAB) procedure and the conversion rates of 1.8% after a MIDCAB surgery [16].

The observed graft failure of 1.5% in our patient cohort echo those of previous trials on graft failure after both traditional and minimally invasive CABG: the meta-analysis by Wang et al. [17] showed a graft stenosis 1 year after surgery in 2.5% of patients after traditional CABG, in 1.8% of patients after TECAB, and in 0.8% of patients in robot-assisted CABG (RACAB). It has to be noted that the complexity of anastomoses performed in our cohort was high with 41.5% being a Y-graft anastomosis.

|           |     |              | Source o | of graft mate | erial |      |         | Target | vessel |    |     |     |     |     |
|-----------|-----|--------------|----------|---------------|-------|------|---------|--------|--------|----|-----|-----|-----|-----|
| n° patier | nts | n (bypasses) | LIMA     | RIMA          | BIMA  | Vein | Y-graft | LAD    | Diag   | CX | MO  | RCA | RPD | PLR |
| Total     | 342 |              | 338      | 258           | 254   | 7    | 142     | 335    | 132    | 57 | 187 | 22  | 86  | 20  |
| 2         |     | 6            | 2        | 1             | 1     | 2    | 1       | 2      | 2      | 0  | 2   | 0   | 2   | 1   |
| 7         |     | 5            | 7        | 6             | 6     | 1    | 6       | 7      | 6      | 6  | 5   | 0   | 4   | 2   |
| 63        |     | 4            | 63       | 63            | 63    | 4    | 47      | 62     | 46     | 21 | 48  | 6   | 34  | 5   |
| 107       |     | 3            | 107      | 105           | 105   | 1    | 66      | 105    | 44     | 19 | 75  | 9   | 42  | 10  |
| 110       |     | 2            | 110      | 79            | 79    | 0    | 22      | 109    | 34     | 10 | 57  | 5   | 4   | 2   |
| 53        |     | 1            | 49       | 4             | 0     | 0    | 0       | 50     | 0      | 1  | 0   | 2   | 0   | 0   |

LIMA, left internal mammary artery; RIMA, right internal mammary artery; BIMA, bilateral mammary artery; LAD, left anterior descending artery; Diag, diagonal artery; CX, circumflex artery; MO, marginal obtuse artery; RCA, right coronary artery; RPD, right posterior descending artery; PLR, posterolateral artery of right coronary artery; Y-graft, all Y-grafts with free RIMA.

# Table 3

Subgroup analysis of surgery details.

|   | Total Group<br>(n=342) | Obese<br>(n = 88) | Diabetics<br>(n = 111) | Elderly<br>(n=36)               |
|---|------------------------|-------------------|------------------------|---------------------------------|
| Number of bypass                                    |                        |                   |                        |                                 |
| 1 bypass, n (%)                                     | 53 (15,5%)             | 9 (10.2%)         | 12 (10.8%)             | 3 (8.3%)                        |
| 2 bypasses, n (%)                                   | 110 (32.2%)            | 30 (34.1%)        | 31 (27.9%)             | 11 (30.6%)                      |
| 3 bypasses, n (%)                                   | 107 (31.3%)            | 26 (29.5%)        | 37 (33.3%)             | 12 (33.3%)                      |
| 4 bypasses, n (%)                                   | 63 (18,4%)             | 18 (20.5%)        | 28 (25.2%)             | 6 (16.7%)                       |
| 5 bypasses, n (%)                                   | 7 (2.0%)               | 3 (3.4%)          | 1 (0.9%)               | 1 (2.8%)                        |
| 6 bypasses, n (%)                                   | 2 (0.6%)               | 0 (0%)            | 1 (0.9%)               | 1 (2.8%)                        |
| Y-graft, n (%)                                      | 142 (41.5%)            | 42 (47.7%)        | 59 (53.2%)             | 17 (47.2%)                      |
| Blood loss (ml)                                     | $407.0\pm466.5$        | $448.0\pm446.4$   | $446.8 \pm 437.8$      | $526.2\pm486.8$                 |
| Transfusion (blood) (units)                         | $0.7\pm3.4$            | $0.7\pm3.0$       | $1.3\pm5.6$            | $1.3\pm1.9$                     |
| Transfusion (thrombocytes) (units)                  | $0.2\pm0.8$            | $0.1\pm0.8$       | $0.2\pm1.1$            | $\textbf{0.4}\pm\textbf{1.0}$   |
| Transfusion (Fresh Frozen Plasma) (unit)            | $0.2\pm1.0$            | $0.1\pm0.6$       | $0.3\pm1.5$            | $\textbf{0.6} \pm \textbf{1.2}$ |
| Occlusion time (min)                                | $52.2\pm31.4$          | $57.0\pm29.7$     | $55.9 \pm 28.6$        | $55.1\pm30.6$                   |
| Perfusion time (min)                                | $98.7\pm38.9$          | $106.3\pm38.6$    | $106.2\pm38.1$         | $106.1 \pm 35.5$                |
| Data are presented as mean $\pm$ SD or numbers (%). |                        |                   |                        |                                 |

#### Table 4

Blood chemistry and hematology.

| Variable                             | Pre-operative  | Post-operative   | <i>p</i> -value |
|--------------------------------------|----------------|------------------|-----------------|
| Leukocytes (x109/L)                  | $8.0\pm0.16$   | $13.4\pm0.27$    | < 0.001         |
| Thrombocytes (x109/L)                | $230.6\pm3.86$ | $181.2 \pm 3.37$ | < 0.001         |
| Hemoglobin (g/dl)                    | $13.7\pm0.09$  | $11.6\pm0.08$    | < 0.001         |
| Hematocrit (%)                       | $39.7\pm0.24$  | $33.8\pm0.24$    | < 0.001         |
| C-reactive protein (mg/L)            | $6.5\pm0.85$   | $48.9\pm2.0$     | < 0.001         |
| Creatinine (mg/dl)                   | $1.3\pm0.11$   | $1.2\pm0.05$     | 0.427           |
| Urea (mg/dl)                         | $40.3\pm1.06$  | $37.8 \pm 0.97$  | < 0.001         |
| Data are presented as mean $\pm$ SD. |                |                  |                 |

Our observed 30-day mortality rate of 1.8% after Endo-CABG is lower compared to traditional CABG. Indeed, two large, highquality randomized controlled trials [18,19] showed a 30-day mortality rate ranging from 2.5% to 2.8%, with no significant difference between off-pump coronary artery bypass and conventional CABG. However, our data are consistent with previously published reports of short-term mortality after minimally invasive CABG. While 30-day mortality rates of 0.8% to 1.9% [16,20] have been reported after a MIDCAB procedure (single-vessel), no deaths were reported within 30 days after minimally invasive CABG via a 4–7 cm left thoracotomy approach [6], a 0.3% mortality rate was shown after either TECAB or RACAB [17], and 1% mortality rate after Endo-ACAB [21].

Although it has been stated that retrograde arterial perfusion may be associated with an increased stroke risk [22], only 2 (0.6%) patients suffered a stroke in our cohort. Moreover, the observed delirium incidence of 5.3% after Endo-CABG is low compared to the reported incidence of 32.4% after traditional CABG [23]. We speculate that a lower need for pain medication, combined with a less pronounced systemic inflammatory response after Endo-CABG may explain these observations. Currently, poor neurocognitive outcome after Endo-CABG procedure is being investigated in a prospective observational cohort study [24].

Surgical revision rate for excessive bleeding (7.3%) in this cohort is at the higher end of the reported spectrum in the literature of 2– 6% after conventional cardiac surgery [25]. After MIDACB and TECAB [10], it ranges from 0% to 8.5% with a pooled incidence of 2.7% and 3.2%, respectively. There may be several explanations for this observation. First, dual antiplatelet therapy was not stopped preoperatively. Second, checking for bleeding from distal anastomoses located at the inferolateral wall is more challenging after releasing the aortic cross-clamp. Third, threshold for surgical revision is low in our hospital. It is also performed through the mini-thoracotomy port and therefore we believe that the impact is lower compared to revision after conventional CABG.

In the past two decades, several minimally invasive techniques have been developed and implemented in cardiac surgery to preserve sternal integrity during CABG. Our newly developed technique, the Endo-CABG, avoids a median sternotomy by combining a thoracoscopic technique via three ~5 mm thoracic ports for LIMA/RIMA harvesting and a mini-thoracotomy utility 3–4 cm port through the intercostal space to enable sufficient view of the heart and all target vessels.

This technique may offer patients significant benefits compared to other minimally invasive CABG techniques. First, in contrast to other minimally invasive CABG techniques [8], all walls of the heart can be easily grafted with Endo-CABG. Our results indicate that Endo-CABG is able to completely revascularize triple-vessel disease. Furthermore, the use of arterial grafts makes this technique the best choice for revascularization with respect to long-term patency. Second, Endo-CABG is less expensive than robotic techniques [10]. Third, it is less time-consuming than robotic techniques. Fourth, in contrast to other CABG techniques [9], individual patient selection is unnecessary, making this a suitable technique to treat also patients with increased risk factors such as old age, obesity, and diabetes. Indeed, 30-day mortality in our cohort of octogenarians (5.5%) is strongly reduced compared to the 16.8% mortality after a conventional CABG procedure in octogenarians [26]. Also, 30-day mortality was absent in our cohort of obese patients, which is strongly reduced compared to the 1.9% and 4.5% mortality after respectively an Endo-ACAB procedure and a conventional CABG in obese patients. Altogether, these data prove that patients with an increased risk profile, can still be treated with an Endo-CABG.

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| Variable  | Total group<br>(n=342)                                   | Obese<br>(n=88)  | Diabetics<br>(n = 111)     | Elderly<br>(n = 36)         | Low-risk group<br>(Euroscore <2.0%)<br>(n= 265) | Moderate-risk group<br>(Euroscore 2.0-5.0%)<br>(n = 62) | High-risk group<br>(Euroscore >5.0%)<br>(n = 8) |
|---|--|--|----------------------------|-----------------------------|---|---|---|
| Ventilation time (h)  | $7.0\pm40.3$   | 7.0 ± 48.8   | $8.0\pm 63.1$              | $9.0 \pm 27.9$              | <b>7.0</b> ±15.8                                | $10.0 \pm 67.3$   | $18.5\pm148.7$                                  |
| Blood loss per 24 h (ml)  | $340.0\pm 628.8$   | $430.0\pm540.3$  | $419.0 \pm 685.9$          | $620.0 \pm 579.9$           | $320.0 \pm 575.7$                               | $430.0 \pm 823.0$                                       | $1040.0 \pm 457.6$                              |
| Atrial Fibrillation, n (%)  | 88 (25.7%)   | 20 (22.7%)   | 28 (25.2%)                 | 13 (36.1%)                  | 65 (24.5%)                                      | 20 (32.3%)  | 1 (12.5%)                                       |
| Surgical Revision, n (%)  | 25 (7.3%)  | 7 (8.0%)   | 10 (9.0%)                  | 4 (11.1%)                   | 13 (4.9%)                                       | 9 (14.5%)   | 3 (37.5%)                                       |
| ICU LOS (hours)   | 66.0 (44.0, 92.0)  | 68.5 (46.0, 96.7)  | 69.0(48.5, 96.0)           | 89.0 (64.0, 110.5)          | 63.0 (43.0, 89.0)                               | 71.5 (49.5, 111.5)                                      | 129.0 107.7, 160.5)                             |
| ICU LOS (days)  | 2.8 (1.8, 3.8)   | 2.9 (1.9, 4.0)   | 2.9 (2.0, 4.0)             | 3.7 (2.6, 4.6)              | 2.6 (1.8, 3.7)                                  | 3.0 (2.0, 4.6)  | 5.4(4.5, 6.7)                                   |
| Prolonged ICU LOS (>4 days), n (%)  | 70 (20.0%)   | 22 (25.0%)   | 27 (24.0%)                 | 13 (36.0%)                  | 43 (16%)  | 18 (29%)  | 8 (100%)  |
| Hospital LOS (hours)  | 192.0 (168.0, 240.0)                                     | 192.0 (168.0, 264.0)                                       | 216.0 (168.0, 264.0)       | 252.0 (216.0, 336.0)        | 192.0 (156.0, 240.0)                            | 216.0 (192.0, 288.0)                                    | 312.0 (270.0, 372.0)                            |
| Hospital LOS (days)   | 8.0 (7.0, 10.0)  | 8.0 (7.0, 11.0)  | 9.0 (7.0, 11.0)            | 10.5 (9.0, 14.0)            | 8.0 (6.5, 10.0)                                 | 9.0 (8.0, 12.0)   | 13.0 (11.2, 15.5)                               |
| Prolonged hospital LOS (>10 days), n (%)  | 72 (21.0%)   | 23 (26.0%)   | 31 (28.0%)                 | 16 (44.0%)                  | 48 (18%)  | 19 (31%)  | 5 (63%)   |
| Graft failure, n (%)  | 5 (1.5%)   | 0 (0%)   | 1 (0.9%)                   | 1 (2.8%)                    | 4(1.5%)   | 1(1.6%)   | 0 (0%)  |
| 30-day mortality, n (%)   | 6(1.8%)  | 0 (0%)   | 4 (3.6%)                   | 2 (5.6%)                    | 0 (0%)  | 4 (6.5%)  | 2 (25%)   |
| Neurological complications  |  |  |                            |                             |   |   |   |
| CVA, n (%)  | 2 (0.6%)   | 0 (0%)   | 0 (0%)                     | 0 (0%)                      | 0 (0%)  | 2 (3.2%)  | 0 (0%)  |
| TIA, n (%)  | 1 (0.3%)   | 0 (0%)   | 0 (0%)                     | 0 (0%)                      | 1 (0.4%)  | 0 (%)   | 0 (0%)  |
| Epilepsy, n (%)   | 1 (0.3%)   | 0 (0%)   | 1 (0.9%)                   | 0 (0%)                      | 0 (0%)  | 1 (1.6%)  | 0 (0%)  |
| Delirium, n (%)   | 18 (5.3%)  | 7 (7.9%)   | 9 (8.1%)                   | 2 (5.6%)                    | 11 (4.2%)                                       | 3 (4.8%)  | 3 (37.5%)                                       |
| Data are presented as mean ± SD, as absolut<br>ICU, intensive care unit; LOS, length of stay; R | te numbers (%) or as medi<br>evascularization (in hospit | an (25th-75th percentile)<br>al), revision of coronary art | ery bypass grafting (CABC  | t) when patients were still | hospitalized; Revasculariz                      | ation (late onset), revision c                          | of CABG when patients                           |
| Mele discliation itolit cite troshicat atta Mel   | ב זב-מתוווורבת יה תוב זוהאו                              | Idl, LVA, CELEDI UVASCULAI                                 | actually, 11A, transient i | SCIEDING ALLACY.            |   |   |   |

Finally, median hospital LOS in our patient cohort (8 days) is reduced compared to the median hospital LOS after a conventional CABG in Belgium (11 days) [27]. In contrast, median ICU and hospital LOS after Endo-CABG is slightly increased compared to the reported median LOS after other minimally invasive CABG techniques [13,15,17]. Although LOS generally reflects hospital efficiency, variations in LOS can also be explained by differences in governmental payment systems [28]. In the Belgian healthcare system, an increased bed occupation is financially beneficial. Also, in our institute, there is no separate intermediate care unit (MCU) and therefore ICU LOS reflects total time spent on both ICU and MCU. Obviously, this makes comparison with other trials difficult.

Our study design also contains some limitations. First, given the retrospective nature of this cohort study, no firm conclusions can be drawn regarding differences in outcomes after CABG techniques. Second, this study does not provide long-term follow-up outcomes or patient-related outcomes (e.g. quality of recovery/ life). These outcomes are planned to be assessed in the near future. Third, as already discussed above, comparison with other trials is difficult with respect to total ICU and hospital LOS since these outcomes are highly influenced by differences in healthcare system and local practice. Finally, since the Endo-CABG technique is performed by a single surgeon in our institute and this technique may require a long learning curve, implementation in daily clinical practice by other surgeons/hospitals might be difficult. Therefore, the generalizability of our results can be questioned. However, collaboration with other institutes is already established and will result in an increased number of patients being treated with this technique.

In conclusion, the Endo-CABG technique can be considered a safe and effective procedure to treat single- and multi-vessel coronary artery disease, even in the absence of individual patient selection. Future research should focus on the transferability of the Endo-CABG technique to other surgeons.

# Author contributions

YA developed the surgical technique and YA, RB, PS performed the surgeries. RS, FP, and BS analyzed the data and wrote the manuscript. YA and PS revised the manuscript and all authors approved the final version.

# **Conflict of interest**

The authors declare that there is no conflict of interest.

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# References

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- Head SJ, Milojevic M, Taggart DP, Puskas JD. Current practice of state-of-the-art surgical coronary revascularization. Circulation 2017;136:1331–45.
- [2] Heilmann C, Stahl R, Schneider C, Sukhodolya T, Siepe M, Olschewski M, et al. Wound complications after median sternotomy: a single-centre study. Interact Cardiovasc Thorac Surg 2013;16:643–8.
- [3] Ezelsoy M, Caynak B, Bayram M, Oral K, Bayramoglu Z, Sagbas E, et al. The comparison between minimally invasive coronary bypass grafting surgery and conventional bypass grafting surgery in proximal LAD lesion. Heart Surg Forum 2015;18:E042–6.

- [4] Ruel M, Shariff MA, Lapierre H, Goyal N, Dennie C, Sadel SM, et al. Results of the minimally invasive coronary artery bypass grafting angiographic patency study. J Thorac Cardiovasc Surg 2014;147:203–8.
- [5] Poston RS, Tran R, Collins M, Reynolds M, Connerney I, Reicher B, et al. Comparison of economic and patient outcomes with minimally invasive versus traditional off-pump coronary artery bypass grafting techniques. Ann Surg 2008;248:638–46.
- [6] Lapierre H, Chan V, Sohmer B, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting via a small thoracotomy versus off-pump: a casematched study. Eur J Cardiothorac Surg 2011;40:804–10.
- [7] Kikuchi K, Mori M. Less-invasive coronary artery bypass grafting international landscape and progress. Curr Op Cardiol 2017;32:715–21.
- [8] Langer NB, Argenziano M. Minimally invasive cardiovascular surgery: Incisions and approaches. Methodist DeBakey Cardiovasc J 2016;12:4–9.
- [9] Bonaros N, Schachner T, Lehr E, Kofler M, Wiedemann D, Hong P, et al. Five hundred cases of robotic totally endoscopic coronary artery bypass grafting: predictors of success and safety. Ann Thorac Surg 2013;95:803–12.
- [10] Cao C, Indraratna P, Doyle M, Tian DH, Liou K, Munkholm-Larsen S, et al. A systematic review on robotic coronary artery bypass graft surgery. Ann Cardiothorac Surg 2016;5:530–43.
- [11] Naito R, Kasai T. Coronary artery disease in type 2 diabetes mellitus: Recent treatment strategies and future perspectives. World J Cardiol 2015;7:119–24.
- [12] Starinieri P, Declercq PE, Robic B, Yilmaz A, Van Tornout M, Dubois J, et al. A comparison between minimized extracorporeal circuits and conventional extracorporeal circuits in patients undergoing aortic valve surgery: is' minimally invasive extracorporeal circulation' just low prime or closed loop perfusion? Perfusion 2017;32:403–8.
- [13] Giambruno V, Chu MW, Fox S, Swinamer SA, Rayman R, Markova Z, et al. Robotic-assisted coronary artery bypass surgery: an 18-year single-centre experience. Int J Med Robot 2018;14:e1891.
- [14] Borde D, Gandhe U, Hargave N, Pandey K, Khullar V. The application of European system for cardiac operative risk evaluation II (EuroSCORE II) and Society of Thoracic Surgeons (STS) risk-score for risk stratification in Indian patients undergoing cardiac surgery. Ann Card Anaesth 2013;16:163–6.
- [15] West D, Flather M, Pepper J, Trimlett R, Yap J, De Souza A. Improved recovery after the endoscopic atraumatic coronary artery bypass procedure compared with sternotomy for off-pump bypass of the left internal thoracic artery to the left anterior descending coronary artery: a case-matched study. Heart Surg Forum 2004;7:E546–50.

- [16] Raffa GM, Malvindi PG, Ornaghi D, Citterio E, Cappai A, Basciu A, et al. Minimally invasive direct coronary artery bypass in the era of percutaneous coronary intervention. J Cardiovasc Med 2015;16:118–24.
- [17] Wang S, Zhou J, Cai JF. Traditional coronary artery bypass graft versus totally endoscopic coronary artery bypass graft or robot-assisted coronary artery bypass graft—meta-analysis of 16 studies. Eur Rev Med Pharmacol Sci 2014;18:790–7.
- [18] Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, et al. Offpump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489–97.
- [19] Diegeler A, Borgermann J, Kappert U, Breuer M, Böning A, Ursulescu A, et al. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. N Engl J Med 2013;368:1189–98.
- [20] Reser D, Hemelrijck M, Pavicevic J, Tolboom H, Holubec T, Falk V, et al. Midterm outcomes of minimally invasive direct coronary artery bypass grafting. Thorac Cardiovasc Surg 2015;63:313–8.
- [21] Vassiliades Jr TA, Reddy VS, Puskas JD, Guyton RA. Long-term results of the endoscopic atraumatic coronary artery bypass. Ann Thorac Surg 2007;83:979–84.
- [22] Modi P, Chitwood Jr WR. Retrograde femoral arterial perfusion and stroke risk during minimally invasive mitral valve surgery: is there cause for concern? Ann Cardiothorac Surg 2013;2:E1.
- [23] Chen Y, Ding S, Tao X, Feng X, Lu S, Shen Y, et al. The quality of life of patients developed delirium after coronary artery bypass grafting is determined by cognitive function after discharge: A cross-sectional study. Int J Nurs Pract 2017;23. http://dx.doi.org/10.1111/ijn.12563.
- [24] Nijs K, Vandenbrande J, Vaqueriza F, Ory JP, Yilmaz A, Starinieri P, et al. Neurological outcome after minimal invasive coronary artery surgery (NOMICS): protocol for an observational prospective cohort study. BMJ Open 2017;7:e017823.
- [25] Biancari F, Mikkola R, Heikkinen J, Lahtinen J, Airaksinen KE, Juvonen T. Estimating the risk of complications related to re-exploration for bleeding after adult cardiac surgery: a systematic review and meta-analysis. Eur J Cardiothorac Surg 2012;41:50–5.
- [26] Ozen A, Unal EU, Songur M, Kocabeyoglu SS, Hanedan O, Yilmaz M, et al. Coronary artery bypass grafting in the octogenarians: should we intervene, or leave them be? | Geriatr Cardiol 2015;12:147–52.
- [27] Federal Public Service Health Food Chain Safety And Environment. Portahealth;http://www.health.belgium.be/nl/gezondheid/ organisatie-van-de-gezondheidszorg/ziekenhuizen/registratiesystemen2016.
- [28] OECD. Average length of stay in hospital. Health at a glance: Europe 2016: State of health in the EU cycle. Paris: OECD Publishing; 2016. p. 186–8.