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Pain Intensity and Graft Patency following Minimally Invasive Coronary Artery Bypass Grafting. A comparison of three different approaches.

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To my grandfather (Mustafa Nihat Sipahi),

The very first generation Dr. Sipahi

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LIST OF ABBREVETIONS

ACS	=	Acute Coronary Syndrome
ACE	=	Angiotensin-Converting Enzyme
ACT	=	Activated Clotting Time
ADP	=	Adenosine Diphosphate
ALT	=	Anterolateral Thoracotomy
ARB	=	Angiotensin Receptor Blockers
ASD	=	Atrial Septal Defect
BMI	=	Body-Mass Index
CABG	=	Coronary Artery Bypass Grafting
CAD	=	Coronary Artery Disease
COPD	=	Chronic Obstructive Pulmonary Disease
CPB	=	Cardiopulmonary Bypass
DM	=	Diabetes Mellitus
ECG	=	Electrocardiography
GEA	=	Right Gastroepiploic Artery
GSV	=	Greater Saphenous Vein
ICS	=	Intercostal Space
ICU	=	Intensive Care Unit
IMA	=	Internal Mammary Artery
ITA	=	Internal Thoracic Artery
LAD	=	Left Anterior Descending Artery
LCA	=	Left Coronary Artery
LV	=	Left Ventricle
MACCE	=	Major Adverse Cardiac And Cerebrovascular Event
MI	=	Myocardial Infarction
MIDCAB	=	Minimally Invasive Direct Coronary Artery Bypass Grafting
MICS CABG	=	Minimally Invasive Coronary Artery Bypass Grafting
NSTEMI	=	Non ST-segment Elevation Myocardial Infarction
OM	=	Obtuse Margin
OPCAB	=	Off-pump Coronary Artery Bypass Grafting
PCI	=	Percutaneous Coronary Interventions
PDA	=	Posterior Descending Artery
PLS	=	Partial Lower Sternotomy
PTCA	=	Percutaneous Transluminal Coronary Angioplasty
RCA	=	Right Coronary Artery
STEMI	=	ST-segment Elevation Myocardial Infarction
TECAB	=	Totally Endoscopic Coronary Artery Bypass Grafting
VSD	=	Ventricular Septal Defect

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1. Introduction

1.1 Background

Coronary artery disease (CAD) is nowadays the leading cause of death, counting worldwide 8.1 million victims in 2013.[1] Despite the presence of the other treatment options such as medications and percutaneous coronary interventions(PCI), coronary artery bypass grafting (CABG) is still remaining as the adopted abolishment of the multivessel CAD. Traditionally, CABG has been performed through a median sternotomy and on cardiopulmonary bypass (CPB).

To renounce the potential systemic complications of CPB, as well as to minimize the risks and problems of a conventional sternotomy by means of the reduction of the wound healing disorders, sternal dehiscence and postoperative pain, several surgical techniques had been developed.

Some of these techniques are off-pump coronary artery bypass grafting (OPCAB), minimally invasive direct coronary artery bypass grafting (MIDCAB) through either a partial sternotomy or a left anterolateral thoracotomy and robotic-assisted totally endoscopic coronary artery bypass grafting (TECAB). Plenty of studies have demonstrated excellent outcomes of minimally invasive coronary artery bypass grafting (MICS CABG) or have compared them with conventional CABG via median sternotomy.[2-4] However the comparison of the minimally invasive techniques between each other has not been performed yet.

1.2 History of the Coronary Artery Bypass Grafting

The search of new blood resource for an ischemic myocardium dates back to the early nineties and has prospered to date with the presentation of surgical and mechanical innovations.

In 1910, Alexis Carrel performed the anastomosis of a carotid artery between the descending thoracic aorta and the left coronary artery (LCA) on beating heart in a canine model.[5] For this work, he was awarded the Nobel Prize.

Claude Beck performed indirect revascularization of the heart with expectancy of developing collateral blood flow to ischemic myocardium in animals[6] and later

in patients[7]. Arthur Vineberg, in the 1940s, used first-time the internal thoracic artery (ITA) as a graft and implanted it into the left ventricular myocardium.[8]
One of the most outstanding milestones in cardiac surgery was the successful use of the CPB in a correction procedure of an atrial septal defect (ASD) by John Gibbon[9], which led later the use of cardioplegia and made a motionless situs possible during the operation. In the same year, Demikhov performed the first successful anastomosis of the internal mammary artery (IMA) to the left anterior descending artery (LAD) in a canine model.[10]
The first surgical procedure on the coronary arteries in man was reported in 1958 by William Longmire, who performed an endarterectomy without the use of CPB.[11] The customization of the CPB for the CABG did not take long time. In 1959, Dubost performed the first in human coronary artery operation, a coronary ostial reconstruction, using CPB.[12] One year later, a "Frankfurter", Robert Goetz performed the first successful clinical coronary artery bypass operation and anastomosed the right ITA to a right coronary artery (RCA) with employing a nonsuture method.[13]
In 1964, Kolesov, a Russian surgeon, performed the first sutured LIMA-LAD bypass without CPB through a left thoracotomy in human.[14] Meanwhile in Houston, the first successful CABG with an autogenous saphenous vein graft was placed from the aorta to the LAD by Garrett, Dennis and DeBakey. They could report this historic event in 1973, following the angiographic confirmation of the graft patency in the seventh year.[15,16] In 1967, Rene Favaloro began to use also a saphenous vein autograft and the proximal of the vein graft was anastomosed to the ascending aorta.[17]
W. Dudley Johnson and colleagues expanded the application of saphenous vein and used it to all major branches of the coronary arteries. After their 1969 dated paper[18], which reported the results of 301 patients, CABG procedure was rapidly adopted worldwide.
In order to avoid the morbidity related to the use of extracorporeal circulation, Trapp and Bisarya reported RCA and LAD grafting on the beating heart.[19] This procedure has been named currently as OPCAB. At the beginning, cardiac surgical professionals were skeptical about OPCAB technique. However, OPCABs performed have reached 30% of all myocardial revascularizations worldwide.

Although complete sternotomy is mostly well tolerated and provides a good accessibility into the thoracic cavity, efforts have been made to minimize the invasiveness of CABG in order to decrease the wound-related comorbidities and improve the postoperative quality of life. With this aspect in 1995, Benetti et al introduced the MIDCAB procedure through an anterolateral thoracotomy.[20] In contrast to his technique with the utilization of a thoracoscope during the preparation of the LIMA, his successors preferred the preparation under direct vision with an aggressive retraction of chest wall, which often resulted in significant postoperative pain. In the late 90s, partial lower ministernotomy was introduced as an alternative access for MIDCAB surgery.[21] In same years, surgical robotics had been adopted in cardiac surgery, firstly in mitral valve surgery and then for assisting the MIDCAB procedure by means of LIMA harvesting. In 1998, Loulmet performed the first successful CABG without opening the chest.[22] Haldun Karagöz, a Turkish cardiac surgeon, was performed the world’s first open heart and coronary artery bypass grafting surgery in the conscious patient without endotracheal general anesthesia, using high thoracic epidural block.[23]

1.3 History of the Minimally Invasive Coronary Artery Bypass Grafting in University Hospital Frankfurt

In university hospital Frankfurt, minimally invasive coronary artery bypass grafting program have been initiated in 1997. In November 1997, the first patient underwent multivessel revascularization through a left anterior small thoracotomy with the assistance of the Port-Access™ system (HeartportInc, Redwood City, CA).[24] In June 1999, our university inaugurated a clinical program using the da Vinci surgical system (Intuitive Surgical Inc, Mountain View, CA) for all surgical disciplines. The first 7 patients either underwent endoscopic LIMA harvest or a robotic coronary artery bypass anastomosis as part of a conventional CABG procedure. Following this preliminary period, the consecutive patients were operated on arrested heart and without opening the chest in the same year. Mostly, LIMA to LAD or RIMA to RCA anastomosis was performed.[25] On November 24, 1999, the first totally endoscopic LITA bypass grafting to LAD and the first diagonal branch in sequential arterial revascularization technique in our institution was performed.[26] In 2001, Tayfun Aybek and colleagues reported the first CABG through complete sternotomy in conscious patients in Germany[27] and then the same group declared further operative techniques including coronary artery bypass grafting through partial lower sternotomy and rib-cage lifting in awake patients.[28] In June 2001, Selami Dogan and colleagues performed the first totally endoscopic LITA to LAD bypass on beating heart at our institution.[29] The same team reported also in 2002 a totally endoscopic bilateral ITA bypass grafting in a 26-year-old diabetic patient.[30]

1.4 Coronary Artery Bypass Grafting as a Treatment of Coronary Artery Disease

CAD can basically be defined as the atherosclerotic alteration of the coronary arteries, which causes a disproportionate relationship between myocardial oxygen demand and blood supply. CAD usually affects the proximal of the larger coronary arteries, especially at or just beyond the branches. The most frequent consequence of CAD is myocardial infarction (MI).
CAD may appear in two different clinical forms: stable angina pectoris (chronic CAD) and acute coronary syndrome (ACS). ACS can itself be divided into three groups: unstable angina pectoris, non ST-segment-elevation myocardial infarction (NSTEMI) and ST-segment-elevation myocardial infarction (STEMI). The diagnosis of CAD can be confirmed by a combination of clinical symptoms and the findings of electrocardiography (ECG), echocardiography, cardiac biomarkers and coronary angiography.

Beside the modification of risk factors therapy of CAD is based on 3 main columns:

1) **Medical management;** includes fundamentally secondary prophylaxis with anti-platelet agents such as Aspirin or Adenosine diphosphate (ADP) receptor-blockers (Clopidogrel, Prasugrel, etc.), enhancement of coronary blood flow with Nitrates and reduction of myocardial oxygen demand with Calcium-channel blockers and Beta-blockers. Lipid lowering therapy with Statins (HMG-Co-A reductase inhibitors) decreases the

storage of lipids and stabilizes the atheromatous plaque in the coronary artery. Angiotensin-converting enzyme (ACE) inhibitors and in case of an intolerance with them, Angiotensin receptor blockers (ARB) are indicated especially in patients, whose left ventricular (LV) systolic function is restricted.

2) **PCI (Percutaneous coronary interventions)**; include percutaneous transluminal coronary angioplasty (PTCA) with or without stent insertion and use of atherectomy devices. The role of the PCI in ACS is beyond any argument very important. An early recanalization of the acute coronary artery occlusion can be life-saving. Another advantage of the PCI is that it can be applied during the coronary angiogram, which is essential to decide for a CABG procedure. According to the latest ESC/EACTS guidelines on myocardial revascularization[31], primary PCI is indicated in patients with ischemic symptoms <12 hours, ACS complicated by cardiogenic shock, objective evidence of a moderate-sized to large area of viable myocardium or moderate to severe ischemia on noninvasive testing and practicability of intervention techniques associated with the anatomy of coronary arteries.

3) **CABG;** is indicated in patients, who have multivessel CAD, one or two-vessel disease with involvement of proximal LAD or left main stem, left ventricular dysfunction, large area of myocardial ischemia (>10% LV) and severe chest pain, which could not be kept under control with medical therapy. In addition to the above-mentioned indications iatrogenic causes (dissection or perforation of a coronary artery during PCI), complications of a myocardial infarction such as ventricular septal defect (VSD), ischemic mitral regurgitation, LV-Aneurysm and free wall rupture may present the patients for CABG. Also the patients, whose coronary anatomy/stenoses do not enable to perform catheterization techniques, should be referred to a cardiovascular surgical procedure.[31]

According to the long-term follow up results of numerous studies[32-40], CABG is superior to PCI regarding the survival rate, freedom from repeat revascularization procedures, freedom from major adverse cardiac and cerebrovascular event (MACCE) and also the occurrence of angina pectoris, especially in patients with diabetes mellitus and impaired left ventricular ejection fraction. Especially in patients with the most severe CAD (SYNTAX Score ≥33), major adverse cardiac and cerebrovascular events, the rate of death, stroke and myocardial infarction increased in PCI group vs. in the CABG group.[41]

1.5 Surgical Methods for Myocardial Revascularization

1.5.1 Off-pump Coronary Artery Bypass Grafting (OPCAB)

A median sternotomy is most frequently performed for multivessel revascularization, however depending on the target-vessel a left or right thoracotomy or partial sternotomy can be used for limited grafting. Following the harvest of necessary graft material the retractor is positioned in the incision, which allows the attachment of the stabilizers. The pericardium is widely incised with an extended “T-shape” and the retraction sutures are placed deeply to improve the exposure. There are a variety of stabilizing adjuncts. Commonly an apical suction device is utilized on the apex of the heart. By moving the apex toward the right sternal half, the LAD, diagonal and obtuse margin (OM) branches come into view. By applying suction to the acute margin of the heart and moving it toward the left shoulder, the distal right coronary artery and its branches are presented. Stabilization of the target-vessel for the distal anastomosis is achieved by utilizing a two-armed vacuum-assisted or metal plate stabilizer. A fine-tipped aspirator or a humidified carbon dioxide blower may be used to clear the blood at the distal anastomotic site. Intracoronary shunts may be used especially constant blood flow in the operating field and to maintain the blood stream into the distal vessel during the construction of the anastomosis. The proximal anastomoses can be performed before or after the distal anastomoses. The advantage of performing the proximal anastomosis first is immediate perfusion of the revascularized myocardium. Typically the LIMA-LAD bypass is performed very first, since the LAD is easiest to access and the blood supply to the anterior wall of the myocardium and septum is restored with this bypass during the other manipulations. Grafting then is continued by performing the easier anastomoses prior to the more difficult ones.

The diagonal arteries, the inferior wall arteries (RCA, posterior descending artery (PDA)) and the lateral wall arteries (OM) are usually revascularized respectively. The proximal anastomoses are generally performed by using a tangential aortic clamp or HEARTSTRING Proximal Seal System (Guidant, Cupertino, CA) that allows carrying out a hand-sewn proximal anastomosis without application of any aortic clamp. Once the adequate hemostasis has been achieved, the drainages are placed and then the thoracic cavity is closed in standard fashion.

There are also different techniques of CABG such as MIDCAB and TECAB. These procedures will be explained in detail in the following chapter of this study.

1.6 Pain Intensity after Cardiac Surgical Procedures

There is no doubt that sufficient pain management plays a decisive role after cardiac surgery. Suboptimal pain killing may impair quality of life and increase both perioperative and long-term morbidity.
Postoperative period can mostly be complicated by pain induced immobility which may lead to atelectasis, pneumonia, increased oxygen consumption, tachycardia, muscle disuse and weakness, deep vein thrombosis, obstipation and urinary retention.[42-43] Early postoperative pain is expressed moderate, severe or even unbearable after cardiac surgery which decreases till discharge and at hospital discharge the majority of patients have no or mild pain.[44] Uymaz et al demonstrated that maximal pain levels were observed on postoperative day two.[45] The visual analog scale can be used to evaluate pain intensity. This scale is from 0, which predicate no pain, up to 10, which is the worst pain experience ever. Lahtinen et al showed that median early postoperative pain was 5 at rest and 7 during coughing, whereas by day four, 2 and 5 points, respectively.[46]
Besides all these, painful experiences imprint themselves on the central nervous system. This can produce chronic pain syndromes.[47] On the other hand, patients with high levels of acute postoperative pain are more likely to suffer from chronic pain than those who have lower pain levels.[42] Eisenberg and

colleagues defined post-CABG pain as chest wall pain of at least 3 months' duration, which first appeared after CABG surgery and which is different from angina pectoris.[48] The incidence of chronic pain after cardiac surgery varies between 21% and 55%.[46,49]

Instruments and surgical technique can influence pain intensity after cardiac surgery. For example: use of sternal retractor may lead to costal fractures or dislocation of costochondral junction. IMA harvesting is associated with increased pain and postoperative amount of morphine.[50-51] Moreover patients with IMA-harvesting tend to develop neuropathic pain syndrome.[52]

To limit the surgical trauma and hence postoperative pain, different surgical accesses have been used in cardiac surgery. MIDCAB surgery, which can be performed through an anterolateral thoracotomy or a partial lower sternotomy, arose from that perspective. Although thoracotomies have been described as one of the most painful surgical procedures, Walther and collegues demonstrated that patients who were operated through an anterolateral thoracotomy suffers from less pain after the initial 2 postoperative days than who had a conventional sternotomy.[44]

1.7 Graft Patency

As a treatment of choice for multivessel CAD, the potency of CABG-procedure is highly associated with the long-term patency of conduits. Arterial (IMA, Radial, gastroepiploic) or venous grafts (greater saphenous) may be used to revascularize the coronary arteries.

Determination of the revascularization strategy plays a vital role in patient's life-expectancy. Age[54], gender, selection of bypass grafts, target-vessel size[55], stenosis severity in native coronary system[54,56], diabetes, smoking and lumen diameter of study graft[57] may influence the graft patency.

Most commonly used graft in CABG surgery is the greater saphenous vein (GSV). Ease of harvest, availability over its entire length and thoroughly investigated long-term results make GSV unique. Disadvantage of GSV is the relatively reduced overall patency. The endothelium of GSV can sustain an injury during the graft harvesting or initial exposure to a high pressure arterial system. This may lead to platelet aggregation and thrombosis in early postoperative period and in the long term intimal hyperplasia and graft atherosclerosis.

Unlike GSV, IMAs develop lesser atherosclerosis and therefore provide an excellent long-term patency that translates into lower risk of late myocardial infarction, hospitalization for cardiac events or reoperation.[65] The radial artery has a thicker wall than the IMA, which contains more myocytes in its media[66] and for that reason is susceptible to spasm during harvesting or perioperative catecholamine therapy. Moreover, atherosclerosis may be detected at the time of harvest more than the IMA. GEA is also a muscular artery but compared to the radial artery its media is less developed.[67,68] The patency of all arterial grafts is strongly associated with the severity of target coronary artery stenosis. More severe native coronary stenosis translates into a better long-term graft patency for arterial conduits.[54,58]

Early and long-term outcomes of mostly used grafts in CABG are compiled in Table 1.

Graft	Patency at 1 year	Patency at 5 years	Patency at 10 years	Ref.
GSV	76-86 %	65-67%	57-61%	54,55,57,58,59
Radial artery	88-92%	89%	83%	55,58,60,61
LIMA	93-98%	88-98%	85-95%	54,57,60,62
RIMA	92%	89-96%	81%	60,63,64

Ref. = References.
GSV = Greater Saphenous Vein, LIMA = Left Internal Mammary Artery, RIMA = Right Internal Mammary Artery

Table 1: Graft patency in CABG at 1, 5, 10 years

1.8 Aim

The aim of this thesis is to follow-up the long term results of the three different minimally invasive coronary artery revascularization techniques. Our interest focused on periprocedural complications, early and late mortality and morbidity as well as rates of reintervention or reoperations. Moreover we aimed to compare these surgical approaches in terms of pain intensity and quality of pain.

2. Methods

2.1 Description of the Entire Patient Cohort

From 1997 to 2006, 126 minimally invasive coronary artery bypass procedures had been performed in our department through different surgical approaches. The surgical procedures performed were totally endoscopic coronary artery bypass grafting (TECAB) (n=63, 50%), minimally invasive direct coronary artery bypass grafting through a left anterolateral thoracotomy (ALT) (n=20, 16%) or a partial lower sternotomy (PLS) (n=43, 34%) (Figure 1). There were 90 males (71.4%) and 36 (28.6%) females with a mean age of 62±11 years (Range 36 to 90) (Figure 2). Mean BMI was 26.9±3.4. Most commonly seen comorbidities were arterial hypertension (79.2%) and hyperlipidemia (77.8%). Twenty-six patients (20.8%) had diabetes. Twenty-six patients (20.8%) had previously suffered a myocardial infarction.

2.1.1. Exclusion Criteria

Patients with acute coronary syndromes requiring emergency revascularization, additional cardiac disease requiring surgical treatment, previous cardiac surgical procedure, peripheral vascular disease or aortic aneurysm, impaired left ventricular ejection fraction (EF<35%) were not considered for MICS-CABG. Other exclusion criteria included chest wall or spinal deformities, congestive heart failure, BMI>30 and impaired pulmonary function tests.

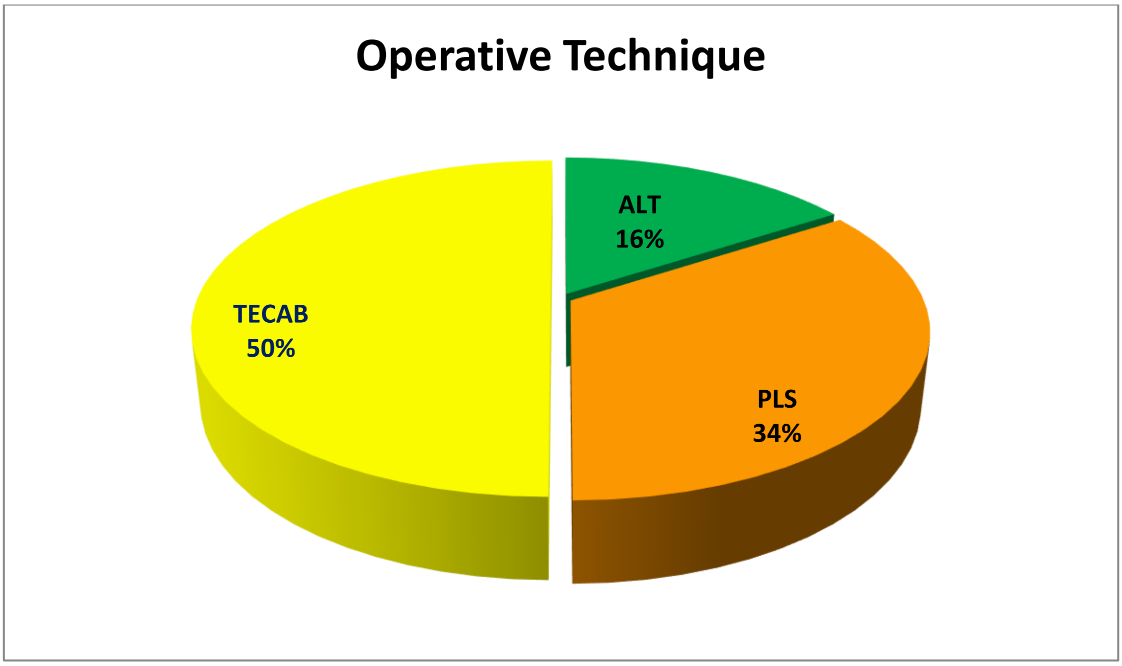


Figure 1: Percental distribution of the minimally invasive myocardial revascularization technique

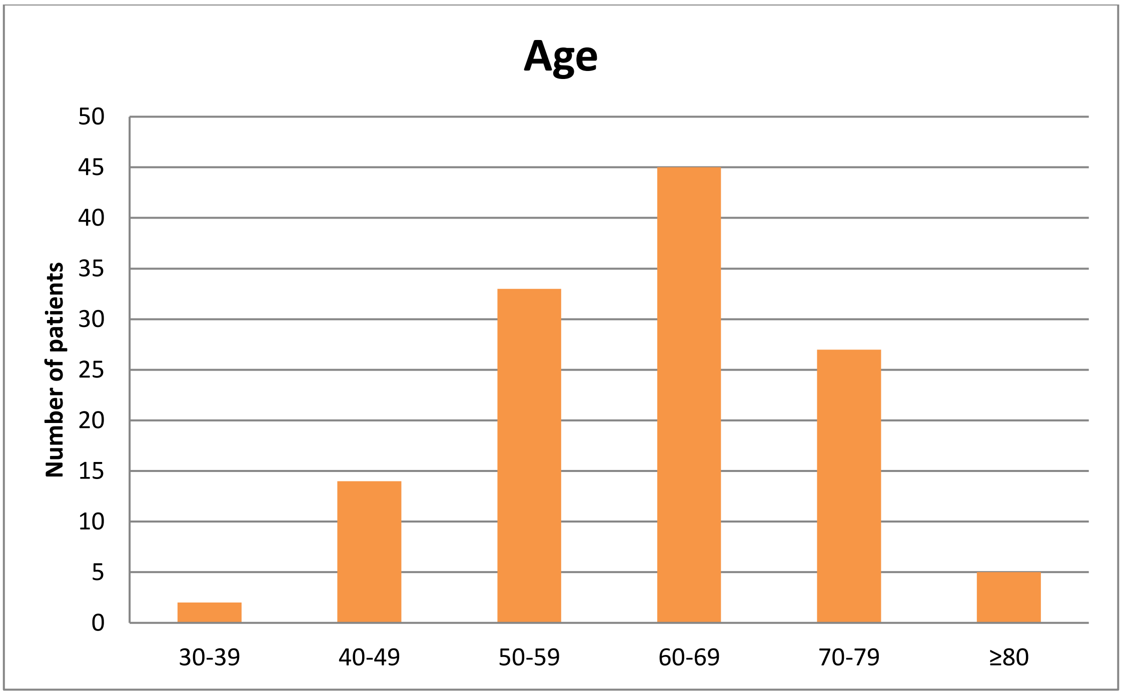


Figure 2: Age distribution of the entire patient cohort

2.2 Anesthesia and Surgical Technique

2.2.1. Preoperative Preparation

All patients were premedicated with benzodiazepines on the day of surgery. Following the establishment of intravenous access and monitoring with electrocardiogram (ECG) lines, pulse-oximetry and continuous invasive blood pressure measurement via insertion of a radial or femoral artery catheter, standard general anesthesia was inducted using sufentanil, etomidate, and pancuronium and maintained with propofol and sufentanil. The endotracheal tubus was placed and secured. All patients planned for TECAB and ALT underwent double-lumen intubation for single lung ventilation; thus, harvest of the left or right IMA could be facilitated. Central venous and pulmonary artery catheter were placed via an internal jugular approach. A transesophageal echocardiography probe was advanced in the esophagus. Furthermore a urinary catheter was placed. Although the peripheral oxygen saturation was continuously controlled using pulse-oximetry, gas exchange was monitored by blood gas analysis periodically.

2.2.2 Minimally Invasive Direct Coronary Artery Bypass Grafting (MIDCAB)

The procedure was performed through a small anterolateral thoracotomy as well as a partial lower sternotomy.

ALT.A 6 to 8 cm anterolateral skin incision is made upon the left fourth rib in males or the inframammary fold in female patients. The pectoralis muscle is divided bluntly with a muscle-sparing approach to avoid potential herniation. The thoracic cavity is entered through the 4^{th} intercostal space.

PLS. A vertical skin incision is made from the forth intercostal space to the xiphoid process (7-8 cm). Sternotomy is performed with an oscillating saw starting from the xiphoid process up to the second or third intercostal space. Once the thoracic cavity has been entered with above-mentioned approaches, the left lung is deflated with the aid of the double-lumen endotracheal tubus and the LIMA is harvested under direct vision or thoracoscopic assistance. Depending on the distal anastomoses planned to conduct, the operation can be performed on-pump or off-pump. Due to the minimally invasiveness of the procedure, cardiopulmonary bypass is achieved by the Port-Access^{TM} system (Figure 3). This system is inserted by the way of dissection of the groin and the cannulation of femoral vessels. Through the right internal jugular vein catheters are inserted into the coronary sinus for retrograde cardioplegia and the pulmonary artery for venting the left heart. A multi-lumen catheter that allows the administration of antegrade cardioplegia and the endovascular occlusion of the aorta is guided into the ascending aorta.

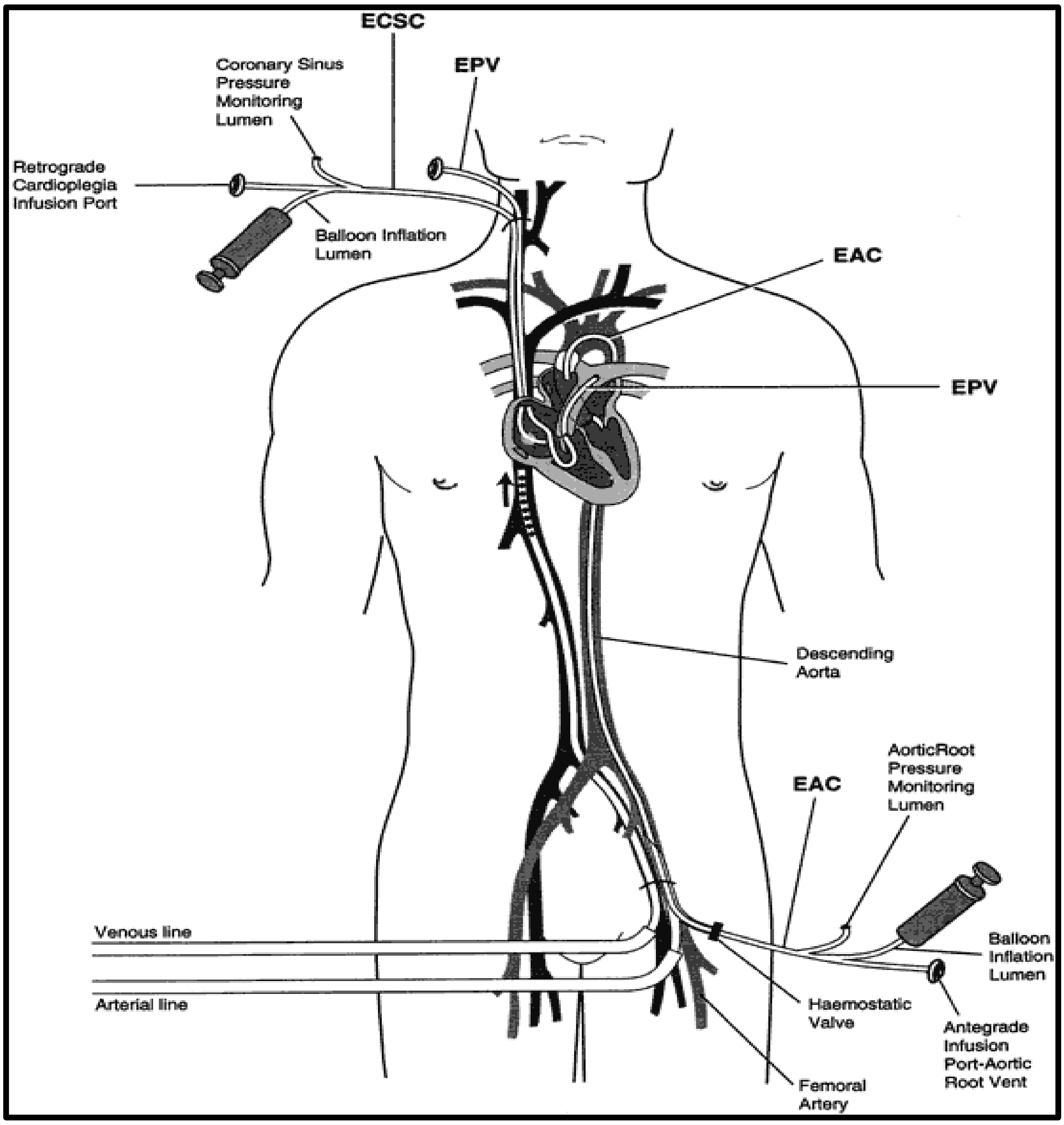


Figure 3: EAC, endoaortic occlusion clamp; ECSC, endocoronary sinus retrograde cardioplegia catheter; EPV, endopulmonary artery vent. (From Toomasian JM, Peters WS, Siegel LC, et al. Extracorporeal circulation for Port-Access cardiac surgery. Perfusion 1997;12:83–93)

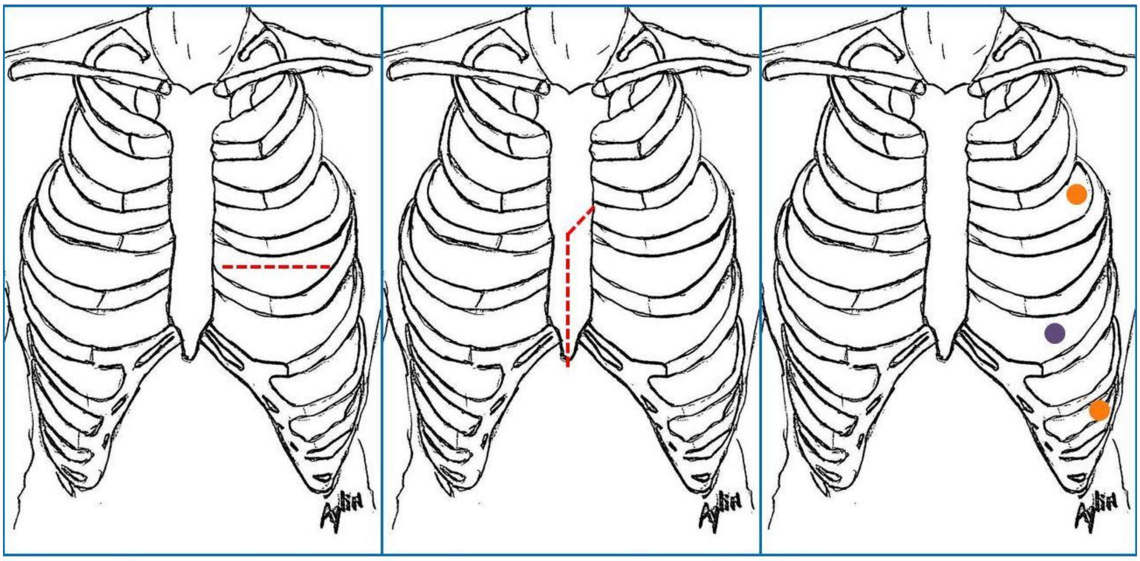
Proximal anastomoses are performed first on beating heart. Then, the ascending aorta is occluded with the endovascular balloon and antegrade as well as retrograde cardioplegia is infused. Following the grafting of the coronary arteries, the endoaortic occlusion balloon is deflated and the patient is weaned from CPB. The femoral cannulas are removed, the drainages are placed and then the thoracic cavity as well as the dissected groin is closed in standard fashion.

2.2.3 Totally Endoscopic Coronary Artery Bypass Grafting (TECAB)

The da Vinci Surgical System. Basically the da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) has two major components: A master console which enables the surgeon to see the surgical field in high definition and a slave unit to manipulate the microinstruments.

Operative Technique for TECAB.
Our institutional protocol for TECAB has been previously described in details.[25,53] Briefly, the patient is placed on the operating table in a supine position. Left hemithorax is slightly elevated. After deflation of the left lung, the central camera port is placed into the fifth intercostal space (ICS). The thoracic cavity is insufflated with carbon dioxide. Two instrument ports are then inserted under direct vision in the third and seventh ICS medial to the anterior axillary line. The LIMA is harvested from the first ICS to the level of the bifurcation using endoscopic instruments. Depending on the planned revascularization, right IMA can also be prepared under the same setting. After heparinization, the distal end of the LIMA is clipped and taken down. To perform the operation on beating heart, a subxyphoidal port for the endostabilizer is inserted. In the contrary case cardiopulmonary bypass is achieved by the cannulation of the femoral vessels with the utilization of the Port-Access™ system. After initiation of CPB heart is decompressed and endoscopic pericardiotomy is safely performed. The target coronary arteries are identified before cardiac arrest. Aorta is cross-clamped via the Port-Access EndoClamp and cardioplegicsolution is administered into the aortic root. Following the completion of the coronary revascularization, the endoaortic occlusion balloon is deflated and the patient is weaned from CPB.

Both femoral cannulas are removed and defects are sutured. Two chest drainages are placed through the camera port and an instrument port.



Anterolateral Thoracotomy: A 6 to 8 cm anterolateral skin incision. The thoracic cavity is entered through the 4th intercostal space.

Partial Lower Sternotomy: A 7-8 cm vertical skin incision. Sternotomy from the xiphoid process up to the third intercostal space.

TECAB:
- Camera Port: 5th ICS, midclavicular line
- Instrument Ports: 3rd and 7th ICS, medial to the anterior axillary line

Figure 4: Three different surgical approaches for MICS-CABG

2.3 Postoperative Course

All patients were transferred postoperatively intubated to the intensive care unit (ICU) where ECG, chest radiography and clinical laboratory test as well as blood gas analysis were immediately performed. Standard postoperative care consisted of mechanical ventilation, cardioactive drugs if indicated, the use of warm air heaters to maintain normothermia and analgesia with a combination of nonsteroidal anti-inflammatory drugs and intravenous morphine boluses as required. Blood gas analyses were repeated half-hourly, the laboratory parameters 4 and 8 h after ICU admission. Hemodynamic monitoring was performed by continuous ECG recording, invasive blood pressure and central venous pressure measurement, monitoring of peripheral and central venous saturation. Mechanical ventilation with biphasic positive airway pressure was turned after the admission to the ICU as soon as possible to continuous positive airway ventilation with low positive end-expiratory pressure. Criteria for weaning from the ventilator included absence of bleeding signs (chest tube drainage <100 ml/h, stable haemoglobin values), stable cardiorespiratory conditions

(mean arterial pressure >60 mmHg, central venous saturation >65 and Horowitz index >200), and absence of high inotropic support. If patients fulfilled these criteria, sedation agents were tapered and continuous positive airway ventilation gradually decreased to a minimum level (FiO2: 35 %, PEEP: 5–6 mbar and ASB: 6–7 mbar). Extubation was performed in the presence of appropriate level of consciousness, adequate airway protection reflexes (cough and swallow) and in the absence of respiratory or cardiac distress. Patients were discharged from the ICU to the cardiothoracic ward at least 4 h after extubation but no later than 09:00 p.m. on the day of surgery. During this period, any increasing requirements for cardioactive drugs, or significant decrease in oxygen saturation (<90 % despite oxygen mask), urine output, or level of consciousness, was considered a contraindication for discharge. In the cardiothoracic ward patients monitor surveillance has been performed for two days after the procedure via continuous ECG, peripheral oxygen saturation control and non-invasive blood pressure measurement in a room that fulfils the conditions of an intermediate care unit.
Reasons for readmission included (1) pulmonary (respiratory distress characterized by tachypnea, decrease in arterial saturation <90 %, Horowitz index <200, use of accessory muscles or abdominal paradox, inability to clear secretion); (2) bleeding or pericardial tamponade; (3) severe agitation requiring extended intravenous sedation; (4) upper or lower gastrointestinal bleeding requiring intervention or surgery; (5) any new permanent neurologic deficits (PNDs); (6) hemodynamic instability (any decrease in blood pressure requiring increasing use of cardioactive drugs).

Surgical reexploration was conducted mostly due to postoperative bleeding or pericardial tamponade. The criteria for resternotomy were as follows: (1) new onset bleeding of more than 200 ml/h; (2) more than 800 ml in the first 6 hours; (3) obvious hemodynamic instability due to pericardial tamponade. Definition and diagnosis of perioperative MI included: (1) new onset changes in ECG (horizontal ST segment depression of 1 mm or more, ST segment elevation more than 1 mm, new T-wave inversions; (2) pathological CK/CK-MB ratio (≥10%); (3) angiographical evidence of graft occlusion. Postoperative new neurological deficits were defined according to the “Modified Rankin Scale” and the patients with a score ≥2 (slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance) was accepted as a new neurological deficit.[69]

2.4 Data analysis

All numerical values are presented as mean values ± standard deviation (SD). Categorical data are presented as absolute numbers and percentages. The statistical analysis was processed with BiAS. für Windows software (BiAS. für Windows™ Version 10.12, epsilon-Verlag GbR Hochheim Darmstadt). Categorical data are analyzed by using Chi-squared test. Comparisons were done with Kruskal-Wallis test for means of normally distributed continuous variables. To consider the statistical significance, a *p* value of less than 0.05 was defined. Survival, freedom from redo-CABG and PCI were calculated with Kaplan-Meier method.

2.5 Follow-up and data collection

Follow-up was obtained from patient himself or attending family doctor by letter and telephone interview. Patients' informed consents were waived. The Institutional Ethics Committee of the Johann Wolfgang Goethe University Hospital, Frankfurt am Main, Germany approved the study protocol. All data available were collected retrospectively and registered in Microsoft Excel® 2010 (Redmond, WA). Data about patient's physical condition, postoperative pain perception and intensity, postoperative myocardial infarction, redo-CABG and PCI were collected with aid of operation-specific questionnaires (Suppl. 1-2). Moreover, the latest coronary angiography findings were collected to assess the graft patency.

3. Results

3.1 Preoperative Characteristics

A total of 126 patients underwent minimally invasive coronary artery bypass grafting with three different approaches (TECAB n=63, PLS n=43, ALT n=20). There were 29 (67.44%), 43 (68.25%) and 18 (90%) males ($p>0.05$) and mean age was 64±11, 60±11 and 66±8 in groups PLS, TECAB and ALT, respectively. There were no significant differences between each group regarding BMI, diabetes, arterial or pulmonary hypertension, renal insufficiency, COPD, hyperlipidemia, arrhythmia, peripheral artery disease and previous myocardial infarction ($p>0.05$). Preoperative characteristics of each group are presented in Table 2.

Tab 2: Demographics	PLS	TECAB	ALT	*p* Value
n	43	63	20	
Male (n)	67.44% (29)	68.25% (43)	90% (18)	>0.05
Mean Age	64±11	60±11	66±8	>0.05
BMI	27.21±3.65	26.15±2.44	26.42±3.59	>0.05
Diabetes Mellitus	25.58%	13.33%	14.29%	>0.05
Renal Insufficiency	9.3%	6.67%	0	>0.05
Pulmonary HT	2.33%	0	0	>0.05
Arterial HT	76.74%	86.67%	78.57%	>0.05
Hyperlipidemia	74.42%	86.67%	78.57%	>0.05
Myocardial Infarction	23.26%	13.33%	21.43%	>0.05
Arrhythmia	9.3%	13.33%	14.29%	>0.05
COPD	4.65%	0	7.14%	>0.05

Table 2: Demographics

3.2 Operative Data

Operative data are summarized in Table 3. Thirty-eight (88.37%) patients underwent single-vessel CABG, 4 (9.3%) patients underwent double-vessel CABG and one patient (2.33%) underwent triple-vessel CABG in PLS group. In TECAB group, 49 (77.78%) and 14 (22.22%) patients underwent single and double-vessel CABG, respectively. In ALT group, only double (n=8, 40%) and multiple-vessel (n=12, 60%) CABG was performed. Mean operating times were 96.53±47.53, 236.32±62.51 and 313.5±55.24 minutes in groups PLS, TECAB and ALT, respectively ($p<0.05$). All binary comparisons of 3 groups (PLS vs. ALT, PLS vs. TECAB, ALT vs. TECAB) were also significant regarding operative time ($p<0.05$). Conversion to sternotomy was required only in one patient in PLS group and conversion to anterolateral minithoracotomy was performed in 2 patients in TECAB group due to intraoperative bleeding.

Tab 3: Operative data	PLS	TECAB	ALT	*p* Value
Operating time (min)	96.53±47.53	236.32±62.51	313.5±55.24	<0.05
- PLS vs TECAB				<0.05
- PLS vs ALT				<0.05
- TECAB vs ALT				<0.05
Conversion to minithoracotomy	0	2	0	>0.05
Conversion to sternotomy	1	0	0	>0.05
Procedure				
Single vessel	88.37% (38)	77.78% (49)	0	<0.05
- PLS vs TECAB				>0.05
- PLS vs ALT				<0.05
- TECAB vs ALT				<0.05
Double vessel	9.3% (4)	22.22% (14)	40% (8)	<0.05
- PLS vs TECAB				<0.05
- PLS vs ALT				>0.05
- TECAB vs ALT				>0.05
Multiple vessel	2.33% (1)	0	60% (12)	<0.05
- PLS vs TECAB				>0.05
- PLS vs ALT				<0.05
- TECAB vs ALT				<0.05

Table 3: Operative Data

3.3 Early Postoperative Outcome

There was no significant difference in postoperative chest tube drainage in the initial 24 hours (390.7±222.8 mL, 537.5±509.8 mL and 555.4±335.7 mL in groups PLS, TECAB and ALT, respectively). Similarly, the difference between groups with respect to mean requirement of red cell concentrates did not reach a statistical significance. Mean red cell transfusion was 0.26±0.66 packs in PLS group, 0.71±1.27 packs in TECAB group and 0.21±0.58 packs in ALT group. Duration of intensive care unit (ICU) stay was 0.93±0.4, 0.8±0.41 and 1.07±0.27 days in groups PLS, TECAB and ALT, respectively. Length of hospital stay was comparable in patients who underwent PLS or TECAB, but both groups had significantly shorter hospital stays than ALT patients ($p<0.05$).

Two patients in group ALT developed neurological complications postoperatively in our whole patient cohort, which was significantly higher than that in groups TECAB (n=0) and PLS (n=0) ($p<0.05$). One patient suffered from temporary dysarthria and one had an acute organic brain syndrome. Both patients were well recovered during their further hospital stays without a permanent neurological deficit. Arrhythmia was observed in 7, 3 and 3 patients in groups PLS, TECAB and ALT, respectively ($p=0.06$). In PLS group, one patient underwent sternum revision because of mediastinitis and on 14th postoperative day and in one patient revision of the LIMA-LAD anastomosis was necessary. Two patients in PLS group and one in ALT group suffered from postoperative wound healing disorder. All patients in TECAB group had an uneventful wound healing. There was no in-hospital mortality among the 126 patients. Postoperative data are presented in Table 4.

Tab 4: Postoperative data	PLS	TECAB	ALT	*p* Value
Chest tube drainage 24 h (ml)	390.7±222.83	537.5±509.8	555.4±335.7	>0.05
Red cell concentrate (mean)	0.26±0.66	0.71±1.27	0.21±0.58	>0.05
Neurological complication (n)	0	0	2	<0.05
Arrhythmia (n)	7	3	3	=0.06
Wound infection (n)	2	0	1	>0.05
PCI (n)	7	9	6	>0.05
Re-Operation (n)	1	2	1	>0.05
•	Re-LIMA-LAD through same incision	CABG CABG	CABG	
Mean ICU stay (d)	0.93±0.4	0.8±0.41	1.07±0.27	>0.05
Mean hospital stay (d)	8.72±4.36	8.87±1.77	11.43±3.37	<0.05
- PLS vs TECAB				>0.05
- PLS vs ALT				<0.05
- TECAB vs ALT				<0.05
In-hospital mortality (n)	0	0	0	

Table 4: Postoperative Data

Tab 5: Follow-up data	PLS	TECAB	ALT	*p* Value
n	32	52	19	
Mean Follow-up (y)	11.73±0.72	11.39±1.88	15.70±0,44	<0.05
- PLS vs TECAB				>0.05
- PLS vs ALT				<0.05
- TECAB vs ALT				<0.05
Long-term Survival	84.4% (27)	88.5% (46)	68.4% (13)	>0.05
Graft Patency	87.5% (28)	86.5% (45)	94.7% (18)	>0.05
Intensity of Sternal Pain (0-10)	2.95±2.67	2.02±2.83	3.08±2.68	>0.05
Intensity of Shoulder/Back Pain (0-10)	1.73±2.76	2±2.66	1.75±2.73	>0.05
Parasternal Pain (n)	31.8% (7/22)	25.6% (11/43)	33.3% (4/12)	>0.05

Table 5: Follow-up Data

3.4 Late Clinical Follow-up

Follow-up data are summarized in Table 5. The mean duration of the follow-up was 12.2±2.1 (range 7.2 to 16.1) years with completed in 81.7 % of the patients (n=103). There were 17 late deaths, four of which died of non-cardiovascular results. There was no significant difference in the long-term mortality between three groups. There were no significant differences regarding reoperations. One patient in PLS group underwent sternal re-fixation due to sternal dehiscence at 7 months.

3.4.1 Graft Patency and Redo-Coronary Artery Bypass Grafting/Percutaneous Coronary Interventions

Graft problem is defined as a significant stenosis of the graft which requires PCI or CABG. Freedom from graft problems was in 87.5%, 86.5% and 94.7% in groups PLS, TECAB and ALT, respectively. Freedom from PCI was 78.1%, 82.7% and 68.4% and freedom from Re-CABG was 100%, 96.1% and 94.7% in groups PLS, TECAB and ALT, respectively. There were no statistical significances regarding freedom from Re-CABG and PCI between groups.

3.4.2 Postoperative Pain Intensity and Quality of Pain

Intensity of sternal pain was 2.95±2.67, 2.02±2.83 and 3.08±2.68 ($p>0.05$) and intensity of shoulder/back pain was 1.73±2.76, 2±2.66 and 1.75±2.73 ($p>0.05$) on the 0–10 numeric rating scale (NRS) in PLS, TECAB and ALT patients, respectively. Percental distribution of parasternal pain in PLS, TECAB and ALT groups were 31.8%, 25.6% and 33.3%, respectively.
Figure 5 presents the duration of sternal pain. A large part of the patients (40%) with sternal pain in TECAB group endured more than one year. Duration of sternal pain in PLS and ALT groups usually limited itself during the first postoperative year. Only in 14.3% of ALT patients and 21.4% of PLS patients suffered from sternal pain over one year.

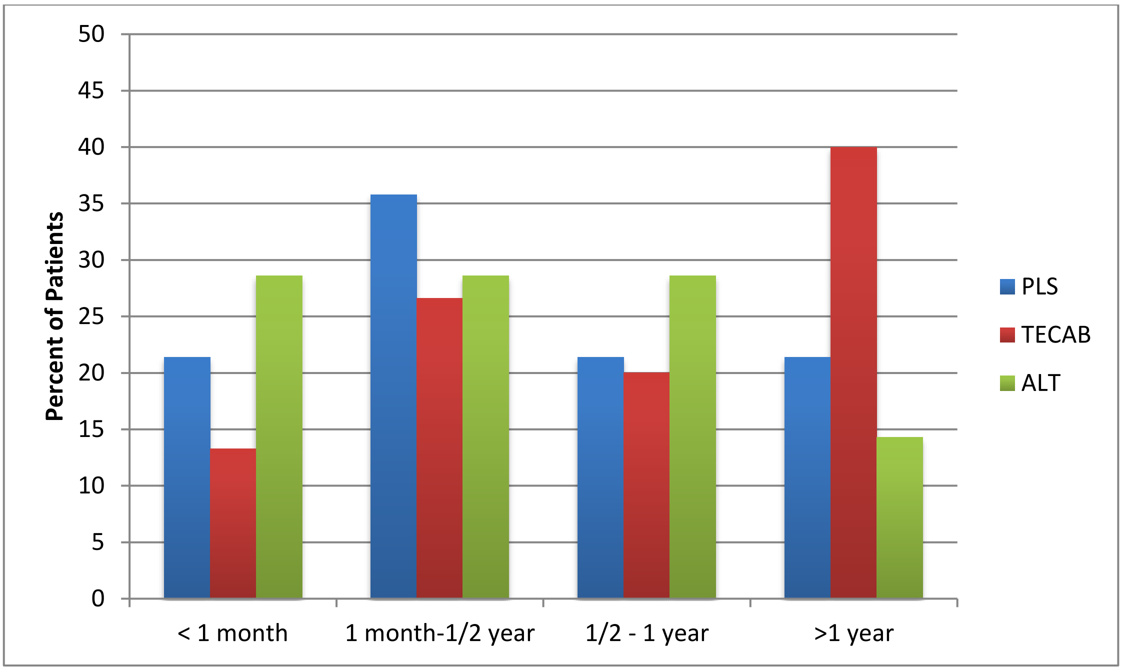


Figure 5: Duration of sternal pain

Frequency of different pain experiences were displayed in Figure 6. Regarding frequency of sternal pain, there were no significant differences between TECAB and ALT groups but frequency of sternal pain in PLS group was significantly higher than both TECAB and ALT groups ($p<0.05$). Frequency of shoulder/back pain was similar in all three groups and could not achieve statistical significance.

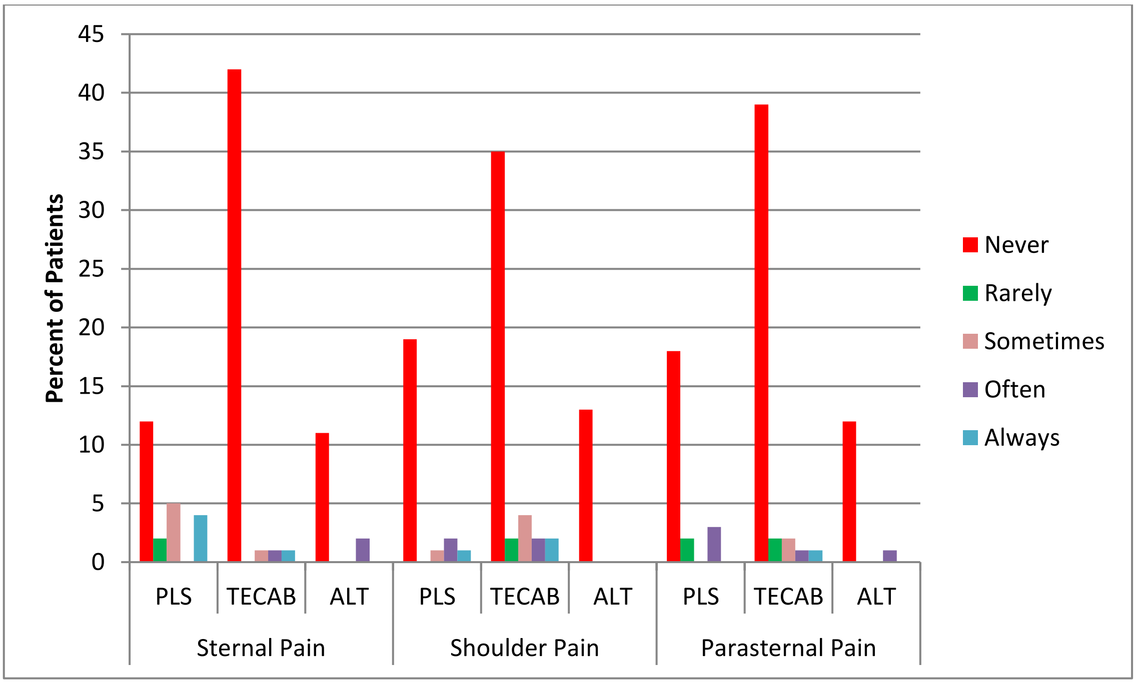


Figure 6: Frequency of different pain types

Quality of postoperative pain was summarized in Table 6. Patients declared their pain experience by using our questionnaire (Suppl. 2) and some marked more than one pain type. Table 5 displays the pain statements of patients. Sternal pain was most commonly seen in PLS patients, who complained predominantly about sticking, pressing and movement induced sternal pain after surgery. Sticking and movement induced sternal pain in PLS group was significantly higher than that in TECAB or ALT group ($p<0.05$). Pressing sternal pain was also higher in PLS group but could not reach statistical significance ($p=0.06$).

Regarding types of shoulder/back pain, statements of the patients were comparable in all groups. Sticking pain was more common in ALT group and movement induced pain was more common in PLS and TECAB groups. Patients, who underwent CABG through a total endoscopic fashion, suffered from pressing pain more than other groups but this trend had no statistical impact.

Quality of parasternal pain was similar in all three groups. Movement induced parasternal pain was obviously more frequent in PLS patients than that in other two groups. ($p=0.0521$).

		Sternal Pain			Shoulder Pain			Parasternal Pain		
		PLS	TECAB	ALT	PLS	TECAB	ALT	PLS	TECAB	ALT
Sticking	No	15	41	10	20	41	10	21	40	10
	Very Mild	4	1	1	1	2	-	1	1	-
	Mild	1	2	1	-	-	2	-	3	2
	Moderate	2	1	1	2	1	-	1	1	1
	Severe	1	-	-	-	1	1	-	-	-
Electrifying	No	22	43	12	22	43	13	22	43	13
	Very Mild	1	-	-	1	1	-	1	-	-
	Mild	-	1	-	-	1	-	-	2	-
	Moderate	-	-	1	-	-	-	-	-	-
	Severe	-	1	-	-	-	-	-	-	-
Burning	No	20	39	12	21	43	12	22	42	12
	Very Mild	1	1	-	2	1	-	-	1	-
	Mild	-	3	-	-	1	-	-	1	-
	Moderate	1	1	1	-	-	-	1	1	1
	Severe	1	1	-	-	-	1	-	-	-
Pressing	No	15	40	10	19	36	11	18	41	11
	Very Mild	3	1	-	-	2	-	3	2	1
	Mild	3	3	2	1	4	-	2	-	-
	Moderate	1	1	1	3	3	1	-	1	1
	Severe	1	-	-	-	-	1	-	1	-
Hammering	No	21	44	12	21	44	12	23	44	12
	Very Mild	1	-	-	-	-	-	-	1	-
	Mild	-	1	-	1	-	-	-	-	-
	Moderate	-	-	1	1	-	-	-	-	1
	Severe	1	-	-	-	1	1	-	-	-
Movement Induced	No	12	37	11	17	34	12	17	41	13
	Very Mild	2	2	1	2	2	-	4	1	-
	Mild	6	3	1	1	5	-	-	2	-
	Moderate	2	1	-	2	3	-	2	-	-
	Severe	1	2	-	1	1	1	-	1	-

Table 6: Quality of pain after MICS-CABG

4. Discussion

There is no doubt that CABG is one of the most important surgical techniques in medical history that has been performed for over half a century and saved millions of lives.[70] Although the obviousness of patient benefit from CABG, invasiveness of this procedure due to median sternotomy and CPB led CABG lose in attractiveness. The accelerated advancement of PCI and its good results in selected cases impeded and partially displaced CABG in single or double vessel CAD, but without reaching the graft patency rates achieved by using especially the left internal mammary artery.[71,72] In order to eliminate the morbidity emanating from the contact of the blood to the extrinsic surface of the extracorporeal circuit, OPCAB technique was introduced at late seventies.[19]
With the aim of reigniting the CABG in patients who have a single or double vessel CAD, several minimally invasive techniques avoiding median sternotomy have been introduced such as PLS, ALT and TECAB.
The above-mentioned minimally invasive techniques intended to combine the advantages of surgical myocardial revascularization with less surgical trauma and therefore to reduce complications like pain and prolonged recovery, bleeding, wound healing disorders and sternal instability.

4.1. Perioperative Morbidity and Mortality

In a long-term follow-up study for ALT, Holzhey and colleagues[73] reported an early postoperative mortality rate of 0.8%, a perioperative neurological complication rate of 2%, a 1.1% conversion rate to sternotomy and a wound infection rate of 0.9%. They found also an angiographic graft patency rate of 95.6% at 6 months and as a result of Kaplan-Meier analysis, 5-year survival of 91.9%. Halkos and colleagues[74] presented the early clinical and angiographic outcomes after OPCAB LIMA-LAD anastomosis through a 3-4 cm minithoracotomy following robotic harvesting of LIMA. In this report, thirty-day mortality was 1.3%, postoperative stroke rate was 0.3%, conversion to sternotomy was 5.2% and wound infection rate was 2%. They performed a pre-discharge follow-up angiography and found a graft patency rate of 95%.
Kappert and colleagues presented their results in a five-year follow-up study

after TECAB.[75] In this study, there was no hospital mortality and overall survival after 5 years was 92.7%.

Our results confirm that MICS CABG can be performed with a great short and long-term outcome. There was no in-hospital mortality. Conversion to minithoracotomy was necessary in 2 (1.6%) patients who underwent TECAB procedure and one (0.8%) partial lower sternotomy was converted to sternotomy. Overall survival was 83.5% after a mean follow-up of 12.2±2.1 years.

The incidence of stroke after CABG was reported in the literature to be 1,2% to 3,8%.[76,77] We observed temporary neurological complications only in 2 (1.6%) ALT patients. A possible explanation may be the older patient population in ALT group. Baker et al researched stroke after CABG and identified the older age as an independent predictor of stroke.[77] Although there was no significant difference between three groups in our study, mean age of the ALT patients was higher than that of the PLS and TECAB patients. Moreover, a recent article reviewed the gender factor in stroke epidemiology and unfolded that stroke is more common among men.[78] In our study, 90 % of the ALT group consisted of males, which may explain the significant increase of neurological complications in that group.

Ng and colleagues[79] compared ALT and complete sternotomy regarding wound complications including incisional hernia, superficial dehiscence, wound infection, chronic pain syndrome and seroma. They found significantly higher wound complications in patients who underwent ALT than that of conventional sternotomy. In our series, wound infections were seen in 2.4% of all patients (one patient in ALT group and two patients in PLS group). Contrary to Ng and colleagues in our study there was no statistical significance between the three groups regarding wound infections.

Certainly, one of the most important issues during postoperative period which can directly influence the outcomes is length of stay in ICU and in hospital. In SYNTAX trial, postoperative length of hospital stay was 9.5 ± 8 days in CABG cohort.[41]

In a very recent study[80] with almost 35,000 patients older than 65 years, Moitra and colleagues found that increasing length of stay in ICU is associated with higher 1-year mortality. Therefore same surgical procedures have been tried to be performed in a minimally invasive manner to recover from the operation faster. Atluri and colleagues reported a significantly shortened hospitalization for MICS CABG when compared to conventional CABG.[81] Lee and colleagues confirmed that increased surgical trauma causes prolonged hospital stay.[82] In this study, conversion to sternotomy was found as a factor, that's presence prolongs the hospital stay. On the other hand, Halkos and colleagues compared sternotomy with non-sternotomy in patients who underwent LIMA-LAD grafting and they found no statistical significance between sternotomy and non-sternotomy patients in terms of hospital stay and ICU stay.[83] In our study, duration of ICU stay was not significant between groups. Length of the hospital stay was comparable in patients who underwent PLS or TECAB, but both groups had significantly shorter hospital stays than ALT patients.

4.2. Follow-up and Long-Term Results

In a review of 13-year single-center experience with ALT, Holzhey and colleagues reported a completeness of 10-year-follow-up for 77% of all possible patients. They found a 10-year-survival rate of 76.6%.[84] In another retrospective study[85], Hoffmann et al compared the short- and long-term follow-up after ALT between octogenarians and a younger group (mean age=64). In this study, the median follow-up time was 5.5 years and follow-up completeness reached 96.9%. The 5-year survival was 90% in the younger group. Kappert and colleagues[75] reported a 5-year follow-up after TECAB and demonstrated an overall survival of 92.7%. In our study, the mean duration of the follow-up was 12.2±2.1 years with completed in 81.7 % of the patients. Our follow-up data demonstrated an overall survival rate of 83.5%. In ALT group, overall survival was 68.4% after a mean follow-up of 15.7 years. In TECAB group after a mean follow-up of approximately 11.4 years, the overall survival was 88.5%. Our experience is in accordance with the literature.

4.3. Postoperative Pain

Patients' preoperative concerns about the operation mostly focus on the anticipated postoperative pain. Postoperative pain can restrict patient's mobility and movements. Moreover it may cause morbidities or even mortalities, prolonged ICU/hospital stay and impaired quality of life. For this reason it is plausible, if possible, to minimize the surgical trauma and thus related postoperative pain. Niinami and colleagues represented the early outcomes and postoperative pain in patients who underwent off-pump single-vessel revascularization through either minithoracotomy or ministernotomy.[86] This study reported that minithoracotomy causes postoperative pain of higher intensity than ministernotomy does. Walther and colleagues compared postoperative pain levels after minimally invasive and conventional cardiac surgery in a prospective study.[44] They found that patients with a lateral minithoracotomy had lower pain levels from the 3rd postoperative day onwards. Lichtenberg et al demonstrated significantly higher levels of postoperative pain following MIDCAB.[87] In a recent study, Uymaz and colleagues studied clinical outcome and pain perception in patients who received off-pump MIDCAB surgery through PLS.[45] Significantly lower intensity of pain was observed in PLS group than in conventional sternotomy group. They also found less need for analgetics in the group of PLS patients. In our study, we could not find any statistical significance regarding intensity of sternum and back/shoulder pain between all three minimally invasive approaches for CABG. Surprisingly, patients who underwent TECAB surgery also suffered from similar pain intensity, although the burden of surgical trauma is plainly smaller than other two approaches. Parasternal pain was observed similar between all groups.

By using operation specific questionnaires, we aimed to determine quality of postoperative pain. Patients were also interested in to share their pain experiences, thus we could reach a return rate of postal questionnaires almost 80% of our cohort. We found sticking and movement induced sternal pain in PLS group was significantly higher than that in TECAB or ALT group. Additionally, PLS patients suffered from pressing sternal pain more than the other groups did but that could not reach statistical significance. Sticking pain was observed more frequently in ALT group and movement induced pain was detected mostly in PLS and TECAB groups. Patients, who underwent CABG through a total endoscopic fashion, suffered from pressing pain more than other groups did but this trend had no statistical impact. In our opinion, identifying the specific type of pain plays during recovery period and in expeditious return to daily activities a very decisive role, since the sufficient pain killing can just be ensured with finding the etiology of pain.

4.4. Study Limitations

This study has some limitations. A major limitation is the absence of a routine angiographic assessment of bypass grafts. For this reason, we obtained follow-up data by using our operation specific questionnaires which also include questions about problems with bypasses and reinterventions/reoperations during postoperative period. The retrospective nature of the manuscript is also a further major limitation.

4.5. Conclusion

MICS CABG can be performed safely and effectively. Short and long-term outcomes of MICS CABG are comparable with those of the gold standard procedure “conventional CABG”. Contrary to our expectations, there were no radical differences regarding pain intensity between all three groups, although all three minimally invasive techniques have completely different surgical accesses. We believe that similar postoperative pain intensity regardless the surgical access may just be induced by harvesting of LIMA, since only this step of surgery was identical in all minimally invasive bypass procedures.

5. Abstract

Background: Minimally invasive coronary artery bypass grafting (MICS CABG) has been introduced to abstain from median sternotomy due to related comorbidities. The aim of this study is to report the long term results of three different MICS CABG strategies: Partial lower sternotomy (PLS), totally endoscopic coronary artery bypass grafting (TECAB) and anterolateral thoracotomy (ALT). Moreover we aimed to compare these surgical approaches in terms of quality of pain and pain intensity.

Methods: From 1997 to 2006, 126 patients underwent MICS CABG surgeries in our department through different surgical approaches: 43 PLS, 63 TECAB and 20 ALT. Preoperative characteristics were similar between groups. There were 90 males (71.4%) and 36 (28.6%) females with a mean age of 62±11 years (Range 36 to 90).

Results: There was no in-hospital mortality. Conversion to minithoracotomy was necessary in 2 (1.6%) patients and conversion to sternotomy was performed in 1 (0.8%) patient. Length of hospital stay was comparable in patients who underwent PLS or TECAB, but both groups had significantly shorter hospital stays than ALT patients ($p<0.05$). Two patients in group ALT developed temporary neurological complications postoperatively, which was significantly higher than that in groups TECAB (n=0) and PLS (n=0) ($p<0.05$). Mean follow-up was 12.2±2.1 (range 7.2 to 16.1) years with completed in 81.7 % of the patients. There were 17 late deaths. Freedom from graft problems was 87.5%, 86.5% and 94.7%; freedom from percutaneous coronary interventions (PCI) was 78.1%, 82.7% and 68.4% and freedom from Re-CABG was 100%, 96.1% and 94.7% in PLS, TECAB and ALT group, respectively. Pain intensity was similar between all three groups.

Conclusion: MICS CABG can be performed safely and effectively. Short and long-term outcomes of MICS CABG are comparable with those of the conventional CABG. There were no major differences regarding pain intensity between all three groups, although all three minimally invasive techniques have completely different surgical accesses.

6. Zusammenfassung

Hintergrund: Die minimalinvasive koronare Bypassoperation (MICS CABG) ist eingeführt worden, um auf die mediane Sternotomie wegen der damit verbundenen Komorbiditäten zu verzichten. In der vorliegenden Studie untersuchten wir die Langzeitergebnisse von drei unterschiedlichen MICS CABG-Strategien: Partielle untere Sternotomie (PLS), total-endoskopische koronare Bypassoperation (TECAB) und anterolaterale Thorakotomie (ALT). Außerdem wurden diese chirurgischen Zugangswege in Bezug auf Schmerzqualität und Schmerzintensität verglichen.

Methoden: Im Zeitraum von 1997 bis 2006 wurden insgesamt 126 MICS CABG-Prozeduren in unserer Klinik durch verschiedene Zugangswege durchgeführt: 43 PLS, 63 TECAB und 20 ALT. Die Patienten waren im Mittel 62 ± 11 Jahre alt (36 bis 90 Jahre), der Anteil der männlichen Patienten betrug 71.4 %.

Ergebnisse: Es gab keine In-Hospital-Mortalität. Konversion zur Minithorakotomie war nötig bei 2 Patienten (1.6%) und Konversion zur Sternotomie wurde bei einem Patienten (0.8%) durchgeführt. Die Krankenhausaufenthaltsdauer war vergleichbar bei PLS und TECAB-Patienten, aber beide Gruppen hatten einen signifikant kürzeren Krankenhausaufenthalt als die ALT-Gruppe ($p<0.05$). Zwei der ALT-Patienten entwickelten postoperativ temporäre neurologische Komplikationen, welche signifikant höher waren als in der TECAB- ($n=0$) und PLS-Gruppe ($n=0$)($p<0.05$). Das durchschnittliche Follow-up war 12.2 ± 2.1 Jahre (7.2 bis 16.1 Jahre) und konnte bei 81.7% der Patienten abgeschlossen werden. Die späte Mortalität betrug 16.5%. Die Freiheit von Bypassproblemen lag bei 87.5%, 86.5% und 94.7%; Freiheit von perkutanen koronaren Interventionen bei 78.1%, 82.7% und 68.4% und die Freiheit von Re-CABG bei 100%, 96.1% bzw. 94.7% in PLS, TECAB und ALT-Gruppe. Die Schmerzintensität war ähnlich in allen Gruppen.

Schlussfolgerung: MICS CABG kann sicher und effektiv durchgeführt werden. Kurz- und Langzeitergebnisse von MICS CABG sind vergleichbar mit denen der konventionellen Bypassoperation. Obwohl alle drei minimalinvasiven Techniken ganz unterschiedliche Zugangswege haben, wurde kein signifikanter

Unterschied zwischen allen Gruppen bezüglich der Schmerzintensität gefunden.

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SUPPLEMENTS

Supplement 1: Operation-Specific Questionnaire for State of Health (in German)

Klinikum der Johann Wolfgang Goethe Universität
Klinik für Thorax-, Herz- und Gefäßchirurgie
Direktor: Prof. Dr. med. Anton Moritz

Fragebogen zur Erfassung des Gesundheitszustandes von Patienten nach einer aortocoronaren Bypassoperation.

Name ______________________ Datum ____________________

- **Haben Sie belastungsabhängige Atemnot?**
  - ☐ Nein
  - ☐ Bei starker körperlicher Belastung
  - ☐ Beim Treppensteigen (2. Stock) und beim Bergaufgehen
  - ☐ Beim langsamen Gehen in der Ebene oder beim Treppensteigen (1. Stock)
  - ☐ Bei geringer Bewegung oder in Ruhe

- **Haben Sie belastungsabhängige Brustschmerzen (Angina Pectoris)?**
  - ☐ Nein
  - ☐ Bei starker körperlicher Belastung
  - ☐ Beim Treppensteigen (2. Stock) und beim Bergaufgehen
  - ☐ Beim langsamen Gehen in der Ebene oder beim Treppensteigen (1. Stock)
  - ☐ Bei geringer Bewegung oder in Ruhe

- **Bestand zum Zeitpunkt der Entlassung oder später eine Wundheilungsstörung?**
  - ☐ Nein
  - ☐ Im Bereich des Brustbeines
  - ☐ Im Bereich der Wunde am Bein

- **Haben Sie nach der Entlassung einen Herzinfarkt erlitten?**
  - ☐ Nein
  - ☐ Vorderwand
  - ☐ Hinterwand
  - ☐ Seitenwand

Datum des Herzinfarktes: ______________________________

Waren Sie deshalb in einem Krankenhaus aufgenommen?

Wann: ______________________ Wo: ____________________

1

Klinikum der Johann Wolfgang Goethe Universität
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- **Haben Sie in der Zwischenzeit eine der folgende Untersuchungen gehabt?**
  - ☐ Herzkatheter, Datum ____________________ Ort ____________________
  - ☐ CT (Computertomographie) des Herzens
    Datum ____________________ Ort ____________________

- **Ergab sich ein Problem an den Bypassgrafts?**
  - ☐ keine
  - ☐ Ja, im Bereich der: ☐ Vorderwand ☐ Hinterwand ☐ Seitenwand

- **Haben Sie seit der Herzoperation einen der folgenden Eingriffe gehabt:**
  - ☐ PTCA der Herzkranzgefäße, Datum ____________ Ort____________________
  - ☐ Stent der Herzkranzgefäße, Datum ____________ Ort____________________
  - ☐ Erneute Herzoperation, Datum ____________ Ort____________________
    Grund ____________

- **Sind in der Zwischenzeit andere, schwere Erkrankungen aufgetreten?**
  - ☐ Schlaganfall ☐ Sonstige ____
    ____
    Datum: ________________

Wir bitten Sie um Erlaubnis, Ihre Daten zur Qualitätskontrolle bei uns zu speichern und gegebenenfalls bei Ihren behandelnden Ärzten uns bei Rückfragen zu erkundigen.

☐ Einverstanden

____
Patientenunterschrift, Telefon

____
Kardiologe o. Hausarzt, Telefon

Supplement 2: Operation-Specific Pain Questionnaire (in German)

Klinikum der Johann Wolfgang Goethe Universität
Klinik für Thorax-, Herz- und Gefäßchirurgie
Direktor: Prof. Dr. med. Anton Moritz

THG

Schmerzfragebogen zur Erfassung von Patienten mit minimaler invasiver Operationstechnik.

Name ______________________ Datum ____________________

- **Hatten Sie in den Wochen nach der Operation Schmerzen am Brustbein?**

Bitte markieren Sie in der unten gezeigten Skala von 0-10 den Schweregrad Ihrer Schmerzen (0 = keine Schmerzen, 10 = unerträgliche Schmerzen)

0	1	2	3	4	5	6	7	8	9	10
Keine		gering		etwas	mittel	schwer		sehr schwer		unerträglich

- **Bitte beurteilen Sie die Qualität Ihrer Schmerzen am Brustbein:**

	Sehr	ziemlich	mittel	wenig	entfällt
Stark	☐	☐	☐	☐	☐
Stechend	☐	☐	☐	☐	☐
Elektrisierend	☐	☐	☐	☐	☐
Brennend	☐	☐	☐	☐	☐
Hämmernd	☐	☐	☐	☐	☐
Drückend	☐	☐	☐	☐	☐
Häufig	☐	☐	☐	☐	☐
Bewegungs-abhängig	☐	☐	☐	☐	☐

1

Klinikum der Johann Wolfgang Goethe Universität
Klinik für Thorax-, Herz- und Gefäßchirurgie
Direktor: Prof. Dr. med. Anton Moritz

- **Wie lange haben diese Schmerzen angehalten?**
  - ☐ < 4 Wochen
  - ☐ ½ Jahr bis 1 Jahr
  - ☐ 1 Monat bis ½ Jahr
  - ☐ > 1 Jahr

- **Hatten/Haben Sie Schmerzen im Bereich der Schultern / des Rückens?**

Bitte markieren Sie in der unten gezeigten Skala von 0-10 den Schweregrad Ihrer Schmerzen (0 = keine Schmerzen, 10 = unerträgliche Schmerzen)

0	1	2	3	4	5	6	7	8	9	10
Keine		gering		etwas	mittel	schwer		sehr schwer		unerträglich

- **Bitte beurteilen Sie die Qualität Ihrer Schmerzen im Bereich der Schultern / des Rückens:**

	Sehr	ziemlich	mittel	wenig	entfällt
Stark	☐	☐	☐	☐	☐
Stechend	☐	☐	☐	☐	☐
Elektrisierend	☐	☐	☐	☐	☐
Brennend	☐	☐	☐	☐	☐
Hämmernd	☐	☐	☐	☐	☐
Drückend	☐	☐	☐	☐	☐
Häufig	☐	☐	☐	☐	☐
Bewegungs-abhängig	☐	☐	☐	☐	☐

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Klinik für Thorax-, Herz- und Gefäßchirurgie
Direktor: Prof. Dr. med. Anton Moritz

- **Hatten/Haben Sie Schmerzen seitlich neben dem Brustbein (im Bereich von gedachten Hosenträgern)?**
  - ☐ Ja
  - ☐ Nein

- **Bitte beurteilen Sie die Qualität Ihrer Schmerzen in diesem Bereich:**

	Sehr	ziemlich	mittel	wenig	entfällt
Stark	☐	☐	☐	☐	☐
Stechend	☐	☐	☐	☐	☐
Elektrisierend	☐	☐	☐	☐	☐
Brennend	☐	☐	☐	☐	☐
Hämmernd	☐	☐	☐	☐	☐
Drückend	☐	☐	☐	☐	☐
Häufig	☐	☐	☐	☐	☐
Bewegungs-abhängig	☐	☐	☐	☐	☐

- **Hatten Sie Schmerzen im Bereich der Einstichstellen im Brustkorb?**
  - ☐ Ja
  - ☐ Nein

Klinikum der Johann Wolfgang Goethe Universität
Klinik für Thorax-, Herz- und Gefäßchirurgie
Direktor: Prof. Dr. med. Anton Moritz

- **Verspüren Sie ein Knacken bei Bewegung im Brustbein?**
  - ☐ Ja
  - ☐ Nein

Datum ________________________

Wir bitten Sie um Erlaubnis, Ihre Daten zur Qualitätskontrolle bei uns zu speichern und gegebenenfalls bei Ihren behandelnden Ärzten uns bei Rückfragen zu erkundigen.

☐ Einverstanden ______________________________
Patientenunterschrift, Telefon

____
Kardiologe o. Hausarzt, Telefon

SCHRIFTLICHE ERKLÄRUNG

Ich erkläre ehrenwörtlich, dass ich die dem Fachbereich Medizin der Johann Wolfgang Goethe-Universität Frankfurt am Main zur Promotionsprüfung eingereichte Dissertation mit dem Titel

**Pain Intensity and Graft Patency following Minimally Invasive Coronary Artery Bypass Grafting.
A comparison of three different approaches.**

in der Klinik für Thorax-, Herz- und Thorakale Gefäßchirurgie unter Betreuung und Anleitung von Herrn PD. Dr. med. Nestoras Papadopoulos ohne sonstige Hilfe selbst durchgeführt und bei der Abfassung der Arbeit keine anderen als die in der Dissertation angeführten Hilfsmittel benutzt habe. Darüber hinaus versichere ich, nicht die Hilfe einer kommerziellen Promotionsvermittlung in Anspruch genommen zu haben.

Ich habe bisher an keiner in- oder ausländischen Universität ein Gesuch um Zulassung zur Promotion eingereicht. Die vorliegende Arbeit wurde bisher nicht als Dissertation eingereicht.

____________________ ________________________

(Ort, Datum) (Unterschrift)