

## EARLY MORBIDITY AND MORTALITY IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT WITH AND WITHOUT CORONARY ENDARTERECTOMY. A SINGLE CENTRE EXPERIENCE

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### ABSTRACT

**Objective:** To compare the early morbidity and mortality in patients undergoing coronary artery bypass grafting (CABG) with and without coronary endarterectomy (CE) in our hospital settings.

**Study Design:** Comparative prospective study.

**Place and Duration of Study:** Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Rawalpindi Pakistan, from Jan 2019 to Jan 2021.

**Methodology:** Consecutive 1820 patients who fulfilled the inclusion criteria and underwent conventional coronary artery bypass grafting (were included in group "A", while 130 patients who underwent coronary endarterectomy during coronary grafting were included in group "B". We identified and compared the preoperative risk factors, early mortality and perioperative complications in our study.

**Results:** In our study the early mortality between both the groups i.e. conventional coronary artery bypass grafting (group A) and coronary artery bypass grafting with coronary endarterectomy (group B) was 3.1% and 5% ( $p=0.07$ ). Amongst the perioperative and postoperative characteristics of patients in both the groups; CPB time, aortic X-clamp time, ICU stay, postoperative Max CKMB, inotropic requirement, hemodynamic instability requiring IABP, dysrhythmias, significant bleeding and LIMA as conduit were significant with the  $p$ -value $<0.05$ . However, ventilation time, requirement of products (FFP, Platelets) and pleural effusion were non-significant.

**Conclusion:** Although early mortality in coronary artery bypass grafting with coronary endarterectomy is higher than the conventional coronary artery bypass grafting, but this difference is statistically insignificant. However, there is an evidence of higher perioperative complications in coronary endarterectomy group in comparison to conventional CABG.

**Keywords:** Coronary artery disease, Coronary endarterectomy, Coronary artery bypass grafting, Cardiopulmonary bypass, Intra-aortic balloon pump, Left internal mammary artery, Creatinine kinase-myocardial band.

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### INTRODUCTION

The incidence of coronary artery disease (CAD) is on the rise and it has become one of the most common causes of death worldwide. There exists a number of procedures to treat CAD including percutaneous coronary intervention (PCI) but coronary artery bypass grafting (CABG) still remains the most valuable modality of treatment for this disease<sup>1</sup>. Today, the incidence of obesity, dyslipidaemias, diabetes and smoking is increasing, as a result it has made CABG surgery more challenging. Coronary endarterectomy (CE) has come up as a useful adjunct in performing CABG surgery in those vessels which are diffusely diseased<sup>2</sup>. As the lumen in these diffusely diseased vessels is completely obliterated or critically narrowed down by the atheromatous plaque, it is very difficult to graft them without removing the atheroma through endarterectomy<sup>3</sup>. The

CE has two types: closed and open. In closed type, the atheroma is pulled out by making a small longitudinal arteriotomy in the native artery wall. Whereas, in cases where this closed removal of plaque is difficult to perform the arteriotomy is extended to lay open the vessel and remove it (open type). The vessel is then reconstructed by either on-lay internal mammary patch or venous patch with or without internal mammary anastomosis. CE was first introduced by Bailey *et al*<sup>4</sup>. Later on, this technique went out of fashion because of the published studies demonstrating considerable mortality and morbidity associated with CE in CABG surgery in comparison to the standard CABG<sup>5-6</sup>. Until late nineteenth century, CE again gained a significant acceptance due to improvement in the surgical techniques. Many studies supported CE and showed that the mortality of CE is comparable to the standard CABG, however, with increased morbidity. Recently a number of studies are showing favourable outcome of CE in CABG surgery<sup>7-10</sup>. This study aims to compare the

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early morbidity and mortality in patient undergoing CABG surgery with and without CE.

## METHODOLOGY

This comparative prospective study was conducted on patients who underwent CE combined with CABG or standard CABG Surgery, at Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi, from January 2019 to January 2021. After seeking approval from the ethics committee of the hospital, data of patients fulfilling the inclusion criteria was entered on the form and patients were divided into two groups. CABG-only (group A) and CABG with CE (group B). Inclusion criteria included all patients irrespective of age and gender who underwent both on-pump and off-pump CABG with and without CE during the study period. However, exclusion criteria comprised of any concomitant procedure other than CABG, Emergency CABG, minimally invasive re-vascularization procedures, dialysis dependent patients, acute pulmonary failure or compensated heart failure and an ejection fraction of <20%. Perioperative indications of CE included either total or subtotal occlusion of a graftable epicardial vessel supplying a viable myocardium, heavy calcification of native coronary artery that made grafting difficult or diffuse disease with multi-segment narrowing. After collection the data was analysed on SPSS-20. Continuous and Ordinal variables were expressed as mean  $\pm$  SD and nominal variables were expressed as frequency and percentage. For comparison of categorical variables between two groups chi-square test was used, while for comparison of continuous variables independent t-test was used.

Early mortality was defined as death within 30 days of surgery, whether in or out-hospital and similarly early morbidities included complications resulting from the CABG surgery, directly or indirectly within 30 days of procedure. Post-operative maximum rise in creatinine Kinase - Myocardial Band (CK-MB) if >10 times of 99<sup>th</sup> percentile URL in addition to either; new ischaemic ECG changes, development of new pathological Q-waves, imaging evidence of loss of viable myocardium thereby indicating perioperative myocardial infarction. Dysrhythmias included new onset rhythm abnormality that was confirmed on ECG and required treatment like atrial fibrillation, ventricular tachycardia and premature ventricular ectopics (PVC's). Significant Bleeding comprised of those patients who received transfusion of >4 units of RCC 's during 30 days of procedure. Prolonged intubation

comprised of ventilatory support for >48 hours of the procedure. ICU stay was the number of days that a patient spent in ITC after CABG. Haemodynamic instability was defined as perioperative requirement of IABP for low pressures not responding to IV pressers. Mild Inotropic support included requirement of one inotrope, moderate contained two inotropes whereas high inotropic support included requirement of more than two inotropes or IABP. Demographic and pre-operative risk factors included age, gender, BMI, hypertension, diabetes, smoking, euro-score and Ejection fraction. Intraoperative data included total CPB time, aortic cross clamp time, number of coronary vessels endarterectomized, Inotropic supports, requirement of IABP. Primary and secondary outcomes included early mortality and morbidities comprising of ventilation time, ICU stay, max CKMB, significant bleeding, dysrhythmias and total hospital stay. Postoperatively all patients received aspirin within 6 hours of CABG and those undergoing CE received both aspirin and heparin which was bridged to warfarin (2.5mg daily) later for the initial three months of CABG surgery.

## RESULTS

There were 1820 patients in group A and 130 patients in group B (1829 vs 130). Both the groups had male preponderance with 82% in group A and 83% in group B ( $p=0.003$ ). Likewise 53% of patients in group A were Hypertensive in comparison to 55% in group B ( $p=0.001$ ), moreover 40% of patients in group A turned out to be diabetic as compared to 53% in group B ( $p=0.001$ ). A total of 583 i.e. 32% of the patients in group A were smokers in comparison to 39 patients i.e. 30% in group B ( $p=0.001$ ). Similarly, in group A 1.3% of patients had an EF <30% in comparison to 4% in group B, 16% vs 46% had an EF ranging from 30-50% and 82% vs 50% had EF >50% ( $p=0.001$ ). In terms of extent of CAD, 3.4% of the patients were suffering from SVCAD, 13% had DVCAD and 84% turned out to have TVCAD in group A in comparison to 0%, 8.4% and 91% in group B, respectively. A total of 361 (94%) patients in group A had associated left main stem disease in comparison to 23 (6%) patients in group B ( $p=0.001$ ). Rest of the preoperative characteristics like age, BMI, CCS class and Euro SCORE II were non-significant as mentioned in the table-I.

Amongst the perioperative and postoperative characteristics of patients in both the groups A and B; CPB time, aortic X-clamp time, ICU stay, postoperative Max CKMB, Inotropic requirement, hemodynamic instability requiring IABP, dysrhythmias, significant

bleeding and LIMA as conduit were significant with the  $p$ -value $<0.05$ . However, mortality, ventilation time, requirement of products (FFP, platelets) and pleural effusion were non-significant as shown in the table-II.

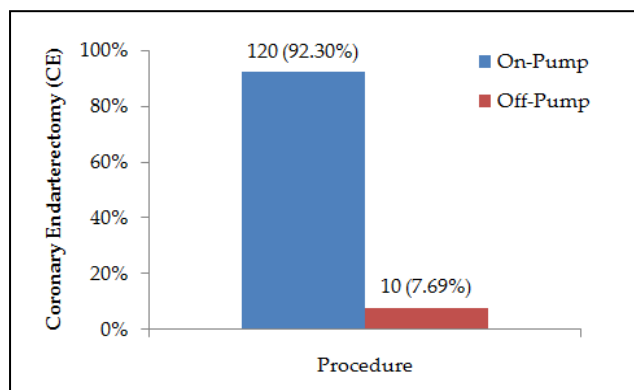
**Table-I: Preoperative characteristics of group A & B.**

Variables	Group A (CABG only) n=1820	Group B (CABG+ CE) n=130	p-value
Age (years)	59.1	58.1	0.832
<b>Gender</b>			
Male	1495 (82%)	108 (83%)	0.003
Female	326 (18%)	24 (17%)	
BMI	27.1± 4.4	27.1 ± 3.5	0.818
Hypertension	971 (53%)	71 (55%)	0.001
Diabetes	729 (40%)	69 (53%)	0.001
Smoking	583 (32%)	39 (30%)	0.001
<b>CCS Class</b>			
I	116 (6.3%)	8 (6.1%)	0.56
II	940 (52%)	69 (53%)	
III	299 (16.4%)	21 (16.1%)	
<b>LMS Disease</b>			
51-70%	116 (91.3%)	11 (8.7%)	0.001
>70%	245 (95.3%)	12 (4.7%)	
<b>Extent of CAD</b>			
SVCAD	62 (3.4%)	-	0.001
DVCAD	234 (13%)	11 (8.4%)	
TVCAD	1525 (84%)	119 (91%)	
<b>EF %</b>			
20-29%	24 (1.3%)	5 (4%)	0.001
30-50%	296 (16.2%)	60 (46%)	
>50%	1500 (82%)	65 (50%)	
Euro Score II	6.7 ± 6.2	7.4 ± 6.2	0.601

**Table-II: Preoperative characteristics of group A & B.**

Variables	Group A (CABG only) n=1820	Group B (CABG+ CE) n=130	p-value
Mortality	55 (3.1%)	7 (5%)	0.07
Ventilation time (hours)	12.4 ± 38.47	19.3 ± 33.86	0.05
CPB time (mins)	74 ± 4.5	95 ± 9.5	0.003
X-clamp time (mins)	52 ± 5	64.6 ± 8	0.0004
ICU stay (hours)	60 ± 77.5	86.2 ± 79.2	0.001
Postop max CKMB (ng/ml)	62.5 ± 80.5	93.05 ± 136.8	0.001
HI-IABP	29 (1.6%)	10 (8%)	0.031
Inotropes	1810 (48.8 ± 54.5)	130 (76.6 ± 70.3)	0.001
LIMA as conduit	1526 (84%)	92 (71%)	0.001
Significant Bleeding	228 (12.5%)	113 (87%)	0.001
<b>Products</b>			
FFP	152 (8.3%)	30 (23%)	0.860
Platelets	182 (10%)	31 (23.5%)	0.077
Dysrhythmias	20 (1.09%)	12 (9.2%)	0.024
Total hospital stay	6.2 ± 4.1	7.3 ± 3.9	0.006
Pleural effusion	23 (1.2%)	4 (3%)	0.823

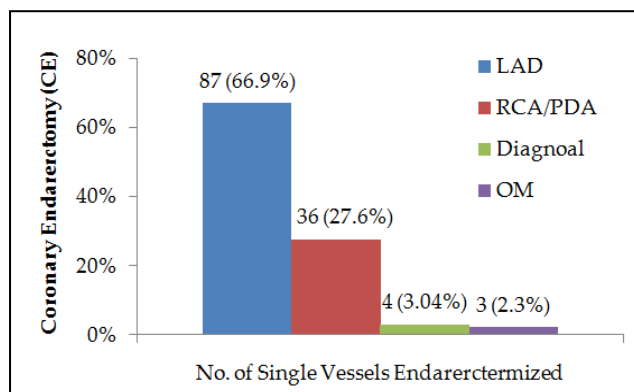
Out of a total of 130 patients who underwent CE in group B, 120 (92.3%) were performed during on-pump CABG, whereas 10 (7.69%) were performed during off-pump CABG (fig-1).



**Figure-1: Frequency of on-pump versus off-pump (n=130).**

LAD was found to be the most frequently endarterectomized vessel accounting for 66.9% of the CE cases. It was followed by distal RCA/PDA that constituted 27.6% of CE and remained the second most common vessel endarterectomized after LAD.

There were only 4 cases representing 3.07% cases in which diagonal artery was endarterectomized and lastly only 3 (2.3%) cases had a CE of obtuse marginal artery. Moreover, single vessel CE was performed in 120 cases i.e. 92.3% while double vessel CE was performed in 10 patients with a percentage of 7.6% (fig-2).



**Figure-2: Site and number of single vessels.**

The most commonly performed CE in double vessels included LAD ± distal RCA/PDA in 7 cases (5.3%) followed by 1 (0.76%) for each distal RCA/PDA + diagonal, LAD + obtuse marginal and LAD + diagonal vessels (fig-3).

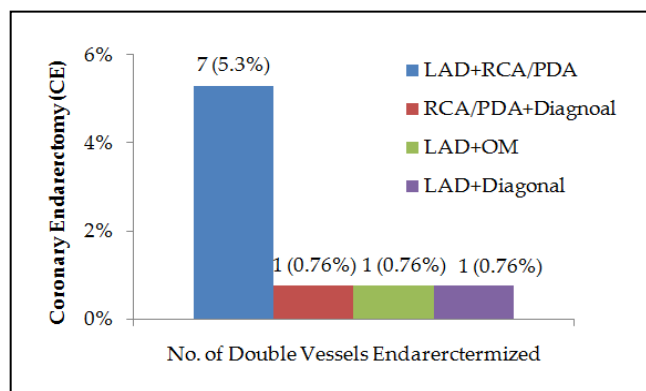


Figure-3: Site and number of double vesselce.

## DISCUSSION

CE is a procedure that is performed on coronary vessels when there are flow limiting localized conditions<sup>11</sup> that might include either an atheromatous plaque<sup>11</sup>, small lumen of vessel normally less than 1mm supplying a large viable myocardium<sup>12-13</sup> or presence of hard calcification which ruptures during suturing there by causing anastomotic compromise or embolic phenomenon<sup>11</sup>.

Practically CE involves removal of internal and middle layers of a coronary vessel affected in atheromatous or calcific process through a limited (closed) or extended (open) arteriotomy and then closing it with either LIMA or saphenous-vein. Onlay-patch grafting of LIMA was introduced by Shapira *et al*<sup>14</sup>, later on Beretta *et al* observed reduced mortality and improved long term survival when LIMA was used in CE in comparison to saphenous vein grafting<sup>15</sup>. Conversely, Myers *et al* found that either LIMA on lay-patch or Saphenous vein patch plus LIMA grafting had no significant impact on survival<sup>16</sup>.

Brenowitz *etal*<sup>17</sup> and Atik *etal*<sup>18</sup> found out that pre-operative characteristics like age >70 yrs, reoperation, IDDM, female sex, left ventricular dysfunction (EF <35%), left main disease and acute MI were statistically significant in CE group as compared to CABG only group. In our study we also found out that comorbid like hypertension, DM, Smoking, significant LM disease, TVCAD and EF <50% had significant association with CE Group as compared to CABG only group ( $p$ -value <0.05). In contrast, our study pointed out rather male gender to be more linked with CE as compared to the female populace. Similar contradictory findings has been observed by various local<sup>2</sup> and international authors<sup>7,18</sup>. Whereas, there was no statistically significant difference between both the groups in terms of age, BMI, CCS class and Euro SCORE II in our study.

In our study we did not find any significant difference between both the groups in terms of ventilation time ( $p$  value 0.05), requirement of products including FFP's and platelets ( $p$ -values 0.86 and 0.077 respectively) and pleural effusions ( $p$ -value 0.823). This results for these variables coincides with other authors<sup>8,10,13,14,19,20</sup>. However, Soylu *et al*<sup>21</sup> showed significant pulmonary complications including ventilation time and pleural effusions in CE group with a  $p$ -value of <0.0001. Similar findings were observed by Wang *et al*<sup>22</sup> and Sirivella *et al*<sup>23</sup> showing poorer short term outcomes after CE during CABG surgery for diffuse CAD.

In this study we found out that the total CPB time and cross clamp time were significantly longer amongst the CE group in comparison to the CABG only group ( $p$  value <0.05). A similar finding was observed by other authors like Wang *et al*<sup>22</sup>, Bitan *et al*<sup>24</sup> and Soylu *et al*<sup>21</sup> who tried to attribute this finding with a higher post-operative complications.

Like wise, our results showed that CABG with CE group is associated with significant ICU stay, Postop Max CKMB, HI-IABP, requirement of Inotropes, significant bleeding requiring transfusions, dysrhythmias and total hospital stay as compared to the conventional CABG group. These findings were similar to large meta-analysis conducted by Soylu *et al*<sup>21</sup> including 54, 440 patients in CE  $\pm$  CABG group vs 47, 074 patients in CABG only group. He showed a higher incidence of dysrhythmias  $p=0.04$ , inotropese  $p < 0.0001$ , blood trans fusion due to bleeding  $p < 0.00001$ , ITU stay  $p=0.001$  and hospital stay  $p < 0.0001$ . Almost similar results were brought forward by meta-analysis carried out by Wang *et al*<sup>22</sup>, and Atik *et al*<sup>18</sup> and other studies<sup>25</sup>. However, more recently a number of studies are coming up with a conflicting evidence showing there by that perioperative characteristics between both CABG with CE and CABG only groups are statistically insignificant<sup>2,7,8,10</sup>.

A great debate exists in literature with regards to the early mortality rates of CE during CABG surgery. Relatively stricter inclusion criteria's, variations in indication, operative technique and postoperative anticoagulation might have translated into differences between the early mortality in both recent as well as older studies. In our study, although the early mortality percentage was higher in CE group (5%) as opposed to CABG only group (3.1%) but it was not statistically significant ( $p=0.07$ ). On the one hand, a few studies reported that adopting stricter criteria for induction of patients in CABG with CE and conventional CABG

only group early mortality was same (3.2% and 3.8%). Similarly, recently MAC *et al*<sup>7</sup> showed relatively higher mortalities of 11.4% and 8% in both the groups respectively but with an insignificant *p* value of 10. Likewise, Alreshidan *et al*<sup>8</sup> found out a figures of 7.9% vs 1.4% in their study with an insignificant *p*-value of 0.06. CE was introduced in LAD artery by Brenowitz *et al*<sup>17</sup> in 1988 and the similar higher mortality i.e. 10% was the concluding point of the study.

Soylu *et al*<sup>21</sup> conducted a meta-analysis that included 20 studies i.e. 54,440 patients (7366 CABG + CE group vs 47,074 CABG only group) and found out that adjunctive CE during CABG was significantly associated with higher 30 days mortality (*p*<0.0001). Similarly, Wang *et al*<sup>22</sup> carried out a meta-analysis of 30 studies comprising a total of 63,730 patients. The CE group was correlated with a significantly higher 30 days postoperative all-cause mortality in comparison to the CABG alone (*p*<0.0001). A common findings in both these meta-analysis was, however, a significant heterogeneity in both the groups there by showing a larger population falling in to high risk category with diffuse CAD amongst the CE group. Further more, to date there are no double-blinded randomized controlled trial that have addressed the heterogeneity, complexity of CAD.

In our study, out of a total (n=130) cases of CE group, 120 were performed on-pump and only 10 were performed off-pump. All the 7 mortalities fell into on-pump CE, however the sample size was too small to draw any reliable conclusion. In literature, most studies revealed no significant statistical difference between on-pump and off-pump CE groups<sup>21</sup>.

With regards to the site of CE, LAD was the most frequent coronary artery requiring endarterectomy in our study group and accounted for almost 70% of the total CE. Various authors also showed LAD as the most common coronary artery being endarterectomized after it was performed by Brenowitz *et al*<sup>17</sup> for the first time<sup>7,8,11</sup>. The frequency of CE site varies in literature. Many studies show increased incidence of CE amongst the right coronary artery (RCA)<sup>2,10</sup>.

Mostly, coronary endarterectomy is performed in a single vessel as this percentage was 92.3% in this study, but Brenowitz *et al*<sup>17</sup>, reported its performance in two, three and even up till seven coronary arteries. Many believe a relation exists between the number of endarterectomies and the greatest morbidity and mortality<sup>23</sup>, but this could not be reproduced in our study nor in others<sup>17,18</sup>.

## CONCLUSION

Diffuse CAD with multiple comorbidities and aiming for complete revascularization is posing a real challenge to cardiac surgeons despite evolving surgical techniques. CE over a period of time has become a useful adjunct in CABG surgery and should be included in the algorithm of surgical revascularization. However, due to higher perioperative complications there is a need to carefully identify and highlight that subset of patients who are prone to be affected from these complications. In the light of our study, it is recommended that the subject needs further research/randomized trials to ascertain the importance of CE, its related complications and methods to reduce the number to make it a useful tool in surgical management of CAD.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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## Coronary Artery Bypass Grafting

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