The Fate of Patent Stents in Patients Undergoing Coronary Artery Bypass Grafting

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Abstract

Objectives: Bypassing a patenty stented coronary artery has a risk of flow competition, and leaving it ungrafted has a high risk of stent restenosis. This study determines the fate of patenty stented coronary arteries bypassed and left ungrafted.

Materials and Methods: Patients undergoing isolated coronary artery bypass grafting (CABG) with previous percutaneous coronary intervention (PCI) were retrospectively scanned between January 1, 2015, and January 1, 2020. Patients undergoing surgery with a patenty stented coronary artery were identified. Postoperative coronary angiography was performed in 52 of these patients.
Introduction

It is still controversial for patently stented coronary arteries to be bypassed or left ungrafted in patients undergoing coronary artery bypass grafting (CABG). There are some concerns about both choices. The first is that bypassing patently stented coronary arteries carries the risk of flow competition between the native vessel and graft; this could lead to thrombosis of one or both of these vessels. The other scenario, which leaves patently stented coronaries ungrafted, has a high risk of in-stent restenosis (ISR). Moussa et al.\(^{(1)}\) reported a study in 2020 that included outcomes of 5,100,394 patients in the United States who underwent percutaneous coronary intervention (PCI) for ISR. The researchers concluded that the rate of ISR was 10.6% after coronary stent implantation, with 25% of these patients presenting with acute myocardial infarction\(^{(1)}\).

Although PCI and CABG results are similar in the early period, CABG is superior as far as freedom from revascularization, cardiac events, and mortality, especially in patients with diabetes in the long term\(^{(2)}\). Studies have reported that the risk of major adverse cardiac events (MACE) is higher in patients undergoing CABG who previously had PCI than in patients undergoing CABG without previous PCI\(^{(3,4)}\), indicating that leaving patently stented coronary arteries ungrafted may be unsafe. In contrast, Grieshaber et al.\(^{(5)}\) reported that the risk of stent stenosis or occlusion in ungrafted patently stented coronary arteries was only 4.7% in the early postoperative period.

In this study, we retrospectively compared patients undergoing CABG with and without graft bypass on a patently stented vessel in terms of mid- and long-term graft and stent patency and incidence of MACE.

Materials and Methods

We retrospectively reviewed the medical records of patients who underwent CABG operations at our institution between January 1, 2015, and January 1, 2020. Patients who underwent concomitant surgery and multiple stents were excluded. Patients who underwent concomitant surgery were excluded because additional procedures needed more retraction and manipulation of the heart. This would be an extra factor influencing the outcome. In addition, we exclude patients with multiple stents in different coronaries. However, patients who had multiple stents in the same coronary artery were included. Patients who had more than 49% ISR were also excluded. There were 106 patients who had open stents in the circumflex artery (Cx) or the right coronary artery (RCA) before CABG. Remaining patients were operated on with two different surgical approaches at our hospital.
While the first approach preferred to bypass the patently stented vessel, the second preferred to leave it ungrafted. Coronary angiography was not performed in 54 patients without angina. Therefore, these patients were excluded from the study. Remaining, 52 patients had postoperative coronary angiography. Invasive coronary angiography (ICA) was performed in 18 patients diagnosed with acute coronary syndrome or likely to have myocardial ischemia and one patient for diagnostic purposes before abdominal aortic surgery. The remaining 33 patients were evaluated with a coronary computed tomographic angiography (CCTA).

There were 24 patients whose patently stented coronary artery was bypassed (bypass group), and 28 patients whose patently stented coronary artery was not bypassed (non-bypass group). Sixteen (66.7%) stents were in the RCA in the bypass group, and eight stents were in the Cx. In the non-bypass group, 22 (78.6%) stents were in the RCA, and six stents were in the Cx. Four out of 24 (16.7%) stents in the bypass group and 16 out of 28 (57.1%) stents in the non-bypass group were drug-eluting stents (DES).

Sixteen bare metal stent (BMS) patients had completed six weeks of Dual antiplatelet therapy (DAPT) from initial stenting, and four DES patients had completed one year. P2Y12 inhibitors were stopped five days before the surgery, but acetylsalicylate (100 mg per day) and low molecular weight heparin (LMWH) (1 mg/kg twice a day) was continued in these 20 patients. Dual antiplatelet therapy was continued in patients who did not reach one year after DES implantation and six weeks after BMS implantation. After the surgery, LMWH and DAPT were initiated in all patients from the postoperative first day until discharge, and DAPT was continued for at least one year from initial stenting. Demographic information, comorbidities, preoperative and postoperative laboratory findings (cardiac enzyme, bun, creatinine), left ventricle ejection fraction (EF) values with transthoracic echocardiography, hospital and intensive care unit (ICU) stay times, time interval stenting to operation, number of bypasses, the extent of coronary artery disease, intraoperative cardiopulmonary bypass (CPB) and cross-clamping (CC) times, mortality rates, and follow-up angiography images were evaluated. Re-exploration due to bleeding, pericardial tamponade, cerebrovascular events, low cardiac output, acute renal failure, and postoperative intra-aortic balloon pump use were defined as major adverse events (MAE). The amount of drainage was classified according to the definition of the American Association for Thoracic Surgery.[6] Deaths within 30 days of surgery were defined as early mortality. The institutional ethics committee of University of Health Sciences Turkey, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Hospital approved this study (01.10.2018/3-1).

Surgical Procedure

According to the clinical protocol, the on-pump CABG procedure was conducted for all patients. Intraoperative anticoagulation was administered with at least 400 sec of activated clotting time[7,8]. Antegrade tepid blood cardioplegia was administered and repeated every 20 min until releasing the cross-clamp to maintain diastolic cardiac arrest[9]. The left internal mammary artery (LIMA) was used for the left anterior descending artery (LAD), and the great saphenous vein was used for other coronary arteries in all patients.

Follow-up

A transthoracic echocardiography was examined before discharge and one month after surgery for all patients. The patients were called for annual control after the first postoperative examination. Postoperative early follow-up of myocardial ischemia was conducted using electrocardiography (ECG) and transthoracic echocardiography. Depending on the patient's symptoms, it was decided which coronary angiography should be performed or would be followed without imaging.

Postoperative Coronary Scanning

Coronary angiography was performed in 19 patients, and CCTA was performed on 33 patients. Twelve of the patients in the non-bypass group and six in the bypass
group were diagnosed with acute coronary syndrome or stable angina with fatigue, dyspnea on exertion, and echocardiographic changes (new onset of atrioventricular valve regurgitation or contractile disfunction) and underwent ICA. ICA was performed in one patient for diagnostic screening in the non-bypass group before abdominal aortic surgery. Thirty-three patients who presented with non-specific chronic angina without the aforementioned symptoms underwent CCTA. The decision on which coronary angiography will be performed was made according to the latest chest pain guideline\textsuperscript{10}. According to the post-operative screening, stenosis was classified for both stents and grafts as follows: 0-49%, 50-69%, 70-90%, and >90%. Those with stenosis below 49% were evaluated as open\textsuperscript{11}. MACE were defined as death due to coronary events, myocardial infarction, stroke, hospitalization because of heart failure, and revascularization (both PCI, and CABG)\textsuperscript{12}. Figure 1 represents the study's flow chart, including patients’ selection criteria and postoperative screening methods.

**Statistical Analysis**

In the study, the distribution of variables was classified, and descriptive results were obtained using SPSS v. 23. The normality of the data was analyzed using the Kolmogorov-Smirnov test. Because the number of patients in each group was limited, we used non-parametric tests for statistical analyzes. Continuous variables have been given as mean ± SD or median with range and categorical variables as frequencies and percentages of the total. Continuous variables were compared using the Mann-Whitney U test, and categorical variables were compared using the chi-

**Figure 1.** Flow chart of the study

CABG: Coronary artery bypass grafting, ICA: Invasive coronary angiography, CCTA: Coronary computed tomographic angiography
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square test. A p-value of <0.05 was considered statistically significant. The effects of covariates on the possibility of vessel occlusion in univariate and multivariate analyses are reported as hazard ratios with a 95% confidence interval using Cox proportional hazards regression. The overall freedom from MACE and open vessel functions of the groups were evaluated with Kaplan-Meier curves, and differences were tested with a log-rank test.

Results

Preoperative and Operative Results

Fifty-two patients underwent surgery; 24 of these had their patently stented coronary artery grafted, and 28 had their patently stented coronary artery left ungrafted. There were 18 (64.3%) patients who had a three-vessel disease and 10 (35.7%) patients who had a two-vessel disease in the non-bypass group. Sixteen (66.6%) patients had a three-vessel disease, and eight (33.3%) patients had a two-vessel disease in the bypass group. There was no statistically significant difference between the patients’ preoperative demographic characteristics and accompanying diseases (p>0.05). Preoperative EF was measured at >50% in 10 (41.6%) patients in the bypass group, and in 18 (64.2%) patients in the non-bypass group. The EF was measured at 35-50% in the remaining patients in both groups, and there was no statistically significant difference (p=0.16). The median preoperative PTCA/CABG interval time was 83 days (45751) in the bypass group and 65 days (61-700) in the non-bypass group. Details are shown in Table 1.

As expected, there was a significant difference in the median number of patient bypass vessels (p<0.001). CPB and CC times were longer in the bypass group, and they were statistically significant between the groups (p=0.004 and p=0.015, respectively). There was no statistically significant difference between postoperative EF measurements (p=0.12). There was no statistical difference in ICU and hospital stays between groups (p=0.19 and p=0.13, respectively). No MAE were observed in either group. There was no early mortality in either group. One late mortality in the bypass group was developed due to cerebral malignancy two years after the operation. Details are shown in Table 2.

Table 1. Patients’ demographic characteristics and preoperative properties

<table>
<thead>
<tr>
<th></th>
<th>Bypass group (n=24)</th>
<th>Non-bypass group (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (46-72)</td>
<td>60 (46-71)</td>
<td>0.68</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>22 (91.6)</td>
<td>20 (71.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI&gt;25 (kg/m²)</td>
<td>12 (50)</td>
<td>18 (64.3)</td>
<td>0.3</td>
</tr>
<tr>
<td>HT</td>
<td>22 (91.6)</td>
<td>26 (92.8)</td>
<td>0.87</td>
</tr>
<tr>
<td>DM</td>
<td>12 (50)</td>
<td>16 (57.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>CPOD</td>
<td>6 (25)</td>
<td>4 (14.3)</td>
<td>0.33</td>
</tr>
<tr>
<td>PAD</td>
<td>4 (16.7)</td>
<td>2 (7.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>CKD</td>
<td>1 (4.2)</td>
<td>2 (7.1)</td>
<td>0.65</td>
</tr>
<tr>
<td>HL</td>
<td>12 (50)</td>
<td>16 (57.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>Preoperative EF (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>10 (41.6)</td>
<td>18 (64.2)</td>
<td>0.1</td>
</tr>
<tr>
<td>35-50</td>
<td>14 (58.3)</td>
<td>10 (35.8)</td>
<td></td>
</tr>
<tr>
<td>Extent of coronary artery disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Vessels</td>
<td>8 (33)</td>
<td>10 (35.7)</td>
<td>0.86</td>
</tr>
<tr>
<td>3 Vessels</td>
<td>16 (66)</td>
<td>18 (64.3)</td>
<td></td>
</tr>
<tr>
<td>Preoperative PTCA/CABG interval (days)</td>
<td></td>
<td>65 (61-700)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Data are presented as the number of patients with percentages and median with range
Follow-up Screening

In the bypass group, postoperative screening showed that 23 (95.8%) patently stented vessels were open; six RCA stents were occluded, but all RCA grafts were open. Two of the Cx stents were occluded, but one of the graft on Cx artery was open. In the non-bypass group, 16 out of 22 (72.7%) RCA stents were open, and four out of six (66.7%) Cx stents were open. A total of 20 (71.4%) stents were open in the non-bypass group. All LIMA-LAD anastomosis was open in both groups. We present the patency of grafts and stents in Table 3. The type of stent is also shown in this table.

The median time from the operation to control screening was 53.5 (18-70) months in the bypass group and 49 (13-67) months in the non-bypass group. The estimated open rate of vessels at three years was 92.8% in the non-bypass group and 95% in the bypass group. The estimated open rate of vessels at five years was 56% in the non-bypass group and 95% in the bypass group (log-rank p=0.01). The Kaplan-Meier results for freedom from vessel occlusion are shown in Figure 2.

A univariate and multivariate Cox regression model was created to determine the effects of four variables (PTCA/CABG interval, stent type, RCA or Cx artery stenting, and bypassing the stented vessel) on vessel occlusion. Univariate and multivariate analyzes showed that grafting the open stented vessel statistically significantly decreased the vessel occlusion (p=0.047 and p=0.03, respectively). The longer PTCA/CABG interval was also favorable for the prevention of vessel occlusion, and it was statistically significant by multivariate analysis (p=0.049). Univariate and multivariate Cox regression model results are shown in Table 4.

MACE developed in 12 (42.8%) patients in the non-bypass group and 6 (25%) patients in the bypass group. While six patients who developed MACE underwent
target vessel revascularization (TVR) in the non-bypass group, only one patient underwent TVR in the bypass group. Kaplan–Meier results for freedom from MACE are presented in Figure 3.

**Discussion**

This study compares two different approaches for patients undergoing CABG with a patently stented coronary artery in terms of graft and stent patency. The main finding of this study was that 95.8% of the open stented coronary arteries with bypass grafts were open postoperatively. Only two saphenous vein grafts bypassed to the open stented vessel were occluded (but a stent in these vessels was still open). However, the patency of preoperatively open stented vessels that were not bypassed was 71.4%. MACE developed in 42.8% of the patients in the non-bypass group, with 21.4% requiring TVR.

The main concern in patients undergoing CABG with an open stented vessel is stent thrombosis due to mechanical manipulation when positioning the heart during surgery. Tovar and Borsari\(^{(13)}\) conducted an animal study investigating the effect of mechanical manipulation on stents during heart surgery. They concluded that the retraction of the heart resulted in severe deformity of all LAD stents, mild deformity of those in the Cx, and mild or no deformity of those in the RCA\(^{(13)}\). Another issue in this patient population is the discontinuation of DAPT, resulting in in-stent occlusion or thrombosis in patients undergoing both cardiac and non-cardiac surgery. On the other hand, undergoing surgery with DAPT has a risk of bleeding. The current approach suggests that it is necessary to continue DAPT in elective non-cardiac operations with low thrombotic risk for at least six weeks for BMS and at least one year for DES\(^{(14)}\). In patients requiring cardiac

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
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<tbody>
<tr>
<td>PTCA/CABG interval (days)</td>
<td>B: -0.003 SE: 0.002 HR (%95 QI): 1.003 (0.99-1.008) p-value: 0.13</td>
<td>B: -0.007 SE: 0.004 HR (%95 QI): 1.007 (1.0-1.01) p-value: 0.049</td>
</tr>
<tr>
<td>DES</td>
<td>B: -1.11 SE: 1.08  HR (%95 QI): 0.33 (0.04-2.74) p-value: 0.3</td>
<td>B: -2.77 SE: 1.57  HR (%95 QI): 0.06 (0.003-1.35) p-value: 0.08</td>
</tr>
<tr>
<td>RCA stent</td>
<td>B: -0.42 SE: 0.84  HR (%95 QI): 0.66 (0.13-3.43) p-value: 0.62</td>
<td>B: -0.59 SE: 0.91  HR (%95 QI): 0.55 (0.09-3.3) p-value: 0.52</td>
</tr>
<tr>
<td>Bypass</td>
<td>B: -2.12 SE: 1.06  HR (%95 QI): 0.12 (0.01-0.97) p-value: 0.047</td>
<td>B: -2.35 SE: 1.07  HR (%95 QI): 0.1 (0.01-0.78) p-value: 0.03</td>
</tr>
</tbody>
</table>

PTCA: Percutaneous transluminal coronary angioplasty, CABG: Coronary artery bypass grafting, DES: Drug-eluting stent, RCA: Right coronary artery, B: Beta, HR: Hazard ratio, CI: confidence interval, SE: Standard error

Table 4. Predictors of vessel occlusion by univariate and multivariate analysis

**Figure 2.** Freedom from vessel occlusion (log-rank p=0.01)

**Figure 3.** Freedom from major adverse cardiac events (log-rank p=0.077)
surgery before the completion of DAPT treatment, it is necessary to discontinue $P_2Y_{12}$ inhibitors for 5-7 days before surgery and maintain antiaggregant treatment with glycoprotein IIb/IIa inhibitors until 4-6 h to surgery\textsuperscript{(14,15)}. The antiplatelet bridging protocol recommended in the latest DAPT guidelines\textsuperscript{(14,15)} was not implemented in this study but, DAPT was continued in patients who did not reach one year after DES implantation and six weeks after BMS implantation. In this context, we hesitated to interrupt DAPT for fear of occlusion of stents that did not complete endothelialization, and we continued DAPT with encouragement we received a report from Karabulut et al.\textsuperscript{(16)}. Similar to Karabulut et al.\textsuperscript{(16)} reported previously, we found that clopidogrel does not increase the risk of bleeding-associated complications in patients undergoing CABG. This showed that $P_2Y_{12}$ inhibitors might be used safely without increasing bleeding complications. Performing CABG with good bleeding control under DAPT might be preferred in patients who did not complete the endothelialization interval with the open stented vessel.

Savonitto et al.\textsuperscript{(17)} published a review article and reported that the incidence of perioperative death, myocardial infarction, and stent thrombosis is up to 30% in the first month, 10-15% between 2 and 6 months, and <10% after 6 months. Therefore, cardiac or non-cardiac surgical intervention in the early period after stenting can lead to death and stent thrombosis-related complications. Surgery can lead to inflammatory, hypercoagulable, and hypoxic states associated with plaque instability and perioperative arterial thrombosis. The case fatality rate was 45% in patients after stent thrombosis\textsuperscript{(18)}. The variables that may affect stent-related complications are the discontinuation of DAPT before endothelization, diabetes, kidney disease, bifurcation lesions, and lower EF\textsuperscript{(18)}. Schouten et al.\textsuperscript{(19)} pointed out that, regardless of the type of stent in patients undergoing early surgery, discontinuation of antiplatelet therapy during the perioperative period may be a major cause of the increase in MACE. In addition, many researchers have reported that previous PCI before CABG increases the risk of MACE\textsuperscript{(14,20)}. On the other hand, as we mentioned before, Moussa et al.\textsuperscript{(1)} reported that the rate of ISR was 10.6% after coronary stent implantation, with 25% of these patients presenting with acute myocardial infarction in patients who underwent PCI for ISR. These reports worry surgeons that leaving open stented vessels ungrafted may be unsafe. Our study results support this concern because there was a higher rate of MACE in the mid-and long term in ungrafted open stented vessels compared with bypassed vessels. In our study, 95.8% of the grafted patently stented vessels were open postoperatively, but 71.4% of the vessels were open in the non-bypass group. Additionally, MACE occurred in 42.8% of patients in the non-bypass group.

We found open stent rates of 71.4% in the non-bypass group and 66.7% in the bypass group. Eight out of 12 (75%) BMS were occluded in the non-bypass group, and six out of 20 (30%) BMS were occluded in the bypass group. All 16 DESs were open in the non-bypass group, and two out of four (50%) DESs were open in the bypass group. The type of stents were unequally distributed in the groups, but stent patency was similar. Undesirable results may have occurred in the non-bypass group because of the high rate of BMS occlusion. However, notably while the rate of occluded BMS is 75% in the non-bypass group, it is 30% in the bypass group. Also, another striking point all DES were remained open in the non-bypass group. Although the rate of DES was higher in the non-bypass group, the results were more satisfactory in the bypass group. Most studies have reported that patients treated with BMS are associated with a higher risk of TVR\textsuperscript{(21-23)}. In this way, the results of this study consider that grafting BMS -implanted vessels may reduce the risk of MACE and ISR. However, the stent type was found to be limited statistical significance in our multivariate regression model.

In contrast with mid- and long-term results, no cardiac events were observed in any patients during the early period. No significant ECG changes or cardiac enzyme elevation were observed in any patient in either group. However, even without ECG or cardiac enzyme changes, graft occlusion may occur. Previous studies have reported that early silent graft failure may occur in about 10% of
venous grafts (24). Stent stenosis or occlusion may also occur without symptoms. Vetrovec et al. (25) reported that about 30% of patients who had undergone CABG suffered from non-specific chronic angina. In our study, 33 out of 106 (31.1%) patients who underwent CABG with patent stented vessels have had CCTA after surgery due to ambiguous symptoms. Eight (24.2%) resulted in coronary artery occlusion or ISR. Grieshaber et al. (5) conducted a study including 107 patients who underwent CABG with an open stented vessel and evaluated graft and stent patency with CCTA and ICA before discharge, reporting that 4.7% of patients had new stent restenosis in the early period. They concluded that perioperative coronary stent stenosis occurs rarely, and it is safe to leave a patently stented coronary artery without grafting. Since we did not perform the imaging in the early period, we do not know our study’s early graft and stent failure rate. However, in contrast with Grieshaber et al. (5), the results of the current study suggest that bypassing open stented vessels, especially vessels with BMS, reduce the risk of cardiac complications and repeated TVR in the mid- and long-term periods. In addition, our multivariate regression model showed that performing surgery in the very early period after stenting may provoke vessel occlusion. As we mentioned before, inflammatory, hypercoagulable, and hypoxic conditions related to surgery can cause plaque instability and arterial thrombosis in stents that do not complete endothelialization. It is an important point to keep in mind that hypercoagulopathy and mechanical manipulations brought about by surgery may cause undesirable results, especially in non-endothelialized stents.

**Study Limitations**

The main restriction of this research is the retrospective study and our limited sample size. Additionally, even though CCTA is less invasive compared to ICA, ICA is the superior method. According to our clinical experience, we have determined that the patients’ coronary artery disease severity is similar. However, it would be more accurate to use an objective method such as syntax or calcium score. Since, DES and BMS rates were unevenly distributed among the groups, we built a regression model in an attempt to overcome this limitation. There is a need for prospective studies with the balanced use of DES and BMS in larger patient groups. We have found 106 patients who underwent CABG with an open stented vessel, but 52 of these patients had coronary screening. We do not know the fate of patients who did not undergo coronary angiography because these patients may have developed silent graft or stent failure.

**Conclusion**

Current data suggest that CABG can be performed with satisfactory medium and long-term results by continuing clopidogrel in patients who have undergone PCI and have not completed DAPT treatment. It may not be safe to leave open stented vessels ungrafted during CABG. In the mid- and long term, the risk of stent thrombosis and MACE are high in cases where open stented vessels (especially with BMS) are left ungrafted. All patients undergoing CABG with patent stented coronaries should be thoroughly discussed by the heart team regarding stent type, time from stent insertion to surgery, and accompanying factors that may relate to stent occlusion.

**Ethics**

**Ethics Committee Approval:** The institutional ethics committee of University of Health Sciences Turkey, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Hospital approved this study (01.10.2018/3-1).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

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Data Collection and/or Processing: Başgöze S, Güner Y, Duman MZ, Demirel A,
Analysis and/or Interpretation: Başgöze S, Güner Y, Duman MZ, Demirel A,
Literature Search: Başgöze S, Şen O, Karacalılar M, Aydın Ü,
Writing: Başgöze S, Bayram M, Aydın Ü.
Conflict of Interest: The authors declare no conflicts of interest concerning the authorship or publication of this article.

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