On-pump beating-heart versus conventional coronary artery bypass grafting for revascularization in patients with severe left ventricular dysfunction: early outcomes

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Background: We sought to evaluate the effects of on-pump beating-heart versus conventional coronary artery bypass grafting techniques requiring cardioplegic arrest in patients with coronary artery disease with left ventricular dysfunction.

Methods: We report the early outcomes associated with survival, morbidity and improvement of left ventricular function in patients with low ejection fraction who underwent coronary artery bypass grafting between August 2009 and June 2012. Patients were separated into 2 groups: group I underwent conventional coronary artery bypass grafting and group II underwent an on-pump beating-heart technique without cardioplegic arrest.

Results: In all, 131 patients underwent coronary artery bypass grafting: 66 in group I and 65 in group II. Left ventricular ejection fraction was $26.6\% \pm 3.5\%$ in group I and $27.7\% \pm 4.7\%$ in group II. Left ventricular end diastolic diameter was 65.6 ± 3.6 mm in group I and 64.1 ± 3.2 mm in group II. There was a significant reduction in mortality in the conventional and on-pump beating-heart groups (p < 0.001). Perioperative myocardial infarction and low cardiac output syndrome were higher in group I than group II (both p < 0.05). Improvement of left ventricular function after the surgical procedure was better in group II than group I.

Conclusion: The on-pump beating-heart technique is the preferred method for myocardial revascularization in patients with left ventricular dysfunction. This technique may be an acceptable alternative to the conventional technique owing to lower postoperative mortality and morbidity.

Contexte: Nous avons voulu comparer les effets du pontage coronarien sur cœur battant sous CEC (circulation extracorporelle) et ceux du pontage coronarien classique exigeant un arrêt cardioplégique chez des patients atteints de coronaropathie et de dysfonction ventriculaire gauche.

Méthodes: Nous faisons état des premiers résultats aux plans de la survie, de la morbidité et de l'amélioration de la fonction ventriculaire gauche chez des patients qui avaient une fraction d'éjection faible et qui ont reçu un pontage coronarien entre août 2009 et juin 2012. Les patients ont été répartis en 2 groupes : le groupe I a été soumis à la technique de pontage coronarien classique et le groupe II a été soumis à la technique à cœur battant sous CEC sans arrêt cardioplégique.

Résultats: En tout, 131 patients ont reçu un pontage coronarien : 66 dans le groupe I et 65 dans le groupe II. La fraction d'éjection ventriculaire gauche était de $26,6\% \pm 3,5\%$ dans le groupe I et de $27,7\% \pm 4,7\%$ dans le groupe II. Le diamètre télédiastolique ventriculaire gauche était de $65,6 \pm 3,6$ mm dans le groupe I et de $64,1 \pm 3,2$ mm dans le groupe II. On a noté une réduction significative de la mortalité dans les groupes soumis à l'intervention classique et à l'intervention à cœur battant sous CEC (p < 0,001). L'infarctus du myocarde peropératoire et le syndrome de faible débit cardiaque ont été plus fréquents dans le groupe I que dans le groupe II (tous deux p < 0,05). L'amélioration de la fonction ventriculaire gauche après l'intervention chirurgicale a été plus marquée dans le groupe II que dans le groupe I.

Conclusion: La technique à cœur battant sous CEC est la méthode préférée de revascularisation myocardique chez les patients atteints d'une dysfonction ventriculaire gauche. Cette technique peut être une solution de rechange acceptable à la technique classique en raison des taux de mortalité et de morbidité postopératoires plus faibles qui y sont associés.

onventional coronary artery bypass grafting (CABG) is routinely used worldwide to treat patients with coronary artery disease. The procedure is associated with several side effects mostly due to the use of aortic cross-clamping, cardioplegic arrest and cardiopulmonary bypass (CPB). In the last 20 years, many efforts have been undertaken to reduce the incidence of major intraoperative and postoperative complications related to the procedure.

Myocardial revascularization in patients with left ventricular dysfunction is often performed to alleviate symptoms, to prevent future ischemic events and to increase survival. Improvement in myocardial protection techniques and complete revascularization procedures has reduced the morbidity and mortality associated with CABG. However, perioperative morbidity and mortality remain high in patients with severe left ventricular dysfunction who undergo this procedure. Recently, beatingheart and noncardioplegic CABG without cross-clamping have been used as alternative surgical techniques in highrisk patients. Patients with left ventricular dysfunction who have extensive areas of hibernating myocardium might be expected to derive the greatest benefits from CABG in terms of left ventricular function improvement. Randomized trials have demonstrated an important survival benefit in patients with low left ventricular ejection fraction who undergo surgical revascularization.^{2,3}

In the present study, we compared improvement of left ventricular function and the early clinical outcomes in patients with left ventricular dysfunction undergoing conventional versus on-pump beating-heart techniques.

METHODS

We conducted this study to determine the early outcomes of consecutive patients who underwent isolated coronary artery bypass surgery between August 2009 and June 2012. We selected patients based initially on their ejection fraction. Patients with an ejection fraction between 25 and 35 were considered to have low ejection fraction and were included in the study. We divided patients into 2 groups according to the technique used during myocardial revascularization: patients in group I underwent conventional CABG and those in group II underwent on-pump beatingheart CABG. All operations were performed by a single surgeon (B.E.). Other surgeons contributed to the preparation and closing stages of the operations. The criteria for preoperative insertion of an intra-aortic balloon pump (IABP) were cardiogenic shock or refractory ventricular failure, hemodynamic instability, refractory angina, ventricular arrhythmia and critical left main stenosis (> 70%). Patients with left ventricle aneurysm, postinfarction ventricular septal defect, ruptured papillary muscle, severe mitral regurgitation or combined surgical procedures were excluded. The investigation was approved by the institutional ethics review

committee, and we obtained informed consent either from the patients or from their closest relatives.

Anesthesia

Anesthesia consisted of propofol (3 mg/kg/h) combined with remifentanyl (0.5–1 g/kg/min). Neuromuscular blockade was achieved using 0.1–0.15 mg/kg of pancuronium bromide or vecuronium. In group I, metaraminol or phentolamine was used to maintain the systemic pressure between 50 and 60 mm Hg and, if necessary, esmolol hydrochloride (11 mg/kg) was used to slow the heart rate.

Surgical techniques

Operations were performed through median sternotomy. Conduits were harvested and prepared. Cardiopulonary bypass was established using ascending aortic cannulation and a 2-stage venous cannulation in the right atrium. In both groups, heparin was administered at a dose of 300 IU/kg to achieve a target activated clotting time greater than 450 s. A standard circuit, including a Bard tubing set with a 40 m filter, a roller pump and a hollow fibre membrane oxygenator, was used. The extracorporeal circuit was primed with 1000 mL of Hartmann solution, 500 mL of gelofusine, 0.5 g/kg of mannitol, 7 mL of 10% calcium gluconate and 60 mg of heparin. Nonpulsatile flow was used. Intermittent antegrade and retrograde coldblood cardioplegia and moderate hypothermia were applied in all patients in group I.

Conventional CABG

Cardiopulonary bypass was established with aortic cannulation and bicaval venous drainage. Systemic temperature was kept between 30° and 32°C (middle hypothermic). The aorta was cross-clamped, and myocardial protection was achieved with intermittent antegrade and retrograde blood cardioplegia. The distal anastomoses were constructed with running sutures of 7–0 or 8–0 polypropylene, and the proximal anastomoses were connected to the ascending aorta with 5–0 or 6–0 polypropylene sutures during a single cross-clamping period. Cumulative regional ischemic times were between 9.1 and 14.2 min. for each anastomosis during cross-clamping. After the patient was weaned from CPB and decannulated, the heparin was reversed with protamine infusion (1/1.5 rate).

On-pump beating-heart CABG

The CPB circuit was the same as that for conventional CABG. The operation was continued with the assisted beating heart. The temperature of patients was kept approximately 36°C without cooling (normothermic). The distal anastomoses were constructed before the proximal anastomoses. The left anterior descending artery (LAD) was revascularized first with the internal thoracic artery

(ITA), followed by the circumflex (Cx) and right coronary arteries (RCA). Regional myocardial immobilization was achieved with a suction stabilizer (Octopus, Medtronic; Guidant Acrobat, Guidant). We did not use an apical suction cardiac positioning device for revascularization. During anastomoses, target vessel homeostasis was obtained with temporary occlusion of the proximal coronary artery, and/or a humidified carbon dioxide blower was used for better visualization. Distal anastomoses were made with running sutures of 7-0 or 8-0 polypropylene. Cumulative regional ischemic times were between 8.7-15.9 min for each anastomosis during beating. After each distal anastomosis, perfusion was maintained with warm blood through the pump using anastomosed saphenous veins. The proximal anastomoses were created with 5-0 or 6-0 polypropylene sutures under a partial occlusion clamp. After weaning from CPB and decannulation, the heparin was reversed with protamine infusion (1/1.5 rate).

Definition and follow-up

We defined in-hospital mortality as death for any reason occurring within 30 days after the operation. Perioperative acute myocardial infarction was defined as the appearance of new Q-waves or a marked loss of R-wave forces and peak creatine phosphokinase (CK-MB) fractions greater than 10% of total creatine kinase. Low cardiac output syndrome (LCOS) was defined as a cardiac index lower than 2.0 L/

min/m² requiring pharmacologic support and/or IABP insertion. Postoperative renal dysfunction referred to an increment of creatinine levels of 1 mg/dL compared with the preoperative value. Neurological complications referred to any transient or permanent neurologic deficit that developed after surgery. Gastrointestinal complications included confirmed diagnosis of upper and lower gastrointestinal hemorrhage, intestinal ischemia, acute cholecystitis and pancreatitis. We recorded mortality; perioperative acute myocardial infarction; IABP usage; incidence of LCOS; renal failure; use of an inotropic agent; intensive care unit and hospital stay; cardiac hemodynamic changes; bleeding; revision rates; gastrointestinal, pulmonary and neurologic complications; infections; and survival rates. All surviving patients underwent postoperative echocardiography within 3 months after the surgical procedure. We determined survival status by contacting all patients or their next of kin by telephone.

Statistical analysis

Group statistics are expressed as means \pm standard deviation. We performed the Mann–Whitney U test for continuous variables and the Wilcoxon signed rank test to compare pre- and postoperative within-group variables. We used the Fisher exact test for nonparametric variables. Survival was calculated using the Kaplan–Meier method. Statistically significant differences are noted for each analysis, and we considered results to be significant at p < 0.05.

	Group		
Variable	Group I†	Group II‡	p value
Sex, M:F	34:22	33:32	0.66
Age, mean ± SD, yr	65.3 ± 4.5	68.1 ± 4.8	0.44
Hypertension	34	31	0.73
Smoker	76	70	0.57
Diabetes	24	22	0.73
Hypercholesterolemia	50	45	0.47
Creatinine level > 1.6 mg/dL	11	10	0.51
CK-MB mean (range), IU/L	66.8 (33–277)	67.1 (44–450)	0.21
COPD	25	24	0.64
CVD	7	6	0.88
PVD	13	12	0.36
Arrhythmias	18	16	0.57
NYHA class, mean ± SD	3.3 ± 0.45	3.2 ± 0.6	0.59
Preoperative PTCA	20	15	0.64
Preoperative IABP	21	17	> 0.99
Stable angina	55	56	0.82
Unstable angina	11	8	0.56
LVEF, mean ± SD	26.6 ± 3.5	27.7 ± 4.7	0.33
LVEDD, mean ± SD, mm	65.6 ± 3.6	64 ± 3.2	0.62

CABG = Coronary artery bypass graft; CK = creatine kinase; COPD = chronic obstructive pulmonary disease; CVD = cerebrovascular disease; F = female; IABP = intra-aortic balloon pump; LVEDD = left ventricle end-diastolic diameter; LVEF = left ventricular ejection fraction; M = male; NYHA = New York Heart Association; PTCA = percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease; SD = standard

*Unless otherwise indicated. †Conventional CABG. ‡On-pump beating-heart CABG

RESULTS

We included 131 consecutive patients in our study: 66 patients in group I and 65 patients in group II. The mean follow-up time was 13 (range 3–18) months. The mean age of patients in group I was 65.3 ± 4.5 (range 52-81) years compared with 68.1 ± 4.8 (range 55-77) years in group II. New York Heart Association classifications were 3.3 ± 0.45 and 3.2 ± 0.6 in groups I and II, respectively. By transthoracic echocardiography, left ventricular ejection fraction was $26.6\% \pm 3.5\%$ in group I and $27.7\% \pm 4.7\%$ in group II. Left ventricular end diastolic diameter (LVEDD) was 65.6 ± 3.6 mm in group I and 64 ± 3.2 mm in group II. In group I, 19 (14.5%) patients had IABP preoperatively compared with 17 (12.9%) patients in group II. The enzymatic evidence of possible myocardial infarction was considered when CK-MB values were greater than 10% of creatine kinase values and when CK-MB values were greater than 25 IU/mL. The preoperative data are summarized in Table 1. There were no differences between the groups in preoperative characteristics. Moreover, the preoperative use of IABP was similar between groups. The time interval from the onset of acute myocardial infarction to CABG was similar between the groups $(11 \text{ h} \pm 2.7 \text{ v}. 10 \text{h} \pm 2.2).$

Table 2 shows the intraoperative characteristics of the patients. The CPB time was similar between the groups. The mean overall number of distal anastomoses was 3.1 ± 0.7 versus 3.0 ± 0.6 (p = 0.76). There was no difference in the number of bypassed vessels, in type of arterial con-

duits or in the sites of surgical anastomoses between the groups. Some patients (5 in group I and 4 in group II) required 2 anastomoses to the LAD artery owing to multiple stenoses. There was no difference between the groups in use of ITA. The ITA could not be used in 4 patients owing to failure or lack of ITA flow. The details on the extent of coronary artery disease are shown in Table 2.

We analyzed data on postoperative survival and complications between the groups (Table 3). Twenty-two patients in the conventional CABG group required new insertion of an IABP compared with 4 patients in the on-pump beating-heart CABG group (p = 0.023). The reason for new IABP insertion was failure to wean from bypass owing to low cardiac output. Although the pulmonary, neurologic, gastrointestinal and infectious complications were identified postoperatively in both groups in our series, the incidence was significantly lower in the on-pump beating-heart group.

Rates of perioperative acute myocardial infarction, new IABP insertion and LCOS were lower in the on-pump beating-heart than the conventional group (all p < 0.05). The increment of postoperative creatinine level greater than 1.5 mg/dL (postoperative renal dysfunction) compared with the preoperative value was notably lower in group II (p < 0.001). Three patients in group I required postoperative ultrafiltration and hemodialysis.

In-hospital mortality was 12.7% (14 patients) in group 1 versus 1.8% (2 patients) in group II (p < 0.001). Operative mortality was also higher in the conventional

Variable	Group; no.*		
	Group I†	Group II‡	p value
CPB time mean ± SD, s	95 ± 20	84 ± 18	0.88
Aortic cross-clamping time mean ± SD, s	22 ± 14	0	< 0.001
No. distal anastomosis mean ± SD	3.1 ± 0.7	3.0 ± 0.6	0.76
LAD bypass	71	69	0.91
Diagonal branches	38	35	0.98
Cx bypass	23	22	0.79
RCA bypass	14	16	0.62
Coronary endarterectomy	17	16	0.81
ITA usage	62	61	0.94
Cumulative regional ischemic times mean ± SD, min.	7.1 ± 4.2	8.2 ± 3.3	0.76
Hemodynamic data			
Arterial pressure mean ± SD, mm Hg	38 ± 13	55 ± 12	0.71
Heart rate mean ± SD, min	0§	64 ± 11	< 0.001
Details of coronary artery disease			
Left main disease	26	22	0.61
Three-vessel disease	22	18	0.82
Two-vessel disease	18	25	0.96
Complete revascularization	57	55	0.65

CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; Cx = circumflex artery; ITA = internal thoracic artery; LAD = left anterior descending artery; RCA = right coronary artery; SD = standard deviation.

^{*}Unless otherwise indicated.

[†]Conventional CABG

[‡]On-pump beating-heart CABG

[§]Cross-clamping.

group (7 patients in group I v. 1 patient in group II). The cause of intraoperative deaths was low cardiac output. In the conventional group, 4 patients died within 48 hours compared with no patients in the on-pump CABG group. The cause of early deaths was progressive cardiac failure unresponsive to inotropic agents and/or IABP support resulting in multiple organ failure. Three patients in group I died later in the postoperative term; the causes of death were renal insufficiency in 2 patients (postoperative days 18 and 25) and recurrent ventricular arrhythmia in 1 patient (postoperative day 3).

The echocardiographic examination within 3 months of surgery revealed improvement of left ventricle function in groups I and II after CABG. The LVEDD also decreased in the 2 groups according to preoperative data. The ejection fraction increase and LVEDD decrease were higher in group II than group I; however, these differences were not significant.

Mean follow-up ranged from 3 to 18 months. The actuarial survival at 1, 12 and 18 months, taking into account all deaths in group I, was 92%, 82% and 70% compared with 97%, 84% and 77%, respectively, in group II (all p > 0.05).

There was an important difference between the groups in terms of intensive care unit and hospital stay; these were significantly shorter in group II than group I (p = 0.032 and p = 0.019, respectively).

DISCUSSION

A dysfunctional left ventricle with low ejection fraction is one of the most important factors for increased morbidity and mortality after and during cardiac surgery. One of the main surgical issues in these patients is myocardial protection. Despite new myocardial protection techniques, anesthesia and surgical techniques, postoperative adverse events related to intraoperative ischemia have not been completely eliminated.^{4,5} Theoretically, the ideal solution to this problem is alternative techniques, such as an off-pump beating-heart technique without CPB or an on-pump beating-heart technique with CPB.

Various studies have shown that an off-pump beating-heart technique is safe and has satisfactory short-term clinical outcomes compared with conventional CABG. 5-9 Despite the efficiency and safety of off-pump techniques over conventional CPB, some critics may argue that patients treated with an off-pump technique are undergoing incomplete revascularization. Although incomplete revascularization has not been reported to increase early risk, it may cause recurrent angina, decrease late survival and require reintervention in the long term. 10-13 Furthermore, one of the important drawbacks of this technique is the hemodynamic deterioration that can occur during manipulation of the heart, which entails urgent conversion to conventional CPB. Conversion from off-pump to

Variable -	Group; no.*		
	Group I†	Group II‡	p value
In-hospital mortality (within 30 d)	14	2	0.001
Operative mortality	7	1	0.022
Early mortality (< 48 h)	4	1	0.002
Later death during postoperative term	3	0	0.007
Perioperative AMI	11	1	0.012
New IABP insertion	22	4	0.023
Duration of inotropic support mean ± SD, d	7.2 ± 4.3	3.1 ± 4.1	0.001
LCOS	16	4	0.025
Postoperative renal dysfunction (creatinine > 1,5 mg/dL)	11	2	0.001
Postoperative hemodialysis	5	0	0.026
Pulmonary complications	6	4	0.66
Neurological complications	4	2	0.78
Gastrointestinal complications	2	0	0.92
ICU stay mean ± SD, d	7 ± 5	3 ± 2	0.032
Hospital stay mean ± SD, d	15 ± 7	7 ± 4	0.019
Time to extubation, h	41.2 ± 15	33.2 ± 14	0.79
Infectious complications	7	5	0.81
Surgical revision for bleeding	11	9	0.69
Postoperative bleeding > 1000 mL	17	16	0.88
LVEF increase > 35%	14	18	0.91
LVEDD decrease < 60 mm	26	30	0.92

AMI = acute myocardial infarction; CABG = coronary artery bypass graft; DSWI = deep sternal wound infection; IABP = intra-aortic balloon pump; ICU = intensive care unit; LCOS = low cardiac output syndrome; LVEDD = left ventricle end-diastolic diameter; LVEF = left ventricular ejection fraction; SD = standard deviation.

^{*}Unless otherwise specified.

[†]Conventional CABG.

[‡]On-pump beating-heart CABG

on-pump bypass has been associated with poor prognosis and may increase in-hospital mortality. 12-17 Owing to the increased cardiac and hemodynamic instability, incomplete revascularization and repeated surgical interventions associated with the off-pump technique, an alternative technique that does not involve aortic cross-clamping with CPB has been developed. We have researched the effectiveness of an on-pump beating-heart technique in reducing both mortality and morbidity in patients with left ventricular dysfunction.

There is evidence that with conventional CABG the arrested heart may not be as well protected from ischemia as the beating-heart. Krejca and colleagues¹⁸ found that troponin T levels were higher with conventional CABG than with on- or off-pump beating-heart techniques. Patients with left ventricular dysfunction may be unable to sustain an adequate intraoperative cardiac output during the beating-heart technique; hence, the theoretical need exists for mechanical support from a CPB circuit as a hybrid procedure. It has been demonstrated that an on-pump beating-heart technique reduces the release of CK-MB and myocardial injury compared with conventional CABG. 12,13,15,19,20 Early surgical outcomes were better in the on-pump beatingheart group in our study, and this result is consistent with those reported in several studies.¹⁸⁻²¹ Postoperative LCOS ratios, perioperative infarction, new IABP insertion (for weaning from the CPB), and duration of inotropic support were significantly lower in the onpump beating-heart group than the conventional group. Postoperatively, intensive care unit and hospital stay as well as hospital costs decreased in the on-pump beatingheart group. The mortality of patients with left ventricular dysfunction undergoing an on-pump beatingheart technique varies from 2%-8%.^{1,3,21} In-hospital mortality was significantly lower in the on-pump beatingheart group than in the conventional group. In our study, mortality was 0.3%, which was low compared with that reported in other studies. These considerations may all be related to the elimination of cardioplegic arrest, which is the main difference between the techniques. No significant differences were detected between the groups in relation to morbidity, including the incidence of stroke, gastrointestinal problems, pulmonary complications, bleeding, mediastinitis and prolonged mechanical ventilation, which are all believed to be related to the use of CPB itself.

Mizutani and colleagues²¹ have indicated that the onpump beating-heart technique may increase the risk for incomplete revascularization due to shorter duration of surgery and CPB time. But we agree with the conclusions of previous studies that the on-pump beating-heart technique is associated with an adequate number of grafts performed and complete revascularization.^{3,22,23} The on-pump beating-heart technique allows optimal exposure of the coronary arteries. This avoids extreme upward retraction of the heart, especially during revascularization of the Cx branch, which might contribute to better myocardial protection.^{3,12,13,21,22}

Renal failure is a frequent complication in patients who have experienced hemodynamic failure or who have undergone conventional CABG. Most authors have shown that on-pump beating-heart CABG presents a low risk for systemic hypoperfusion during surgery and better renal protection, as demonstrated by a low incidence of postoperative renal complications.^{3,24} Because most patients with left ventricular dysfunction are hemodynamically unstable and have poor perfusion of their visceral organs, the appropriate circulatory support system, such as CPB, should be applied to improve their hemodynamic status and compensate for visceral organ perfusion.^{3,6,14,15,20,21} Therefore, the on-pump beating-heart technique offers a lower risk of systemic hypoperfusion during surgery and, as a consequence, superior renal protection.^{3,24–26} Although postoperative renal dysfunction was identified in both groups in our series, the incidence was significantly lower in the on-pump beating-heart group. Furthermore, there was no renal dysfunction requiring hemodialysis in the on-pump beating-heart technique group in our series. Despite the use of CPB in both groups, CPB time was shorter in the on-pump beating-heart group. Shortening of the duration of CPB may reduce the renal and visceral injury. In addition, the systemic heat of patients was approximately 36°C in the on-pump beating-heart group, whereas the patients were cooled to 30°C in the conventional group. Therefore, the renal and visceral damage that may have occurred due to systemic cooling would have been more significant in the conventional group.

Limitations

There are some limitations to the present study. First, the sample was nonrandomized. However, using specific statistical evaluations allowed for relatively precise risk and outcome assessment and comparison. Second, its retrospective nature and small sample limited the validity of the clinical results. Further studies are needed, particularly to determine the benefit achieved by increasing myocardial revascularization among patients who underwent onpump beating-heart CABG. Finally, although a larger number of patients would be needed to guarantee more significant results, we believe that our study already shows interesting short-term results.

CONCLUSION

We performed an on-pump beating-heart technique to revascularize the myocardium in patients with left ventricular dysfunction and compared the early outcomes with those of conventional CABG. Our experience suggests that an on-pump beating-heart technique is the preferable method of myocardial revascularization for patients with acute myocardial infarction and low ejection fraction who might tolerate cardioplegic arrest poorly. The main advantages of the on-pump beating-heart technique are complete revascularization without hemodynamic instability and low morbidity and mortality in patients with left ventricular dysfunction.

Competing interests: None declared.

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