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Association of Fragmented Wide QRS Complex with Coronary Artery Disease in Patients with Left Bundle Branch Block

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Abstract

Introduction. Complete Left bundle branch block (LBBB) increases the risk of cardiac mortality, and the prognosis is primarily determined by the underlying coronary artery diseases. LBBB creates a problem for detecting coronary artery diseases (CAD) on ECG and represents a clinical challenge for detecting myocardial ischemia. The presence of a fragmented wide QRS complex on surface ECG in LBBB may be related to myocardial ischemia, scarring, or fibrosis.
Purpose. To investigate the relationship between the presence of fragmented wide QRS complex (fw-QRS) and significant obstructive CAD in patients with LBBB.
Materials and methods. A cross-sectional study has been carried out on 100 patients with LBBB who are admitted into cardiac centers (Ibn Al-Bitar Center for Cardiac Surgery and Nassyireha Cardiac Center) to do coronary angiography as part of the workup for the diagnosis of CAD. Demographic features, classical risk factors of CAD, coronary angiography, ECG, and Echocardiography had been evaluated for all patients enrolled in the study.
Results. The mean age of the patients was 61.2±10.5 years and 55 (55%) were male. A significant obstructive CAD had been detected in 53 (53%) patients. About 50% of all patients enrolled in the study were hypertensive, diabetics (36%), obese (60%), dyslipidemia (46%) and (33%) were smokers. Family history with CAD found in 30%. About (53%) of all study subjects had significant obstructive CAD. Subjects group with significant CAD had a higher frequency of hypertension (56%, P=0.54), diabetes (55.6%, P=0.7), dyslipidemia (65.2%, P=0.02), and smoking (54.5%, P=0.82), and 56.7% of patients were obese (P=0.36). The mean of left ventricular ejection fraction (LVEF) was 51.5±8.6%, and 40% of involved patients in the study had impaired LV systolic function (EF less than 50%) (P=0.03 and P=0.017), respectively. The fragmented wide QRS complex was presented in 46 (46%) of all patients involved in the study, of them 78.3% cases with significant obstructive CAD (P<0.00001). Regarding angiographic data, a substantial difference was found between the groups with significant obstructive CAD and those without obstructive CAD for the presence of few-QRS [(36%) vs. (10%), respectively; p<0.00001)]. There was a significant

association between the presence of fragmented LBBB and significant obstructive CAD. There was a significant association between LV systolic function status and the presence of fw-QRS complex in which 31 (31%) of patients group with fw-QRS had impaired ejection fraction (P<0.00001).
Conclusion. In LBBB cases, there is a significant association between the fragmented QRS complex with the presence and severity of CAD. In ischemic LBBB, there is an inverse relationship between LV systolic function and the presence of fragmented QRS.
Keywords: QRS complex, Coronary artery disease, Left Bundle Branch Block, ischemic heart disease, ST-elevation, ECG

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Связь фрагментации широкого комплекса QRS с ишемической болезнью сердца у пациентов с блокадой левой ножки пучка Гиса

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Резюме

Введение. Полная блокада левой ножки пучка Гиса (БЛНПГ) повышает риск смертности от сердечной недостаточности, прогноз которой в значительной степени обусловлен сопутствующими коронарными заболеваниями. При БЛНПГ возникают сложности с выявлением ишемической болезни сердца (ИБС) на ЭКГ, что затрудняет клиническую диагностику ишемии миокарда. Фрагментация широкого комплекса QRS на поверхностной ЭКГ у пациентов с БЛНПГ может свидетельствовать об ишемии миокарда, рубцевании или фиброзе.
Цель. Исследование связи фрагментации широкого комплекса QRS (fw-QRS) и выраженной обструктивной ИБС у пациентов с БЛНПГ.
Материалы и методы. Проведено перекрестное исследование 100 пациентов с БЛНПГ, поступивших в кардиологические центры в Ибн Аль-Битар и Насирии для проведения коронарной ангиографии в рамках обследования с целью диагностики ИБС. У всех пациентов, включенных в исследование, была проведена оценка демографических характеристик, типичных факторов риска ИБС, а также результатов коронарной ангиографии, ЭКГ и эхокардиографии.
Результаты. Средний возраст пациентов был в пределах 61,2±10,5 года, 55 (55% от общего числа испытуемых) составляли мужчины. У 53 (53%) пациентов была выявлена выраженная обструктивная ИБС. Почти 50% всех пациентов, включенных в

исследование, страдали гипертонией, у 36% был диабет, у 60% – ожирение, у 46% – дислипидемия, 33% были курильщиками. 30% испытуемых имели ИБС в семейном анамнезе. Примерно 53% всех участников исследования имели выраженную обструктивную ИБС. В группе испытуемых с выраженной ИБС чаще выявляли гипертонию (56%, P=0,54), диабет (55,6%, P=0,7) и дислипидемию (65,2%, P=0,02), курильщиками были 54,5% (P=0,82), 56,7% испытуемых страдали от ожирения (P=0,36). Средняя фракция выброса левого желудочка (ФВЛЖ) составляла 51,5±8,6%, нарушение систолической функции ЛЖ (ФВ менее 50%) было выявлено у 40% включенных в исследование испытуемых (P=0,03 и P=0,017) соответственно. Фрагментация широкого комплекса QRS наблюдалась у 46 пациентов (46% всех испытуемых, участвовавших в исследовании), из них в 78,3% случаев она сопровождалась выраженной обструктивной ИБС (P<0,00001). Анализ ангиографических данных выявил достоверные различия в обнаружении фрагментации широкого комплекса QRS (fw-QRS) в группах с выраженной обструктивной ИБС и без нее (36% по сравнению с 10% соответственно; p<0,00001). Установлена достоверная связь между наличием фрагментированной БЛНПГ и выраженной обструктивной ИБС. Также отмечена достоверная связь между показателями систолической функции ЛЖ и наличием комплекса fw-QRS, при этом у 31 (31%) пациента из группы с fw-QRS имелись нарушения фракции выброса (P<0,00001).

Заключение. Установлена достоверная связь между фрагментацией широкого комплекса QRS у пациентов с БЛНПГ и наличием и степенью тяжести ИБС. При БЛНПГ, вызванной ишемией, существует обратная зависимость между систолической функцией ЛЖ и наличием фрагментации QRS.

Ключевые слова: комплекс QRS, коронарное заболевание, блокада левой ножки пучка Гиса, ишемическая болезнь сердца, подъем сегмента ST, ЭКГ

■ INTRODUCTION

The left bundle branch block (LBBB) occurs when normal electrical conduction through the left bundle of the His-Purkinje system is interrupted, which results in a drastic alteration of the normal sequence of activation in the left ventricle [1, 2]. LBBB can be present in young asymptomatic subjects without any structural heart disease (isolated LBBB) and is then generally associated with a good prognosis. However, at a higher age, LBBB often co-exists with underlying heart disease (e.g. ischemic, infiltrative, hypertensive, or valvar), where it acts as an independent predictor of poorer cardiovascular outcomes [3].

Thus, the incidental finding of LBBB is currently considered a potential marker of underlying heart disease, especially CAD, prompting further non-invasive or invasive diagnostic procedures to detect underlying myocardial pathology [4, 5].

Some epidemiological studies have associated LBBB with coronary artery disease (CAD), suggesting a causal role of CAD in most patients with LBBB, while other studies did not support or confirm this relationship. Thus, the association of LBBB with CAD remains unclear [6–8].

The diagnosis of CAD in patients with LBBB represents a clinical challenge. The non-invasive evaluation of CAD in these patients has several limitations. The available modalities include exercise ECG, stress echocardiography, and myocardial perfusion imaging, which

all become less accurate in the presence of LBBB. Because of these limitations, patients with LBBB are often referred to invasive coronary angiography (ICA) to exclude CAD [9–11].

Coronary angiography remains the 'gold standard for identifying the presence or absence of stenosis due to coronary artery disease and provides the most reliable anatomical information for determining the appropriateness of medical therapy, percutaneous coronary intervention, or coronary artery bypass graft in patients with ischemic heart disease [9, 12].

It should be noted that this study, like many studies, used the 70% diameter stenosis cutoff to define "significant stenosis" even though extensive data demonstrate the unreliability of diameter stenosis as a measure of the physiological relevance of stenosis in terms of impairment in flow reserve [13].

Based on QRS complex duration, fragmented QRS complexes are subclassified into fragmented narrow QRS complexes (fqrs; QRS duration <120 ms) and fragmented wide-QRS complexes (f-w-QRS; QRS duration >120 ms) [14, 15].

Fragmented narrow QRS complex includes various RSR' patterns with different morphologies of the QRS complexes, with or without the Q wave on a resting 12-lead ECG. Various RSR' patterns include an additional R wave (R') or notching in the nadir of the S wave, or the presence of >1 R' (fragmentation) in 2 contiguous leads corresponding to a major coronary artery territory [14].

In complete LBBB, a fragmented wide QRS complex was defined by the presence of >2 notches in the R wave, or >2 notches in the S wave, in two contiguous leads corresponding to a major coronary artery territory [15].

Das et al proved that the presence of fw-QRS predisposed susceptible patients to a higher propensity of adverse cardiac events like MI, the need for revascularization, or cardiac death [16].

Several studies have suggested that the fragmentation of the QRS complex is caused by a change in the ventricle's normal depolarization. On surface ECG, the presence of a fragmented QRS (f-QRS) complex has been linked to myocardial ischemia, scarring, or fibrosis. The ischemia effect on Purkinje fibers could be the cause of this QRS fragmentation. Due to variably depolarized myocardium and decreased action potential upstroke velocities, the chronically ischemic myocardium activates slowly, this feature is also responsible for the ventricles' non-homogeneous activation. As evidenced by endocardial mapping and computer modeling, ischemia affects ventricular depolarization patterns, which most likely represents fragmentation in the QRS complex on the surface 12-lead ECG [13, 16, 17].

In the previous studies, the presence of fragmented QRS was found to be useful in the detection of myocardial scar, and the prediction of myocardial infarction and reperfusion parameters [18–20].

■ PURPOSE OF THE STUDY

To investigate the relationship between the presence of fragmented wide QRS complex (fw-QRS) and significant obstructive CAD in patients with LBBB.

■ MATERIALS AND METHODS

This is a cross-sectional study, a total of 100 patients with LBBB, 55 males and 45 females were referred for coronary angiographic examination as part of the investigation for CAD.

The study was conducted at Ibn Al-Bitar Center for Cardiac Surgery and Nassyireha Cardiac Center during the period from January 2021 to February 2022.

After giving informed written consent, all patients underwent the following: Preliminary evaluation which included the clinical characteristics of the patient's age, gender, family history of CAD, smoking, body weight, height, body mass index, systemic hypertension and diabetes mellitus, and dyslipidemia.

Complete 12-leads electrocardiography (0.5–150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV), the QRS width was calculated. According to AHA recommendations for the Standardization and Interpretation of the Electrocardiogram; a complete LBBB was diagnosed by the following criteria [21]:

1. QRS duration greater than or equal to 120 ms in adults.
2. Broad or slurred R' wave in leads I, aVL, V5, and V6.
3. Absent q waves in leads I, V5, and V6, but in the lead aVL, a narrow q wave may be present in the absence of myocardial pathology.
4. R' peak time greater than 60 ms in leads V5 and V6 but normal in leads V1, V2, and V3, when small initial r waves can be discerned in the above leads.
5. ST and T wave opposite in direction to QRS.

The diagnosis of fragmented wide QRS in LBBB was established in the presence of more than two notches in the R or S wave, on at least two adjacent leads corresponding to a major coronary artery territory; inferior (II, III, aVF), lateral (I, aVL, V5, V6) or anterior (V1 to V6) leads [15].

Transthoracic echocardiography examination was done for all patients by using standardized equipment (GE Vivid E9 Ultrasound Machine). The biplane method of Simpsons was used to estimate ejection fraction [22].

Coronary angiography was done by Seldengers technique on all patients involved in the study. The extent of coronary artery disease (CAD) was assessed concerning the number of diseased vessels, and the grading of stenosis was assessed by the percentage of coronary arterial lumen occluded visually and or by QCA measurement.

A significant obstructive CAD is defined as [23]:

- ≥70% luminal diameter narrowing, of epicardial artery stenosis measured in the "worst view" angiographic projection.
- ≥50% luminal diameter narrowing, of the left main stenosis measured in the "worst view" angiographic projection.

Patients were excluded from the study if they had one or more of the following:

- Moderate or severe aortic valve heart disease.
- Left ventricular outflow obstruction and hypertrophic cardiomyopathy.
- Previous cardiac surgery or PCI.
- Acute STEMI.
- Paced rhythm.

Data Analysis was done on SPSS version 26, for the determination of statistical significance among different variables; a P-value of less than 0.05 was considered significant.

■ RESULTS

A total number of 100 patients were enrolled in this study, 55% of them were male and 45% were females, and the mean age of the study population was 61.2±10.5 years.

The comparison betwee cases with significant obstructive CAD (n=53) and normal or non-obstructive CAD (n=47) was listed in Table 1. About 50% of all patients enrolled in the study were hypertensive, diabetics (36%), obese (60%), dyslipidemia (46%) and (33%) were smokers. Family history with CAD found in 30%. About (53%) of all study subjects had significant obstructive CAD. Subjects group with significant CAD had a higher frequency of hypertension (56%, P=0.54), diabetes (55.6%, P=0.7), dyslipidemia (65.2%, P=0.02), and smoking (54.5%, P=0.82), and 56.7% of patients were obese (P=0.36). The mean of left ventricular ejection fraction (LVEF) was 51.5±8.6%, and 40% of involved patients in the study had impaired LV systolic function (EF less than 50%), (P=0.03 and P=0.017), respectively. The fragmented wide QRS complex was presented in 46 (46%) of all patients involved in the study, of them 78.3% cases with significant obstructive CAD (P<0.00001).

Statistically, there was no significant difference in the distribution of age (P=0.78) (Table 2) and gender (P=0.77) (Table 3) between groups with the fragmented and non-fragmented wide QRS complex.

Regarding angiographic data, a substantial difference was found between the groups with significant obstructive CAD and those without obstructive CAD for the presence of few-QRS ((36%) vs. (10%), respectively; p<0.00001)). There was a significant association between the presence of fragmented LBBB and significant obstructive CAD (Table 4).

Table 1
The baseline characteristics of patients involved in the study

Characters	All subjects (n=100)	Significant obstructive CAD (n=53)	Normal or non-obstructive CAD (n=47)	Chi-square (X^2)	P-value
	No. (%)/ mean±SD				
Gender (Male: Female)	55 (55):45 (45)	35 (63):18 (37)	20 (44): 27 (56)	5.55	0.018
Age (year)	61.2±10.5	62.3±10.4	56.8±9.5	0.19	0.08
DM	36 (36)	20 (55.6)	16 (44.4)	0.14	0.7
HTN	50 (50%)	28 (56)	22 (44)	0.36	0.54
Smoking	33 (33%)	18 (54.5)	15 (45.5)	0.04	0.82
BMI (kg/m^2)	35.6±6.5	34.7±4.7	31.2±3.8	0.44	0.07
Obesity	60 (60)	34 (56.7)	26 (43.3)	0.8	0.36
Dyslipidemia	46 (46)	30 (65.2)	16 (34.8)	5.1	0.02
Family history of CAD	30 (30)	17 (56.7)	13 (43.3)	0.23	0.63
Ejection Fraction <50%	40 (40)	27 (67.5)	13 (32.5)	5.6	0.017
Ejection fraction (EF %)	51.5±8.6	48.6±7.7	55.4±6.9	4.39	0.03
LBBB with fw-QRS complex	46 (46)	36 (78.3)	10 (21.7)	21.8	<0.00001

Table 2
The presence of LBBB with fw-QRS complex according to age groups

Age groups (years)	fw-QRS complex (No. (%))		Total
	Yes	No	
30–64	20 (20)	22 (22)	42 (42)
≥64	26 (26)	32 (32)	58 (58)
Total	46 (46)	54 (54)	100
X^2=0.07; P=0.78			

Table 3
The relationship between gender and LBBB with the fw-QRS complex

Sex	fw-QRS complex (No. (%))		Total
	Yes	No	
Male	26 (26)	29 (29)	55 (55)
Female	20 (20)	25 (25)	45 (45)
Total	46 (46)	54 (54)	100
X^2=0.08; P=0.77			

Table 4
The association between significant obstructive CAD and the presence of LBBB with fw-QRS complex

LBBB with fw-QRS	Significant obstructive CAD (No. (%))		Total
	Yes	No	
Yes	36 (36)	17 (17)	53 (53)
No	10 (10)	37 (37)	47 (47)
Total	46 (46)	54 (54)	100
X^2=21.8; P<0.00001			

The sensitivity of LBBB with fw-QRS complex in detecting significant obstructive CAD was 68%, specificity 79%, positive predictive value 78% and negative predictive value 69% (Table 5).

Comparison between fragmented and non-fragmented LBBB groups according to the numbers of significantly obstructive vessels (Table 7); revealed that 16 (30.2%) patients who had fw-QRS had triple vessels or LMS disease, followed in decreasing order by double vessels disease 12 (22.6%) and single-vessel disease 8 (15.1%), with no significant difference (P=0.056).

There was a significant association between LV systolic function status and the presence of fw-QRS complex in which 31 (31%) of patients group with fw-QRS had impaired ejection fraction (P<0.00001) (Table 7).

Table 5
Validity of fw-QRS complex in predicting significant obstructive CAD

Sensitivity	Specificity	PPV: positive predictive value	NPV: negative predictive value
68%	79%	78%	69%

Table 6
Comparison of the number of vessels with significant CAD between fw-QRS and non-fw-QRS groups among patients with LBBB (n=53)

No. of vessel diseased with significant obstruction	Fw-QRS (No. (%))		Total
	Fw-QRS (+VE)	Fw-QRS (-VE)	
1 vessel diseased	8 (15.1)	9 (17.0)	17 (32.1)
2 vessels diseased	12 (22.6)	5 (9.5)	17 (32.1)
≥3 vessels diseased and or LMS diseased	16 (30.2)	3 (5.6)	19 (35.8)
X^2=5.76; P=0.056			

Table 7
The distribution of LV systolic function in patients with fragmented and non-fragmented wide QRS in LBBB

Fw-QRS complex	Left ventricular systolic function (EF %) (No. (%))		Total
	EF <50%	EF ≥50%	
fw-QRS	31 (31)	16 (16)	47 (47)
Non-fw-QRS	10 (10)	43 (43)	53 (53)
X^2=22.83; P<0.00001			

Table 8
Relationship of a risk factor with the fragmented wide QRS complex

Risk factor	Fw-QRS complex (No.)		Odds ratio	95%CI	P-value
	Yes	No			
Diabetes	20	16	1.174	0.51–2.66	0.7
Hypertension	29	21	1.496	0.68–3.29	0.32
Smoking	16	17	0.763	0.33–1.76	0.53
Obesity	32	28	1.034	0.46–2.3	0.93
Dyslipidemia	26	20	1.3	0.59–2.86	0.52
Family history of CAD	18	12	1.5	0.62–3.57	0.36

However, there was a higher incidence of patients with fragmented wide QRS among the groups with diabetes (20/36), hypertension (29/50), smoking (16/33), obesity (32/60), dyslipidemia (26/46), and family history of CAD (18/30). Statistically, these differences were not significant (Table 8).

■ DISCUSSION

In our study, LBBB was common among old age groups; the incidence was 58% at ages more than 64 years, and the mean age of the study was 61.2±10.5 years, which was close to that illustrated by other studies [24, 25]. LBBB was more common in males than females in which (55%) of the overall patients were males, Ghaffari et al's study yielded similar results [26].

Patients with LBBB and concomitant coronary artery disease (CAD) have a worse prognosis than those with LBBB without coronary heart disease (CHD). Patients with LBBB who were followed had increased mortality as compared with those without LBBB, but this worsened survival was observed only in those with concomitant CAD, Patients with LBBB and no CAD had a reasonably good prognosis [3, 27].

However, identifying CAD in these patients has been the subject of many studies and remains a clinical challenge. Exercise ECG, a non-invasive test that is often used in the investigation of CAD, but has limited diagnostic value in LBBB patients. The ACC/AHA Guide recommends the use of imaging stress tests for the investigation of ischemia in LBBB cases. Moreover, stress testing in the presence of LBBB is challenging due to higher rates of false-positive findings, even if imaging modalities are employed. Because of these limitations, patients with LBBB are often referred to as invasive coronary angiography (ICA) to exclude CAD [1, 9, 28–30].

The imaging stress tests used in the investigation of CAD in cases of LBBB are generally expensive and not widely available in our country. More than half of the patients enrolled

in the current study had significant obstructive CAD. This is in agreement with other studies' findings [31, 32], in contrast, other studies showed a lower incidence of CAD in patients with LBBB [31, 33].

In the current study, we evaluate the presence of a fragmented QRS complex as a marker of CAD in patients with LBBB. According to the findings of this study, there was a substantial link between a fragmented QRS complex in LBBB and CAD with significant stenosis on coronary angiography. Our findings revealed that fragmented LBBB had a sensitivity of 68% in detecting significant obstructive CAD, a specificity of 79%, a positive predictive value of 78%, and a negative predictive value of 69%.

The above outcome of a significant relationship between fragmented LBBB and CAD was similar to other studies done by Mohamed M. Al-Daydamony [34] and Bayar and his colleague [35].

Also, Das et al have demonstrated a high correlation between the incidence of fragmented LBBB and the presence of myocardial scar related to CAD proved by SPECT imaging in LBBB cases. They found that the sensitivity of fragmented left bundle branch block in predicting myocardial ischemic scar was 88.6%, specificity was 90.2%, positive predictive value was 95.1%, and negative predictive value was 78.7% [16]. The figures found by Das et al. were higher than ours. These differences may be explained by the higher number of patients involved in the study. Another explanation is the multiple parameters they used to detect myocardial ischemia including gated SPECT analysis while we depend on invasive coronary angiography to detect CAD [16].

Chronic ischemia has been documented to cause myocardial patchy fibrosis which could lead to the emergence of fragmented QRS on ECG [36, 37]. Our results are supported by the study of Pietrasik et al who proposed that a fragmented QRS complex could be used to identify ischaemic myocardium [38, 39].

On the other hand, the angiographic severity of CAD was evaluated by calculating the number of vessels with anatomically significant obstruction, sixteen patients (44%)with ischemic fragmented LBBB had triple or LMS disease. This positive relationship between anatomically assessed severe CAD and fragmented LBBB in our study was in concordance with a study done by Caliskan et al., which showed a significant correlation between fw-QRS and functionally significant myocardial ischemia assessed by SPECT [40].

Furthermore, there was a significant link between LV systolic function and the presence of fw-QRS complex in which three-quarter of patients group with fragmented LBBB had impaired ejection fraction while only one-quarter of patients group without fw-QRS had ejection fraction below <50%, this was in the correlation of Reddy CV and his colleague who found that the presence of fragmented QRS complex on an ECG is a reliable indicator for the LV systolic dysfunction [41] and this inverse relationship between the fragmented QRS complex and LV systolic function also has been demonstrated by other studies [24, 42].

Das et al., reported that fw-QRS has emerged as an independent predictor for major adverse cardiovascular events in individuals with CAD, study that included patients with LBBB and RBBB, the survival time in patients with fragmented LBBB was determined to be significantly shorter than that in patients with non-fragmented LBBB, RBBB, and fragmented RBBB [43].

The adverse prognostic value of fragmented LBBB tested by Dae et al can be partially explained in our study by the expected occurrence of adverse cardiac events caused

by more severe CAD involvement and impaired LV systolic function among the studied patient group with the fragmented QRS complex.

Although there was a higher incidence of patients with fragmented LBBB among the group with DM (20/36), HTN (29/50), smoking (16/33), obesity (38/60), and dyslipidemia (26/46), statistically, were not significant. This non-significant link between fragmented LBBB and different risk factors for CAD is in concordance with other study results [2].

■ CONCLUSION

There is a link between a fragmented QRS complex with the presence and severity of CAD in LBBB patients. In ischemic LBBB, there is an inverse relationship between LV systolic function and the presence of fragmented QRS. The presence of a fragmented QRS complex on the surface ECG in cases of LBBB is a valuable, non-invasive diagnostic tool that can be used to identify the presence of significant obstructive CAD.

Limitation of the study

1. The study's patient population is small.
2. Because the study did not include case follow-up, the effect of fragmented wide QRS on prognosis could not be assessed.

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