ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.5336/cardiosci.2022-95172

# Effect of Previous Stent Implantation in Elective Coronary Artery Bypass Grafting Operation; Multivariate Analysis of 1,259 Patients: Retrospective Clinical Trial

## Geçirilmiş Stent İmplantasyonunun Elektif Koroner Arter Baypas Greft Operasyonundaki Etkisi; 1.259 Hastanın Multivaryant Analizi: Retrospektif Klinik Çalışma

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**ABSTRACT Objective:** This study aims to investigate the effect of previous stent implantation on early mortality in patients undergoing elective coronary artery bypass grafting (CABG). **Material and Methods:** A total of 1,259 patients who underwent elective isolated CABG between January 2015 and December 2016 were included. There were 970 patients in the CABG without stent group and 289 patients in the CABG with stent group. Preoperative, intraoperative, and postoperative data of both groups were compared. Predictors of early mortality in CABG were examined using the logistic regression analysis. **Results:** Early mortality rates after surgery between the groups were similar (CABG without stent group vs. CABG with stent group; 2.9% vs. 3.1%, p=0.998). The length of intensive care unit stay, the use of intraaortic balloon pump, tracheotomy, new dialysis, revision and the use of extracorporeal membrane oxygenator were also comparable between the groups (p>0.05). The mean number of grafts was significantly lower in the CABG with stent group than the CABG without stent group (2.62±0.91 vs. 2.87±0.9; p<0.001 respectively). Multivariate analysis revealed that an ejection fraction of ≤40% [odds ratio (OR): 3.8; 95% confidence interval (CI): 1.9-7.7; p<0.001], preoperative renal failure (OR: 3.7; 95% CI: 1.5-8.8; p=0.003), and advanced age (OR: 1.07; 95% CI: 1.03-1.1; p<0.001) were independent predictors of early mortality. Previous stent implantation has not been found out as a risk factor for early mortality (OR: 1.08; 95% CI: 0.5-2.3; p=0.998). **Conclusion:** Previous stent implantation was not found to be a factor affecting early mortality in patients undergoing elective CABG operations.

**Keywords:** Coronary artery bypass; cardiopulmonary bypass; extracorporeal membrane oxygenation; percutaneous transluminal coronary angioplasty; stents

**ÖZET Amaç:** Bu çalışmada, koroner arter baypas greftleme (KABG) yapılan hastalarda geçirilmiş stent implantasyonunun erken dönem mortaliteye olan etkisi araştırıldı. **Gereç ve Yöntemler:** Ocak 2015-Aralık 2016 yılları arasında elektif izole KABG yapılan toplam 1.259 hasta çalışmaya dâhil edildi. KABG stentsiz grupta 970 hasta yer alırken, KABG stentli grupta 289 hasta vardı. Her iki grup ameliyat öncesi, ameliyat sırası ve ameliyat sonrası özellikler açısından karşılaştırıldı. Lojistik regresyon analizi ile KABG'de erken dönem mortaliteyi etkileyen faktörler araştırıldı. **Bulgular:** Ameliyat sonrası erken mortalite oranları her iki grupta benzerdi (KABG stentsiz gruba oranla KABG stentli grup; %2,9'a karşı %3,1, p=0,998). Yoğun bakım ünitesinde kalış süresi, intraaortik balon pompası kullanım oranı, trakeostomi, yeni diyaliz, reviyon ve ekstrakorporeal sirkülasyon kullanım oranları her iki grupta karşılaştırılabilir düzeydeydi (p>0,05). Ortalama greft sayısı, KABG stentli grupta, KABG stentsiz gruba göre anlamlı düzeyde daha düşüktü (2,62±0,91'e karşı 2,87±0,9; p<0,001). Çok değişkenli analizde ≤%40 ejeksiyon fraksiyon [göreceli olasılıklar oranı (odds ratio "OR"): 3,8; %95 güven aralığı (confidence interval "CI"): 1,9-7,7; p<0,001], ameliyat öncesi böbrek yetersizliği (OR: 3,7; %95 CI: 1,5-8,8; p=0,003) ve ileri yaş (OR: 1,07; %95 CI: 1,03-1,1; p<0,001) erken dönem mortaliteyi etkileyen bağımsız öngördürücüler olarak bulundu. Geçirilmiş stent implantasyonu, erken mortaliteyi etkileyen bir risk faktörü olarak saptanmadı (OR: 1,08; %95 CI: 0,5-2,3; p=0,998). **Sonuç:** Elektif koroner arter baypas operasyonu yapılan hastalarda, geçirilmiş stent implantasyonu erken mortaliteyi etkileyen bir faktör olarak bulunmamıştır.

**Anahtar Kelimeler:** Koroner arter baypas; kardiyopulmoner baypas; yapay dolaşım membran oksijenasyonu; perkütan translüminal koroner anjiyoplasti; stentler

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Peer review under responsibility of Turkiye Klinikleri Cardiovascular Sciences.

***Received:*** 29 Dec 2022 ***Accepted:*** 26 Sep 2023 ***Available online:*** 10 Oct 2023

The number of patients with previous stent implantation has been increasing among coronary artery bypass grafting (CABG) patients. As of 2000, these patients account for >20% of the all CABG cases.[1-4] Increasing rate of stent implantations in multivessel patients have played an important role in these results.[5]

The CABG procedure can be performed in patients with previous stent implantation due to several factors such as restenosis, early thrombosis, and de novo atherosclerosis. In some patients, indications for CABG after previous stent implantation may be due to both restenosis and de novo atherosclerosis.[6] It is still controversial whether previous stent implantation affects early mortality in CABG patients. In many studies, it has been shown to increase early major morbidities or early mortality especially in selected patient populations. Previous stent implantation adversely affects early outcomes in patients with multi-vessel disease, multiple stenting, diabetes and diabetic three-vessel disease.[7-10]

In the present study, we aimed to investigate the effect of previous stent implantation on early morbidity and mortality in patients undergoing elective CABG operations and to identify whether previous stenting was a predictor of early mortality.

## MATERIAL AND METHODS

This single-center retrospective study was conducted between January 2015 and December 2016. A total of 1,259 patients who underwent isolated CABG were included. The number of patients who did not undergo percutaneous coronary intervention (PCI) before CABG was 970, forming the CABG without stent group. The number of patients who underwent PCI before CABG was 289, forming the CABG with stent group. The basic indications for surgical intervention in the CABG with stent group were identified as de novo atherosclerosis, stent restenosis and in-stent thrombosis. The majority of the patients in our study comprised of patients who underwent coronary angiography under elective conditions regardless of any previous stent implantation and who underwent CABG without undergoing any new stent implantation. On the other hand, a minor portion of our patients included those who underwent PCI and CABG during the same hospitalization period and who have also been operated electively. All patients underwent elective isolated CABG. Patients who required urgent or rescue CABG and those who underwent CABG after myocardial infarction (MI) within a week were excluded. In addition, those undergoing an additional valve procedure, carotid and ascending aortic intervention, and having CABG+mitral reconstruction and/or replacement for ischemic mitral insufficiency and redo CABG operations were excluded. PCI procedures and CABG operations were performed by multiple cardiologists and multiple surgeons. A written informed consent was obtained from each patient. The study protocol was approved Clinical Research Ethics Committee (date: October 19, 2021; number: 2021/14/546). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The left anterior descending (LAD) artery, circumflex artery (Cx), and right coronary artery (RCA) were considered as the 3 different vessel systems. One-vessel stent was defined as one-vessel system intervention group, two-vessels stent to 2 different vessels systems as 2 vessels systems interventions group, and three-vessels stent to 3 different vessels systems or left main coronary artery (LMCA) stenting as 3 vessels systems or LMCA interventions group. The diagonal branch stent was examined as part of the LAD stent group, (obtuse marginal branch) stent was examined as part of the Cx coronary artery group, and right coronary posterior descending and right coronary posterolateral stents were examined as part of the RCA stent group. Re-stenting into the same vessel system in separate sessions did not affect the classification. Multiple stenting interventions were performed either during the same session or in separate sessions.

Data of the patients were retrieved from the hospital database. In-hospital mortality was defined as mortality during hospitalization following CABG. Chronic renal failure was defined as a creatinine level of >1.2 μg/dL in men and >1.4 μg/dL in women without preoperative dialysis or undergoing renal replacement. Postoperative renal failure was defined as the need for renal replacement after surgery, while

not receiving before surgery. Revision was defined as the re-transfer of the patient from the intensive care unit (ICU) to the operating room due to uncontrollable bleeding or the need for cardiopulmonary bypass (CPB) or redo surgery.

### STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean±standard deviation, median (minimum-maximum) or number and frequency, where applicable. The Shapiro-Wilk test was used to examine normal distribution of the variables. The Student t-test was used to compare normally distributed data, while the Mann-Whitney U test was used to compare non-normally distributed data between the groups. The chi-square test and continuity (Yates) correction were performed to compare quantitative variables. Univariate and multivariate logistic regression analyses were used to identify preoperative independent predictors of in-hospital mortality. A p value of <0.05 was considered statistically significant.

### OPERATIVE TECHNIQUE

A median sternotomy was performed in all patients. Vast majority of the patients have been operated under on-pump conditions. For on-pump patients, hypothermia was maintained at 30 to 32 °C in patients under CPB. Antegrade or antegrade+retrograde blood cardioplegia was used for myocardial protection. Proximal anastomoses were performed using cross-clamping or side-clamping. For off-pump patients, activated clotting time ACT was kept above 200 second.

## RESULTS

A total of 1,259 isolated CABG cases were included. Of the patients, 289 underwent CABG with previous PCI; forming CABG with stent group, while 970 underwent CABG without PCI; forming CABG without stent group.

Baseline demographic and clinical characteristics of the patients are shown in Table 1. There was no significant difference in demographic characteristics, risk factors, and comorbidities between the groups (p>0.05). About 30% of the patients in both groups had a body mass index of >30 kg/m$^2$. A total of 14% of the patients in the CABG-PCI group and 16% of the patients in the CABG-non-PCI group had an ejection fraction (EF) of <40%, indicating no significant difference (p>0.05).

Table 2 shows the intraoperative findings between the 2 groups. The median aortic cross clamp

**TABLE 1:** Preoperative patient characteristics in terms of groups.

| | All patients n=1,259 | | |
|---|---|---|---|
| | CABG without stent (n=970) | CABG with stent (n=289) | p value |
| Age | 61.07±9.38 | 60.03±8.92 | [1]0.095 |
| Height, X̄±SD | 167.77±8.10 | 167.88±8.65 | [1]0.843 |
| Weight, X̄±SD | 79.51±12.76 | 79.25±12.15 | [1]0.755 |
| BMI, X̄±SD | 28.28±4.35 | 28.15±4.07 | [1]0.649 |
| Women, n (%) | 177 (18.2) | 51 (17.6) | [2]0.816 |
| DM, n (%) | 439 (45.3) | 146 (50.5) | [2]0.115 |
| CKD, n (%) | 57 (5.9) | 24 (8.3) | [2]0.140 |
| EF≤40%, n (%) | 160 (16.5) | 43 (14.9) | [2]0.512 |
| Number of stent, n (%) | | | |
| 1 vessel | - | 198 (68.5) | |
| 2 vessels | - | 72 (24.9) | |
| 3 vessels and LMC | - | 19 (6.6) | |
| BMI>30, n (%) | 292 (30.1) | 85 (29.4) | [2]0.822 |
| Hyperlipidemia, n (%) | 419 (43.2) | 114 (39.4) | [2]0.281 |

[1]Student t-test; [2]Chi-square test; CABG: Coronary artery bypass grafting; SD: Standard deviation; BMI: Body mass index; DM: Diabetes mellitus; CKD: Chronic kidney disease; EF: Ejection fraction; LMC: Left main coronary.

**TABLE 2:** Operative patient characteristics in terms of groups.

| | All patients n=1,259 | | |
|---|---|---|---|
| | CABG without stent (n=970) | CABG with stent (n=289) | p value |
| Mean number of distal anastomosis | 2.87±0.9 | 2.62±0.91 | [1]p<0.001 |
| Number of grafts n (%) | | | |
| 1 graft | 62 (6.4) | 28 (9.7) | [2]0.056 |
| 2 grafts | 246 (25.4) | 97 (33.6) | [2]0.006* |
| 3 grafts | 430 (44.3) | 119 (41.2) | [2]0.343 |
| 4 grafts | 214 (22.1) | 40 (13.8) | [2]0.002* |
| 5 grafts | 19 (2.0) | 4 (1.4) | [3]0.696 |
| ACCT (minimum), X̄±SD | 60.15±25.71 (59) | 56.81±28.22 (55) | [1]0.03* |
| TPT (minimum), X̄±SD | 100.44±38.20 (98) | 95.24±45.08 (95) | [1]0.016* |
| On-pump CABG, n (%) | 948 (97.7) | 276 (95.5) | |
| Off-pump CABG, n (%) | 22 (2.3) | 13 (4.5) | [3]0.069 |

[1]Mann-Whitney U test; [2]Chi-square test; [3]Continuity (Yates) correction; *p<0.05 significant; CABG: Coronary artery bypass grafting; ACCT: Aortic cross clamp time; SD: Standard deviation; TPT: Total perfusion time.

**TABLE 3:** Evaluation of the groups in terms of postoperative complications and mortality.

| | All patients n=1,259 | | |
|---|---|---|---|
| | CABG without stent (n=970) | CABG with stent (n=289) | p value |
| ICU length of stay, X±SD (hours) | 62.25±45.68 | 60.25±46.62 | [1]0.131 |
| IABP, n (%) | 44 (4.5) | 18 (6.2) | [2]0.311 |
| Tracheotomy, n (%) | 14 (1.4) | 1 (0.3) | [3]0.214 |
| New dialysis, n (%) | 21 (2.2) | 10 (3.5) | [2]0.303 |
| Revision, n (%) | 68 (7.0) | 20 (6.9) | [4]0.958 |
| ECMO, n (%) | 10 (1.0) | 2 (0.7) | [3]1.000 |
| Early mortality, n (%) | 28 (2.9) | 9 (3.1) | [4]0.998 |

[1]Mann-Whitney U test; [2]Continuity (Yates) correction; [3]Fisher's exact test; [4]Chi-square test; CABG: Coronary artery bypass grafting; ICU: Intensive care unit; SD: Standard deviation; IABP: Intraaortic balloon pump; ECMO: Extracorporeal membrane oxygenator.

time (ACCT) and CPB time values were significantly higher in the CABG without stent group than CABG with stent group (60.13 vs. 56.81 minimum, p=0.03 and 100.44 vs. 95.24 minimum, p=0.016, respectively). The rate of two-vessel grafting was significantly higher (25.4% vs. 33.6%, p=0.006) and four-vessel grafting was significantly lower (22.1% vs. 13.8%, p=0.002) in the CABG with stent group than the CABG without stent group. The mean number of grafts used was significantly higher in the CABG with stent group (2.87±0.9 vs. 2.62±0.91; p<0.001). The rate of off-pump CABG was also higher in the CABG with stent group; however, it did not reach statistical significance (4.5% vs. 2.3%, p=0.069).

Table 3 reveals the length of ICU, postoperative early major morbidities and early mortalities. There was no statistically significant difference in the early mortality rates after surgery between the groups (CABG without stent Group vs. CABG with stent group 2.9% vs. 3.1%, p=0.998 respectively). The length of ICU stay and early morbidities indicating the use of IABP, tracheotomy, new dialysis, revision and the use of extracorporeal membrane oxygenator were also comparable between the groups (p>0.05).

Logistic regression analysis was performed to identify preoperative predictors of early mortality (Table 4). Univariate regression analysis revealed that preoperative renal failure, advanced age, and an EF of <40% were found to be risk factors of early mortality. Multivariate analysis showed that all three factors were found to be independent predictors of increased early mortality. However, previous PCI

**TABLE 4:** Factors affeccting in hospital mortality; univariate and multivariate analysis.

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | Odds ratio (95% CI) | p value | Odds ratio (95% CI) | p value |
| Women | 1.472 (0.685-3.164) | 0.436 | | |
| EF≤40 | 4.217 (2.160-8.231) | <0.001* | 3.883 (1.943-7.759) | <0.001* |
| DM | 0.979 (0.508-1.887) | 1.000 | | |
| Hyperlipidemia | 0.567 (0.278-1.159) | 0.115 | | |
| CKD | 4.342 (1.917-9.836) | 0.002* | 3.743 (1.590-8.808) | 0.003* |
| Previous stent implantation | 1.081 (0.594-2.319) | 0.998 | | |
| On-pump CABG | 1.031 (1.021-1.041) | 0.622 | | |
| Off-pump CABG | 0.970 (0.960-0.979) | 0.622 | | |
| BMI>30 | 0.537 (0.234-1.234) | 0.192 | | |
| 1 graft | 0.354 (0.048-2.609) | 0.512 | | |
| 2 grafts | 0.989 (0.473-2.065) | 1.000 | 8.88 (0.742-106.359) | 0.085 |
| 3 grafts | 1.378 (0.716-2.652) | 0.335 | 10.867 (0.920-128.412) | 0.058 |
| 4 grafts | 1.094 (0.494-2.424) | 0.988 | 11.739 (0.905-152.326) | 0.60 |
| 5 grafts | 0.979 (0.961-0.980) | 0.400 | | |
| Age | 1.082 (1.041-1.125) | <0.001* | 1.076 (1.034-1.120) | <0.001* |

*p<0.05 significant; CI: Confidence interval; EF: Ejection fraction; DM: Diabetes mellitus; CKD: Chronic kidney disease; CABG: Coronary artery bypass grafting; BMI: Body mass index.

was not found to be a significant predictor of early mortality [odds ratio (OR): 1.081, 95% confidence interval (CI): 0.594-2.319; p=0.998].

## DISCUSSION

In the present study, we examined the effect of previous stent implantation on early morbidity and mortality in patients undergoing CABG and identified predictors of early mortality. Our study results showed that previous stent implantation was not an independent predictor of increased early mortality in CABG patients. Advanced age, an EF of <40%, and preoperative renal failure were also the risk factors of early and mortality.

The effects of PCI on coronary arteries have been subject to various studies. Stent implantation has been shown to be associated with neoatherosclerosis,[11] increased systemic inflammation,[12] and endothelial dysfunction[13] in the long term. Such conditions can lead to a more progressive form of atherosclerosis, potentially requiring CABG in these patients in future years. Furthermore, various comparative CABG studies have demonstrated higher rates of hyperlipidemia and hypercholesterolemia in patients with a previous history of PCI compared to those with no such history.[9,14,15] As indicated by some author, this condition may lead to the progression of de novo atherosclerosis that is refractory to medical treatment.[9] These patients may require CABG in later years. Therefore, previous stenting has been a matter of debate for CABG in the long term.

In our study, we included all CABG patients performing electively. In other words, we considered all patients without selecting them into specific patients' characteristics such diabetes or multiple stents.

Studies involving selected patients with multivessel disease multipl PCI, diabetes, diabetic three-vessel disease indicate that previous PCI increases early mortality.[7-10,16] A multi-center study including more than 37,000 patients has shown that 2 or more PCIs increase early mortality in CABG. In this study comprising the years of 2000-2005, it was suggested that different outcomes can be obtained with different stents due to the developing stent technology.[16] In another study involving diabetic patients only, previous PCI was associated with increased early mortality as well as increased major cardiac events including early mortality, perioperative MI, intraaortic balloon pump and postoperative cardiogenic shock after CABG.[9]

On the other hand, similar to our findings, studies including large series involving non-selected patients have demonstrated no effect of previous PCI on early mortality.[14,15,17,18] A study including more than 48,000 patients has indicated that previous PCI did not increase early mortality in CABG [OR 1.00 (95% CI: 0.82-1.22), p=0.995].[15] The same study has not identified stent administration as a risk factor for the composite outcome that included stroke, bleeding revision, renal insufficiency requiring dialysis, deep sternal infection and prolonged ventilation.[15]

However, overall, the common feature of studies including either selected or non-selected patients is the exclusion of CABGs performed emergently, urgently, new MI within two four weeks.[8-10,14,15] The reason for this is to eliminate the probability of intergroup bias that may arise due to inclusion of patients having a poor condition after emergent or urgent PCI. It is well known that morbidity and mortality are higher particularly in emergency patients undergoing CABG directly after PCI performed in the catheter laboratory. Thus we evaluated elective CABGs in our study and excluded urgent or rescue CABGs and cases of MI occurring 1 week ago. In this perspective, outcomes from many studies including ours are also closely associated with the characteristics of patients included or excluded based on their clinical conditions.

In our study, the rate of 2-vessel grafting was significantly higher and 4-vessel grafting was significantly lower in the CABG with stent group than the CABG without stent group. In addition, the mean number of grafts used was significantly higher in the CABG without stent group than CABG with stent group (2.87±0.9 vs. 2.62±0.91; p<0.001), consistent with the literature.[19,20] The low rate of bypass in CABG with stent group can be explained by 2 factors. First, neoatherosclerosis[11] and increased inflammation[12] can adversely affect the vessel quality. This may cause not to perform bypass to the vessel and leading to incomplete revascularization. Indeed, in stented vessels, distal vessel anastomosis is technically more challenging and is performed more distally than usual.[21] In some cases, coronary endarterectomy combined with removal of proximal stent may be required before distal anastomosis.[22] Second, the stented vessels may be patent and, therefore, revascularization may not be required. Consistent with the literature, we do not perform grafting in patent vessels with stents.[23] Irrespective of the aforementioned factors, in our study, the number of grafts did not affect early morbidity and mortality in CABG patients.

In the present study, we only evaluated early outcomes, but not the long-term outcomes. But some studies reported that multiple stenting and diabetic 3-vessel disease were associated with late mortality in CABG patients with previous PCI.[24,25] Moreover, as above mentioned, the number of the grafts was lower in the CABG without stent group. According to the logistic regression analysis, the number of grafts did not affect early morbidity and mortality. However, long-term results are unclear.

There are some limitations to this study. First, we did not evaluate drug-eluting stents and bare stents separately. During the study period (2015-2016), drug-eluting stents were used in the majority of cases in our center. But the types of drug eluting stents didn't define in the study. Second, the time from the final stenting to CABG was not determined. In some studies, patients undergoing stent implantation 5 years before CABG were excluded.[17] The stent load and inflammatory reaction may vary according to the stenting time, which may have affected the results of this study.

## CONCLUSION

In conclusion, previous stent implantation did not significantly affect early mortality in elective CABG patients. Multivariate analysis revealed that three factors as; an EF of ≤40%, preoperative renal failure, and advanced age were independent predictors of early mortality. But previous stent implantation has not been found as an independent factor affecting the early mortality.

However, the number of grafts was lower in the CABG with stent group than in the CABG without stent group. This finding may affect the long-term outcomes.

### Acknowledgments

*The authors would like to thank Mrs. Ebru OSMANOĞLU for the statistical analysis of the study.*

### Source of Finance

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

***Idea/Concept:*** *Mehmet Erdem Toker;* ***Design:*** *Mehmet Erdem Toker, Muharrem Dağlı, Cüneyt Arkan;* ***Control/Supervision:*** *Mehmet Erdem Toker, Muharrem Dağlı, Cüneyt Arkan, Ömer Faruk Akardere;* ***Data Collection and/or Processing:*** *Mehmet Erdem Toker, Muharrem Dağlı, Cüneyt Arkan, Ömer Faruk Akardere;* ***Analysis and/or Interpretation:*** *Mehmet Erdem Toker, Muharrem Dağlı, Cüneyt Arkan;* ***Literature Review:*** *Mehmet Erdem Toker;* ***Writing the Article:*** *Mehmet Erdem Toker;* ***Critical Review:*** *Mehmet Erdem Toker.*

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