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Original article

The Role of Transarterial Bland Embolization in Management of Hepatocellular Carcinoma in Child-Pugh-Turcotte (B) Patients

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Abstract

Background: HCC is a major global health challenge. TACE is the first-line non-curative therapy for certain cases. However, patients in CPT-B or C are cautioned against TACE due to an increased risk of liver failure and mortality, particularly with non-selective lobar chemoembolization approaches. Advances in super-selective embolization techniques have mitigated these risks, creating new therapeutic options for patients with compromised liver function. This study aimed to evaluate the tumor response of transarterial bland embolization in (CPT-B) patients with HCC. **Methods:** This prospective study evaluated the tumor response of TABE in 25 CPT-B patients with HCC over one year. The TABE procedure, conducted under fluoroscopic guidance, involved hepatic arteriography and super-selective embolization using size-specific embolic materials. Post-treatment and tumor response were assessed through imaging and alpha-fetoprotein levels in serum. **Results**: participants with a single lesion were more likely to achieve a complete response. In contrast, the mean largest lesion dimension was significantly smaller in participants who achieved a complete response compared to those who did not (4.2 ± 1.4 cm vs. 6.2 ± 1.9 cm, P = 0.007). The best cutoff point of Child-Paugh score to predict incomplete response was > 8, at which sensitivity, specificity, PPV, and NPV were 66.7%, 100%, 100%, and 84.2%, respectively. Child-Pugh score remained a significant predictor OR = 10.891, 95% CI: 1.097–108.116, P = 0.041). **Conclusion:** TABE is an effective treatment modality for HCC in CPT-B patients, achieving a complete response in most cases with Child-Pugh score being the strongest predictor.

Keywords: HCC, TABE, Child-Pugh-Turcotte score, liver cirrhosis.

Introduction

Hepatocellular carcinoma (HCC) is a standout amongst the most widely recognized cancers (1). Most patients are diagnosed at middle of the road or progressed clinical stages, which rejects them from possibly curative treatment such as resection, liver transplantation, or local ablation (2).

Cirrhotic liver function is most categorized according to the Child-Pugh-Turcotte score (CPT) which has a strong prognostic value for HCC patients and is included in all integrated HCC staging systems (3). The Barcelona Clinic Liver Cancer (BCLC) system is the integrated HCC staging system most used worldwide (4).

Patients with well-preserved liver function (CPT-A) are considered suitable for virtually all treatment modalities and are easily and rigorously treated according to the BCLC stage (4). Patients with severely compromised liver function (CPT-C) are instead considered terminal patients suitable only for palliative care (if not transplantable) and, as such, are managed in nearly all instances following the guidelines (4).

Concerning the (CPT-B) class, it corresponds to an intermediate, partially compromised situation, in between well preserved and terminal condition and accordingly these patients have a fragile liver function (5).

Depending on the tumor burden and/or the performance status, CPT-B patients can fall into various BCLC stages (3). However, they are frequently not ideal candidates for the first line treatments recommended in general for their respective stages as resection, transplantation, radio-frequency ablation and transarterial chemoembolization (6).

As arterial neo-angiogenesis is one of the hallmarks of hepatocellular carcinoma (HCC), tans-arterial bland embolization (TABE) lead to tumor ischemia and inhibition of tumor growth through tumor blood flow shut down (7).

As TACE can induce irreversible liver failure in patients with compromised liver function (CPT-B patients) (8), Transarterial bland embolization (TABE) can block the hepatic artery with embolic agents (e.g., lipidol, Gel Foam sponge, and blank particles) having therapeutic effects on HCC by the induction of ischemia and necrosis in the tumor area with no such chemotherapeutic burden on liver cells (9). In this study we will discuss the role of TABE in management of HCC in CPT-B patients

The aim of this study is to evaluate the tumor response of transarterial bland embolization in (CPT-B) patients with HCC.

Patients and methods

Patients:

This prospective study included twenty-five CPT-B patients attending Radiodiagnosis and Hepatology Departments-Benha University Hospital and meeting the inclusion criteria for Tans-Arterial Bland Embolization (TABE) of HCC from November 2022 to October 2023.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Inclusion criteria were patients of both sex of any age who attended to Radiodiagnosis and Hepatology Departments, Faculty of Medicine, Benha University, with liver cirrhosis with Child-Pugh score B and diagnosed with HCC that is multinodular tumors without vascular invasion or extrahepatic spread.

Exclusion criteria were Patients with Child-Pugh-Turcotte score of A or C. Patients with portal vein thrombosis, arterio-portal shunts or any collateral vessels pathways potentially endangering normal territories during embolization were excluded from the study. In addition, patients with malignancies other than HCC, with extra-hepatic spread or with contra-indication to contrast media administration were excluded. Patients who refused to participate in the study were also excluded from the study.

Methods:

All studied cases were subjected to the following: Detailed history taking, including [Personal history; name, age, gender and body mass index (BMI), Present history: course of the disease and duration, Past history of any medical condition or previous hospital admission and Family history of similar condition]. **Full clinical examination: General examination including [**General comment on patient conscious and mental state, Jaundice or pallor, Vital signs: pulse, blood pressure, capillary filling time, respiratory rate and temperature]. **local abdominal examination** also was done. **Routine laboratory investigations [**complete blood count (Hb, WBCs, Platelets), random blood sugar, total bilirubin, INR, prothrombin time, albumin kidney function tests and liver function tests].

All patients underwent radiological examination including ultrasound scan and contrast-enhanced CT to evaluate the size, number, location, and extension of the tumor, patency of the portal vein and tumoral arterial supply. All patients were categorized according to Child-Pugh-Turcotte score into A, B, or C to predict mortality in cirrhosis and guide the selection of patients. Conventional TABE procedure was performed under fluoroscopy guidance. Firstly, under

sterile conditions, the femoral artery was punctured under local anesthesia using a needle, and a 5F-sheath was inserted via the Seldinger technique. Secondly, the coeliac trunk and superior mesenteric artery were catheterized using a 4F catheter. An indirect portography was made to evaluate the portal venous system and exclude portal vein thrombosis. Afterward, the catheter was placed in the common hepatic artery and then the right or left hepatic artery was selectively catheterized, depending on the location of the lesion. A 2.4F microcatheter was used to super-selectively catheterize the tumor-feeding arterial branches. When the target artery was reached, the embolizing agent was carefully injected under fluoroscopy for the embolization of the tumor until blood stasis was reached.

Approval code of ethical committee: MS 32-9-2022

Statistical analysis

Statistical analyses were done using SPSS version 28 (IBM Inc., Armonk, NY, USA). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. Quantitative data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Quantitative data were compared according to response to embolization using the independent t-test or Mann-Whitney U test for normally and non-normally distributed quantitative variables, respectively. Categorical data were compared using the Chi-square or Fisher's exact test. ROC analysis was done for the Child-Paugh score to predict incomplete response. Area Under the curve, 95% confidence interval, best cutoff point, and diagnostic indices were calculated. Multivariate logistic regression analysis was done to predict incomplete response. The odds ratios with 95% confidence intervals were calculated. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Results

This study was conducted on CPT-B patients attending the Radiodiagnosis and Hepatology Departments for TABE of hepatocellular carcinoma.

The study included 25 participants with a mean age of 64 ± 8 years. Most of the participants were males, comprising 20 individuals (80%), while females accounted for 5 participants (20%). The lesion characteristics revealed that most participants had a single lesion (19 participants, 76%), while 4 participants (16%) had two lesions, and 2 participants (8%) had three lesions. The largest lesion dimension across the study population had a mean size of 4.9 ± 1.8 cm. The laboratory findings indicated that the mean total bilirubin level was 2.7 ± 0.5 mg/dL, with a mean international normalized ratio (INR) of 1.6 ± 0.4 and a mean serum albumin level of 3.4 ± 0.4 g/dL. **Table 1**

The clinical characteristics showed that the ascites was absent in 14 participants (56%), mild in 10 participants (40%), and moderate in 1 participant (4%). None of the participants exhibited encephalopathy. The median Child-Pugh score was 7, with a range of 7 to 9, indicating that the study population predominantly consisted of patients with compensated or mildly decompensated liver disease. Among the embolizing agents used, Lipiodol was the most common, utilized in 14 participants (56%), followed by a combination of Lipiodol and Gel Foam in 8 participants (32%). Particles were used in 2 participants (8%), and Embospheres in 1 participant (4%). A complete response to the treatment was achieved in 16 participants (64%). **Table 1**

No significant differences were reported regarding age (P = 0.288) and gender (P = 1.0) between those with complete and incomplete responses to embolization. The analysis of factors associated with a complete response showed that participants with a single lesion were more likely to achieve a complete response (87.5% vs. 55.6%). However, this difference was not statistically significant (P = 0.167). In contrast, the mean largest lesion dimension was significantly smaller in participants who achieved a complete response compared to those who did not (4.2 ± 1.4 cm vs. 6.2 ± 1.9 cm, P = 0.007). No significant differences were reported between those with complete and incomplete responses regarding total bilirubin (P = 0.446), INR (P = 0.735), and albumin (P = 0.223). **Table 2**

The association between clinical characteristics and complete response showed no significant difference in ascites status between participants with and without a complete response (P = 0.377). However, the median Child-Pugh score was significantly lower in participants with a complete response (7 [range: 7–8]) compared to those without (9 [range: 7–9], P < 0.001). Participants with a complete response most received either Lipiodol (43.8%) or a combination of Lipiodol and Gel Foam (43.8%), whereas those without a complete response predominantly received Lipiodol alone (77.8%). Embospheres were only used in one participant without a complete response (11.1%), and particles were exclusively used in participants who achieved a complete response (12.5%). Although the potential trend favoring the combination of Lipiodol and Gel Foam in achieving better outcomes, this was not statistically significant. **Table 2**

ROC analysis was done for the Child-Paugh score to predict incomplete response. It revealed a significant AUC of 0.903, with a 95% CI of 0.757 – 1.0 (P = 0.001). The best cutoff point to predict incomplete response was > 8, at which sensitivity, specificity, PPV, and NPV were 66.7%, 100%, 100%, and 84.2%, respectively. **Table 3&Figure.1**

Univariate and multivariate logistic regression analyses identified factors

associated with incomplete response. We included significant variables in the above comparisons. In the univariate analysis, the largest lesion dimension (OR = 2.118, 95% CI: 1.104–4.065, P = 0.024) and the Child-Pugh score (OR = 17.158, 95% CI: 2.235–131.72, P = 0.006) were significantly associated with a complete response. However, in the multivariate analysis, only the Child-Pugh score remained a significant predictor (OR = 10.891, 95% CI: 1.097–108.116, P = 0.041). **Table 4**

Table 1: Demographic characteristics, Lesion characteristics, Laboratory findings and Clinical characteristics of the studied patients

Demographics	**Mean ±SD**	**n (%)**
Age (years)	Mean ±SD	64 ±8
Sex		
Males	n (%)	20 (80)
Females	n (%)	5 (20)
Lesion characteristics		
Number of lesions		
One	n (%)	19 (76)
Two	n (%)	4 (16)
Three	n (%)	2 (8)
Largest dimension (cm)	Mean ±SD	4.9 ±1.8
Total bilirubin (mg/dl)	2.7 ±0.5	
INR	1.6 ±0.4	
Albumin (g/dl)	3.4 ±0.4	
Clinical characteristics		
Ascites		
No	n (%)	14 (56)
Mild	n (%)	10 (40)
Moderate	n (%)	1 (4)
Encephalopathy	n (%)	0 (0)
Total Child-Pugh	Median (range)	7 (7 - 9)
Embolizing agent		
Embospheres		1 (4)
Lipidol		14 (56)
Lipidol & Gel Foam		8 (32)
Particles		2 (8)
Complete response		16 (64)

Table 2:Demographic characteristics, Number of lesions, Laboratory findings, Clinical characteristics and Embolizing agent according to embolization response

		Complete response		
		Yes (n = 16)	**No (n = 9)**	**P-value**
Age (years)	Mean ±SD	66 ±9	62 ±6	0.288
Sex				
Males	n (%)	13 (81.3)	7 (77.8)	1.0
Females	n (%)	3 (18.8)	2 (22.2)	
		Yes (n = 16)	**No (n = 9)**	**P-value**
Number of lesions				
One	n (%)	14 (87.5)	5 (55.6)	0.167
Two	n (%)	1 (6.3)	3 (33.3)	
Three	n (%)	1 (6.3)	1 (11.1)	
		Yes (n = 16)	**No (n = 9)**	**P-value**
Total bilirubin (mg/dl)	Mean ±SD	2.6 ±0.5	2.8 ±0.6	0.446
INR	Mean ±SD	1.6 ±0.4	1.6 ±0.4	0.735
Albumin (g/ml)	Mean ±SD	3.4 ±0.4	3.2 ±0.3	0.223
		Yes (n = 16)	**No (n = 9)**	**P-value**
Ascites				
No	n (%)	10 (62.5)	4 (44.4)	0.377
Mild	n (%)	6 (37.5)	4 (44.4)	
Moderate	n (%)	0 (0)	1 (11.1)	
Encephalopathy	n (%)	0 (0)	0 (0)	-
Total Child-Pugh	Median (range)	7 (7 - 8)	9 (7 - 9)	**<0.001**
		Yes (n = 16)	**No (n = 9)**	**P-value**
Embolizing agent				
Embospheres	n (%)	0 (0)	1 (11.1)	0.11
Lipidol	n (%)	7 (43.8)	7 (77.8)	
Lipidol & Gel Foam	n (%)	7 (43.8)	1 (11.1)	
Particles	n (%)	2 (12.5)	0 (0)	

Significant P-value; SD: Standard deviation; INR: International normalized ratio

Table 3: ROC analysis for Child-Paugh score to predict incomplete response

ROC characteristics	
AUC	0.903
95% CI	0.757 – 1.0
Best cutoff point	> 8
Sensitivity	66.7%
Specificity	100%
PPV	100%
NPV	84.2%
P-value	<0.001

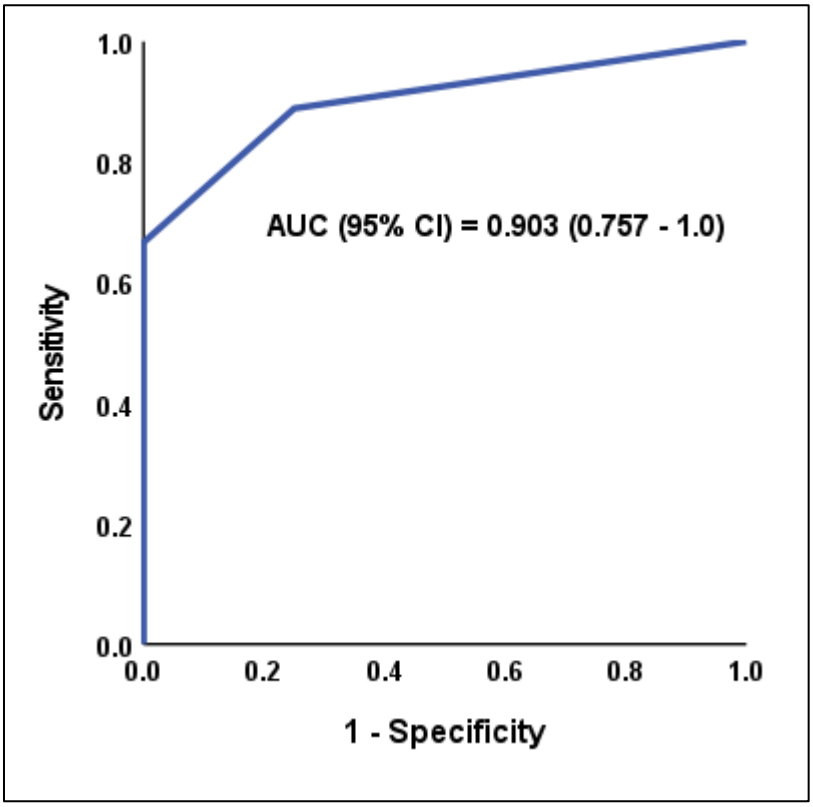

Figure 1: ROC analysis for Child-Paugh score to predict incomplete response

Table 4: Univariate and multivariate logistic regression analysis to predict incomplete response

	Univariate		Multivariate	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Lesion number (ref = One)				
Two	8.4 (0.701 - 100.595)	0.093	2.62 (0.035 - 194.055)	0.661
Three	2.8 (0.146 - 53.706)	0.495	1.755 (0.063 - 48.983)	0.741
Largest dimension (cm)	2.118 (1.104 - 4.065)	**0.024***	1.344 (0.528 - 3.417)	0.535
Total Child-Pugh	17.158 (2.235 - 131.72)	**0.006***	10.891 (1.097 - 108.116)	**0.041***

Significant P-value; OR: Odds ratio; 95% CI: 95% Confidence interval

Discussion:

The present study reported a complete response rate of 64%, highlighting the potential efficacy of TABE in treating HCC in CPT-B patients. This response rate is consistent with the therapeutic potential of TABE in achieving tumor necrosis by occluding arterial blood supply to the tumor, a critical mechanism given the hyper vascular nature of HCC.

Interestingly, **Guo et al.** carried out a propensity-score matching analysis to compare the initial responses and safety of TABE and drug-eluting beads-TACE (DEB-TACE) in the management of HCC. They studied 26 patients treated with TABE and 52 matched patients treated with DEB-TACE for primary or ruptured HCC, focusing on initial tumor responses and adverse effects of one-month post-procedure. In contrast, while **Guo et al.** reported no cases of complete response (CR) in either the TABE or DEB-TACE groups due to the large tumor burden and single embolization session, our study demonstrated a higher rate of complete response, potentially attributed to differences in patient selection, lesion sizes, or embolization strategies, such as the combination of Lipiodol and Gel Foam, which showed a trend towards improved outcomes in our study (9).

Correspondingly, randomized controlled study was objectively designed by **Chang et al.** to evaluate transcatheter arterial embolization with or without cisplatin treatment of HCC. The patients were divided into two groups by random sampling. In group I, 22 patients received TAE with the regimen of cisplatin (50 mg) mixed with Lipiodol 5-15 ml followed by gelfoam pieces. In group II, 24 patients, as a controlled group, used the regimen of Lipiodol and gelfoam pieces only. They reported tumor response rate of group I was 68% (15/22) and group II was 67% (16/24) similar to our results (10).

Our analysis revealed that participants with smaller lesion dimensions were significantly more likely to achieve a complete response compared to those with larger lesions which is consistently evident through the univariate analysis for factors predicting complete response indicating the clinical importance of early detection and intervention in HCC, as smaller tumors are more likely to be fully embolized due to their limited vascular complexity and reduced likelihood of collateral blood supply. The result aligns with the known biology of HCC, where larger lesions often exhibit intratumorally heterogeneity and partial hypo-vascularity, potentially reducing the efficacy of arterial embolization.

In consistency with our results, **Takayasu et al.** conducted a study for assessment of super selective approaches in treatment of HCC. They reported that multivariate analysis revealed that Child-Pugh class, tumor number, size, alpha-fetoprotein, and des-gamma carboxy-prothrombin were independent predictors of response. The survival rate decreased as the tumor number (p=0.0001) and size increased (p=0.04 to p=0.0001) in all but one subgroup in both Child-Pugh-A and -B. better outcomes were seen in those with fewer tumor numbers, smaller tumor size, and better liver function (11).

Furthermore, **Lo et al.** conducted a randomized controlled trial to assess the efficacy of transarterial Lipiodol chemoembolization in Asian patients with unresectable HCC. They studied 80 patients randomly assigned to receive either chemoembolization with a variable dose of cisplatin-Lipiodol emulsion and Gel Foam-sponge particles (40 patients) or symptomatic treatment (39 patients). Chemoembolization was repeated every 2-3 months unless contraindications arose, and survival was the primary endpoint. They found that chemoembolization resulted in significantly improved survival rates compared to the control group (1-year survival: 57% vs. 32%; 2-year survival: 31% vs. 11%; 3-year survival: 26% vs. 3%; P = 0.002) (12).

In their study, tumor response rates were higher in the chemoembolization group, with an objective response rate of 72% in serum alpha-fetoprotein levels and 39% in tumor size. They also identified tumor size as a critical factor influencing survival outcomes, emphasizing the importance of smaller lesions for better therapeutic response. In contrast, Lo et al. observed a higher overall survival benefit with chemoembolization, which is attributable to the added cytotoxic effect of cisplatin combined with Lipiodol, enhancing ischemic necrosis of the tumor. Our study focused on TABE, which lacks the chemotherapeutic component, potentially explaining the difference in long-term survival outcomes (12).

Our study findings indicate that a lower Child-Pugh score is a significant predictor of achieving a complete response to TABE, as participants with a

median score of 7 were more likely to respond compared to those with a score of 9. While univariate analysis identified both smaller lesion dimensions and lower Child-Pugh scores as significant factors, multivariate analysis confirmed that the Child-Pugh score was the strongest independent predictor. This emphasizes the critical role of liver function in determining treatment efficacy, as better hepatic reserve may enhance the ability to tolerate embolization and promote effective tumor necrosis.

Further confirming the value of CPT score, the ROC analysis for the Child-Pugh score demonstrated its strong predictive value for incomplete response to TABE, with a significant AUC indicating excellent discrimination ability. A cutoff score > 8 was identified as the optimal threshold, providing high specificity and PPV, ensuring precise identification of patients unlikely to achieve a complete response highlighting clinical utility of the Child-Pugh score in stratifying patients for TABE and suggest that those with scores > 8 may benefit from alternative or combined treatment strategies due to their reduced likelihood of achieving optimal outcomes.

Confirming our study, **Dorn et al.** conducted a retrospective analysis to evaluate the safety and efficacy of TACE as a first-line therapy for HCC in cirrhotic patients with compromised liver function (Child-Pugh B/C) compared to those with preserved liver function (Child-Pugh A). They included 190 patients, assessing tumor necrosis via mRECIST criteria and post-TACE survival. They found that tumor necrosis was comparable between Child-Pugh A and B/C groups. However, survival outcomes were inferior in the Child-Pugh B/C group (median survival: 13.7 months vs. 21.9 months, P = 0.03) (13). Additionally, they emphasized the importance of liver function as a predictor of outcomes, as reflected in our study where a lower Child-Pugh score was significantly associated with a complete response to TABE. While both studies underscore the feasibility of embolization therapies in cirrhotic patients with compromised liver function, the survival disparity observed by **Dorn et al.** aligns with our stress on careful patient selection based on liver reserve. Differences in embolization techniques (bland embolization in our study vs. chemoembolization in theirs) and tumor biology could explain the variation in long-term outcomes (13).

Parallel to our findings, **Guo et al.**'s study supports the efficacy and safety of TABE, particularly in reducing adverse effects, and underscores the importance of tumor size and liver function as key predictors of therapeutic response. The differences in response rates and patient outcomes between the studies could be attributed to variations in study populations, tumor burden, and treatment protocols (9).

Consistently, **Saif-Al-Islam et al.** conducted a retrospective analysis aimed

at identifying factors influencing post-treatment outcomes in HCC patients treated with various modalities. Their study included 407 patients over five years, analyzing clinical, radiological, and laboratory predictors of favorable and unfavorable outcomes. The favorable outcomes included patients who were cured or had stable disease. Conversely, the unfavorable outcomes included patients who deteriorated or had a recurrence. They found that fewer hepatic focal lesions, smaller lesion size, early-to-intermediate stages of disease severity, and better liver function (Child-Pugh class A, and early B) were significant predictors of favorable outcomes (14).

This study has some limitations. The study included only 25 participants, which may limit the generalizability of the findings to a broader population of CPT-B patients with HCC. The study focused primarily on immediate and short-term tumor response, without evaluating long-term outcomes such as overall survival or progression-free survival. Conducting the study at a single institution may introduce selection bias and limit the external validity of the results.

Conclusion

Our study demonstrated that TABE is an effective treatment modality for HCC in CPT-B patients, achieving a complete response in most cases. Key predictors of treatment response included smaller lesion size and lower Child-Pugh scores, with a score > 8 significantly associated with incomplete response. Child-Pugh score was reported as the strongest independent predictor of response highlighting the importance of careful patient selection based on tumor characteristics and liver function to optimize outcomes of TABE in this patient population.

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