ORIGINAL RESEARCH ARTICLE

Prenatal ultrasound monitoring and diagnostic accuracy rates of fetal congenital heart disease: A meta-analysis

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Abstract

Congenital heart disease (CHD) is the most common birth defect that is caused by genetic and acquired factors. Accurate prenatal diagnosis of congenital heart disease (CHD) can ensure proper delivery and in-time postpartum management, but the diagnostic rate is not clear. PubMed, CNKI, Web of Science, Wanfang, and VIP databases were searched for publications investigating CHD during prenatal ultrasound scans. Original studies with strict screening and diagnostic criteria were included. Fixed effect model or random effect model was used according to homogeneity statistical test. A total of 859 CHD cases were diagnosed by ultrasound, and 1394 cases were confirmed by induced labor autopsy or at birth. The heterogeneity of the analysis was 100% and the accuracy of CHD diagnosis using prenatal ultrasound was 76% (95%CI: 50.00%-102%). The diagnostic yield of fetal CHD screening using ultrasound alone is still not very high, which lower than the combined diagnostic yield of other studies. This suggests the need to combine other monitoring methods that do not harm fetal development. When economic conditions permit, the diagnosis of CHD can be recommended to use no less than two monitoring methods. *(Afr J Reprod Health 2023; 27 [6]: 33-40).*

Keywords: Prenatal ultrasound monitoring; antenatal surveillance (as); diagnostic rates; congenital heart disease; meta-analysis

Résumé

La cardiopathie congénitale (CHD) est l'anomalie congénitale la plus courante causée par des facteurs génétiques et acquis. Un diagnostic prénatal précis des cardiopathies congénitales (CHD) peut garantir un accouchement approprié et une prise en charge post-partum à temps, mais le taux de diagnostic n'est pas clair. Des recherches ont été effectuées dans les bases de données PubMed, CNKI, Web of Science, Wanfang et VIP pour trouver des publications portant sur la maladie coronarienne lors d'échographies prénatales. Des études originales avec des critères de dépistage et de diagnostic stricts ont été incluses. Un modèle à effet fixe ou un modèle à effet aléatoire a été utilisé selon le test statistique d'homogénéité. Au total, 859 cas de coronaropathie ont été diagnostiqués par échographie et 1394 cas ont été confirmés par autopsie provoquée par le travail ou à la naissance. L'hétérogénéité de l'analyse était de 100 % et la précision du diagnostic de coronaropathie par échographie prénatale était de 76 % (IC à 95 % : 50,00 % - 102 %). Le rendement diagnostique du dépistage des maladies coronariennes fœtales par échographie seule n'est toujours pas très élevé, ce qui est inférieur au rendement diagnostique combiné d'autres études. Cela suggère la nécessité de combiner d'autres méthodes de surveillance qui ne nuisent pas au développement du fœtus. Lorsque les conditions économiques le permettent, le diagnostic de coronaropathie peut être recommandé d'utiliser pas moins de deux méthodes de surveillance. *(Afr J Reprod Health 2023; 27 [6]: 33-40).*

Mots-clés: Surveillance echographique prenatale ; surveillance prenatale (sa); tarifs diagnostiques ; maladie cardiaque congenitale; meta-analyse

Introduction

Congenital heart disease (CHD) refers to cardiovascular malformations caused by abnormal cardiac and vascular development in the fetal period, and is the most common heart disease in children. It is the most common birth defect worldwide[1-3], mainly caused by extracardiac and/or chromosomal abnormalities, leading to not only impaired embryonic development of the heart and blood vessels, but also multiple abnormal clinical phenotypes which may largely impact the development and quality of life of children. The incidence of CHD is about 0.6%-0.9% of all live births. It is estimated that 150,000 newborns with various types of CHD are born in China every year, among which the proportion of ventricular septal defect, patent ductus arteriosus, atrial septal defect and pulmonary valve stenosis are about 20.0%, 15.0%, 12.0% and 10.0%, respectively[4]. Furthermore, CHD is a common cause of neonatal morbidity and mortality. Such phenomenon is even

more serious in low- and middle-income countries such as sub-Saharan Africa[5]. There are 4 to 50 out of a thousand live births carrying CHD, representing a wide range of variation in its incidence across different studies[6,7]. CHD accounts for nearly a third of neonatal deaths with congenital defects due to its complexity and difficulty of postpartum surgeries[8,9]. Congenital heart disease occurs in 4-13 of every 1,000 births in the United States, and while many risk factors for coronary heart disease have been identified, more than 90% of cases occur in low-risk patients[10].

CHD can be classified into four types according to the obstetric ultrasound cardiac view required for diagnosis, which are outflow tract view (e.g., tetralogy of Fallot, d-transposition, truncus arteriosus), 4-chamber view (e.g., hypoplastic left heart syndrome, Ebstein's anomaly, single ventricle), 3-vessel or other non-standard cardiac views (e.g., coarctation, anomalous pulmonary veins), and isolated ventricular septal defects using any view[11], respectively. It is generally believed that most congenital heart diseases are caused by the interaction of multiple gene abnormalities and environmental factors[12]. The factors with strong correlation with cardiovascular malformations are: (1) early intrauterine infection, such as rubella, influenza, mumps and coxsackievirus infection; (2) the mother had a history of exposure to large doses of radiation and medication (antineoplastic drugs, antiepileptic drugs, etc.); (3) maternal metabolic disorders (diabetes, hypercalcemia, etc.); (4) chronic diseases causing hypoxia in utero; (5) alcoholism and drug abuse during early pregnancy[12].

Epidemiological investigation revealed a high incidence rate of CHD in high-risk groups, i.e., pregnant women with diabetes, hypertension and hyerlipidemia, while 85% to 90% of all CHD cases are sporadic without any obvious risk factor. A Japanese study showed that prenatal cardiac diagnosis reduces geographic and chronological risks of emergency transfer for moderate to severe CHDs[13]. Therefore, screening for cardiac malformations has now become a routine practice. High-risk groups of CHD will be defined through screening and sent to further examination. Proper evaluation during prenatal diagnosis is helpful to optimize the prognosis of newborns[14]. Timely prenatal detection, diagnosis and intervention are very important. Fetal cardiovascular malformations have been widely focused and screened, but the accuracy of screening is not satisfactory. Prenatal screening for CHD is commonly performed by the following methods: (1) B-mode ultrasound[15] can be performed between 11-13 weeks +6 in early pregnancy to check the thickness of the transparent layer of fetal neck , that is, the NT value. If the thickness of NT value exceeds 3mm, congenital heart disease is likely to occur. (2) Down's screening[16] can detect whether the fetus is likely to have chromosomal abnormalities, including trisomy 18 syndrome and trisomy 21 syndrome, both of which are associated with congenital heart disease. (3) Fetal heart color ultrasound[17], through which the structure of the fetal heart can be understood and congenital heart disease can be excluded.

In the past 30 years, due to the application of echocardiography, cardiac catheterization, cardiography, as well as the development of open heart surgery under low temperature anesthesia and extracorporeal circulation, the majority of CHD have been accurately diagnosed, most of them can be completely cured, and the prognosis has been greatly improved[18,19]. However, in recent years, the incidence of fetal cardiovascular malformations has increased and the prognosis is very poor. Early diagnosis is critical, and the main methods for diagnosing fetal malformations include computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound[17,20-22]. Among them, ultrasound has become the first choice for diagnosing fetal congenital cardiovascular malformations because of its simple operation, low cost, no ionizing radiation and real-time dynamic characteristics[17]. In combination with maternal age, serum biochemistry, and ultrasound abnormalities, ultrasound screening can identify most chromosomal or in vivo abnormalities. The risk of congenital heart disease is significantly increased if the fetal nuchal translucency is found to be increased and the karyotype is normal during the first trimester examination. Ultrasound diagnosis for early pregnancy screening is very important for fetuses with CHD. When diagnosed prenatal, proper evaluation can help optimize neonatal outcomes.

Hence, the purpose of this meta-analysis was to determine the relationship between prenatal ultrasound testing and the rate of diagnosis of coronary heart disease, which would be beneficial to

evaluate and help optimize maternal and infant outcomes.

Methods

Retrieval strategy

This study was based on searching PubMed, CNKI, Web of Science, Wanfang, VIP and other electronic databases. "Congenital heart disease", "prenatal diagnosis" and their corresponding English expressions were used as search keywords. No attempt was made to retrieve unpublished studies.

Inclusion and exclusion criteria

Inclusion criteria: Cases were collected for field investigation; the study was population-based, not volunteer; clear diagnostic criteria and study implementation date; multiple studies with the same sample included the most detailed research data. All included studies should use the same diagnostic criteria to exclude studies where data are not available.

Research quality

We use the framework recommended by the Cochrane Collaboration to assess the quality of studies. For inclusion decisions, the quality assessment was carried out independently by three reviewers. The study could only be included after agreement by at least two of them. All data included in the study were clearly tabulated and deviations were considered and identified during the quality assessment stage.

Statistical methods

This meta-analysis was performed using RevMan 5.3. The diagnostic rate of CHD was calculated, and fixed effect model or random effect model was used in according to I^2. Heterogeneity was divided into low, medium, and high levels according to 25%, 50% and 75% of I^2. Fixed effect model was applied to low heterogeneity, while random effect model was applied to medium and high heterogeneity. Publication bias was evaluated through funnel plot, Mr. Begg's inspection, and Egger's regression asymmetry evaluation. Data analysis was performed using Stata 14.0 (StataCorp, College Station, TX, USA). Diagnostic accuracy and 95%CI for ultrasound diagnosis of fetal CHD were calculated for each study, and the year of publication was also available. A total of 859 CHD cases were diagnosed by ultrasound, and 1394 cases were confirmed by induced labor autopsy or at birth. The final combined ultrasound diagnostic rate was 76% (95%CI: 50.00%-102%). The heterogeneity of the analysis was 100% (Figure 2). The quality evaluation of the included literature was shown in Figure 3.

Results

Figure 1 summarized the literature selection process of this study. A total of 352 relevant articles were retrieved at the initial stage, and the remaining 71 were read through after eliminating duplicates and reading titles and abstracts. Finally, a total of 14 literatures published from 2014 to 2021 were included. The analysis was not confined to papers that confirmed ultrasound diagnosis at birth or at postmortem. Table 1 showed the characteristics of the study.

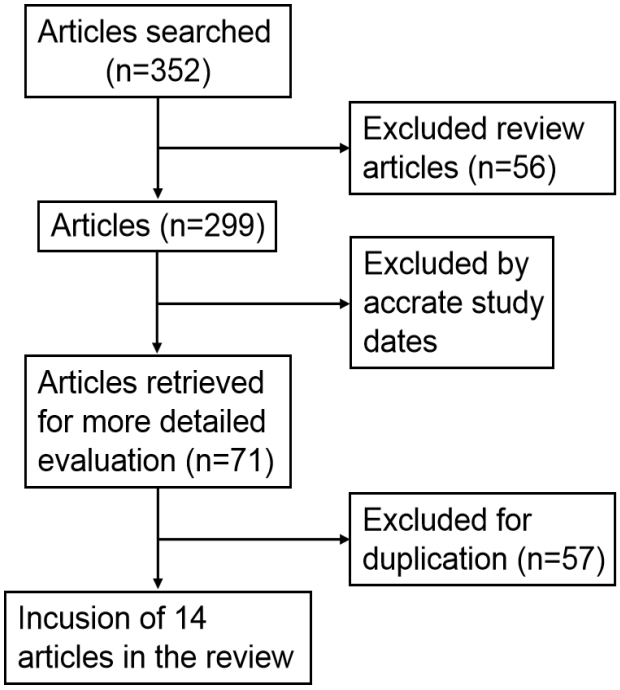


Figure 1: Flow of information through the different phases of a systematic review

Table 1: Characteristics of the studies (n=14)

No.	Author, Year	Region	Number of prenatal diagnoses	Confirmed the number
1	Xia Tao 2021[23]	Sichuan, China	51	60
2	Shuang Gao 2019[24]	Beijing, China	149	171
3	S Turan 2014[25]	USA	20	22
4	Bing Han 2021[26]	Shandong, China	40	454
5	Carvalho H 2021[27]	/	13	44
6	Mei Bingchuan 2021 [28]	Jiangxi, China	75	79
7	Lin Muzhen 2021[29]	Guangdong, China	47	55
8	Zhang li 2021[30]	Henan, China	70	75
9	Song Junning 2021[31]	Henan, China	38	40
10	Yuan Dan 2021[32]	Jiangxi, China	24	30
11	Chen Min 2021[33]	Henan, China	110	126
12	Marijo Aguilera 2017[34]	USA	74	106
13	Rahul Krishnan 2021 [35]	USA	61	63
14	Mei Mei 2019[36]	Heilongjiang, China	87	99

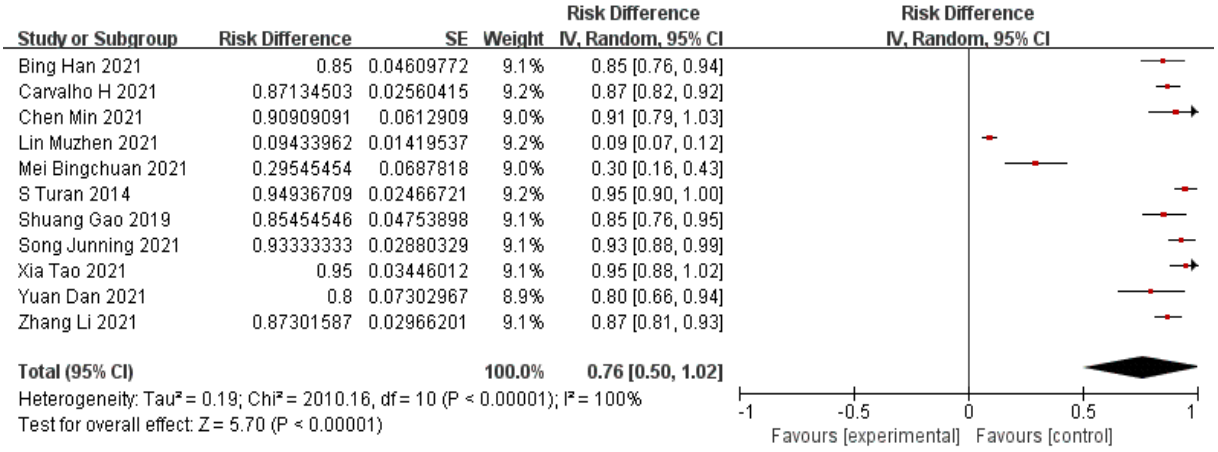


Figure 2: Forest map of prenatal ultrasound monitoring and diagnostic rates of fetal congenital heart disease

Sensitivity analysis and publication bias evaluation

Sensitivity analysis was conducted to exclude the influence of each study on the results of meta-analysis, and the results showed that each study had little change in the combined effect value. However, the funnel plot (Figure 4**)** showed bias, which may be related to large heterogeneity.

Discussion

Despite significant improvements in the quality of life of patients due to medical advances, there are indications of an increase in the incidence of developmental problems in children with CHD[37]. The hospital mortality rate of middle and late preterm infants with coronary heart disease remains high[38]. In order to effectively reduce the disease burden and achieve early detection and diagnosis, interventions such as prenatal diagnosis and intervention by ultrasound scan are necessary and need further attention[39].

The meta-analysis of the present study found that the diagnostic rate of prenatal ultrasound for fetal CHD was 76%, similar to a study (76.2%) reported in 2020[40], higher than 58% reported in Kaur A *et al*.[11] but lower than that (85%) in a previous multicenter study among women during the second trimester[41], furthermore, the diagnostic rate of prenatal ultrasound diagnosis of complex and simple CHDs was 90.50–91.66% and 98.68%[40], these results all indicated that ultrasound monitoring was an effective strategy for fetal CHD . Some researchers have advocated for routine fetal echocardiography in pregnancy[42] as well because of the unsatisfactory performance of obstetric screening for fetal CHD.

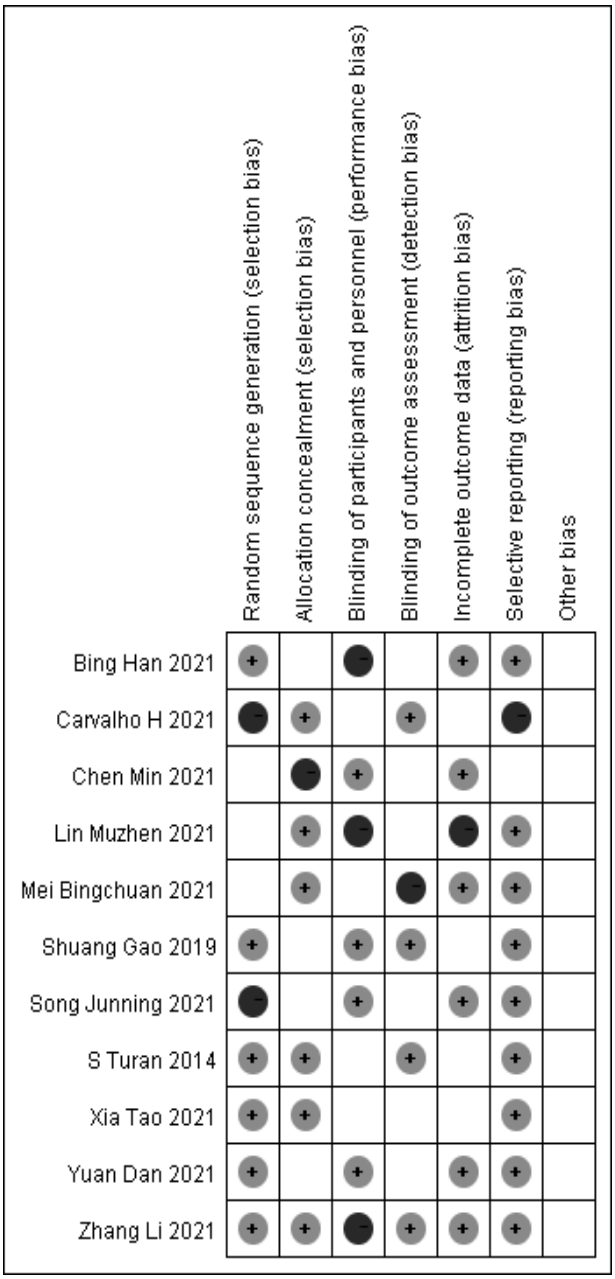


Figure 3: Quality evaluation of included literature

Early prenatal screening using ultrasound can significantly reduce neonatal mortality due to CHD. However, the need for fetal cardiologist expertise and the large number of screening cases limit the actual detection rate that can be achieved[43]. It was worth noting that ultrasound screening incorporating multiple cardiac views for fetal cardiac malformations was the mainstream diagnostic measures in the USA[44], while ultrasound screening examinations were performed by physicians experienced in obstetric ultrasonography rather than sonographers, and are typically conducted in regional tertiary obstetric centers and secondary obstetric hospitals in China[42].

A study[45] has suggested that both maternal and fetal factors may prompt referral for fetal echocardiography. Prompt referral for fetal echocardiography should be made when maternal indications are present, such as congenital heart disease in a first-degree relative, maternal systemic disease (e.g., diabetes, lupus), in vitro fertilization, exposure to teratogens, and familial genetic disorders (e.g., Marfan syndrome). Fetal signs that should suggest referral include chromosomal abnormalities, extracardiac abnormalities, hydrops, arrhythmias, monochorionic twins, and polyhydramnios. CHD can be predicted by abnormal cardiac screening at routine fetal ultrasound at 18-20 weeks, and follow-up fetal echocardiography, including four-chamber views of the heart and outflow tract, has identified 60% to 80% of cardiac defects[46], while nearly 30% of lesions remain unanticipated at birth. Patients should be referred for genetic counseling and offered appropriate genetic testing when CHD is detected by prenatal screening. At the same time, a close communication between prenatal diagnosis of genetic syndromes associated with CHD, obstetricians, geneticists, and pediatricians can help optimize maternal and infant outcomes[47].

Early fetal echocardiography is feasible and can detect most coronary artery disease, but congenital heart defects vary in appearance at different stages of pregnancy and may develop in utero with gestational age. Therefore, early fetal echocardiography should always be followed by echocardiography in the second trimester[48]. Despite advances in ultrasound equipment, fetal position, maternal obesity, scarring of maternal abdominal wall from previous surgery, and amniotic fluid passing can severely impair visualization of fetal heart structure. It has been reported that fetal ECG reflects the close relationship between the cardiac nerve conduction system and the structural morphology of the heart. It also appears to be particularly useful for detecting the electrophysiological effects of anatomical defects of the heart, such as malnutrition, hypertrophy, and conduction disruption[49].

In the United States, fetal magnetic resonance imaging (MRI) and steady-state free precessional (SSFP) sequences may be useful for

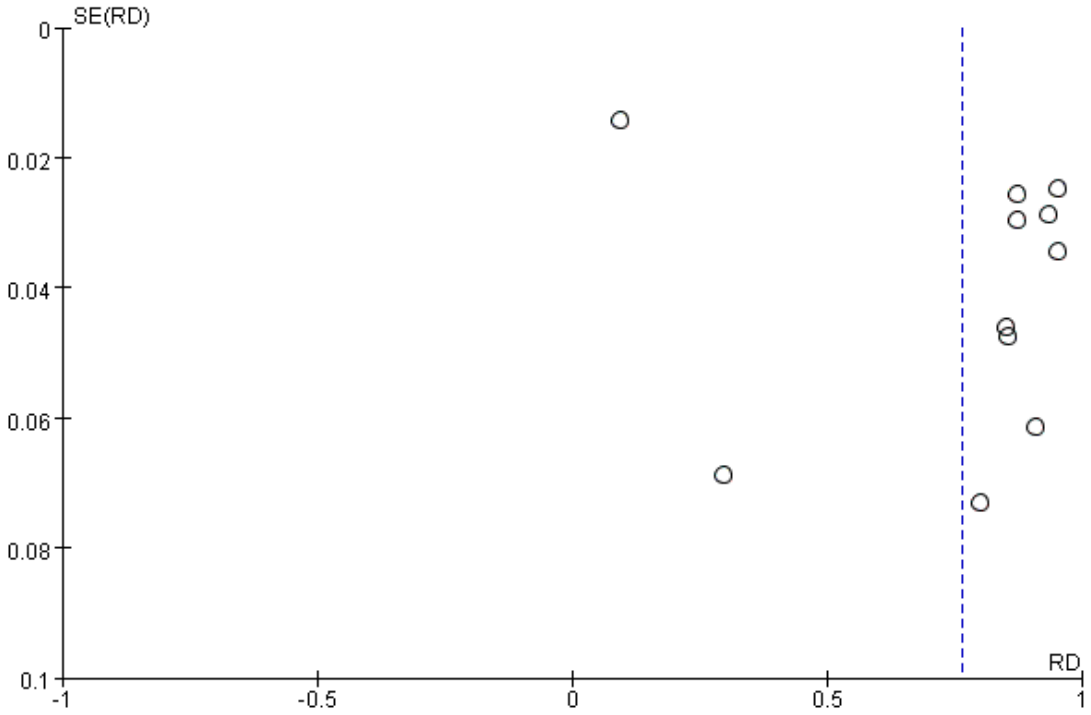


Figure 4: Funnel plot of prenatal ultrasound monitoring and diagnostic rates of fetal congenital heart disease

assessing normal fetal heart and identifying major morphological changes associated with coronary heart disease when examination is limited to fetal position, maternal obesity, and hydramnios. Both obstetric ultrasound and fetal MRI have good correlation and can be used as auxiliary imaging techniques[50]. These diagnostic methods are promising clinical tools that can complement the shortcomings of ultrasound in CAD screening programs. Thus, multidisciplinary consultation in prenatal diagnosis can be considered a beneficial method for CHD in the fetus[40].

At present, fetal CHD can not be effectively treated, and the treatment methods are still in the experimental stage and have not entered the clinical practice. Women should know whether there are genetic diseases in their spouses during the preparation of pregnancy. If there is a genetic disease factor, consider whether it will affect the fetus, need to find experts for consultation.

There was significant heterogeneity among the articles included in this study, so this result should be treated with caution. Meanwhile, some limitations should be mentioned. Firstly, the results were based on unadjusted estimates. Secondly, the number of studies included were insufficient, especially the subgroup analysis. Thirdly, only literature published in English and Chinese was included, so important studies published in other languages may be ignored, which may lead to potential language bias.

Conclusion

The result of our analysis showed that the diagnostic yield of fetal CHD screening using ultrasound alone is still not very high, which lower than the combined diagnostic yield of other studies. This result suggests it is necessary to combine other monitoring methods that do not harm fetal development. Meanwhile, the diagnosis of CHD can be recommended to use no less than two monitoring methods if economically feasible.

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