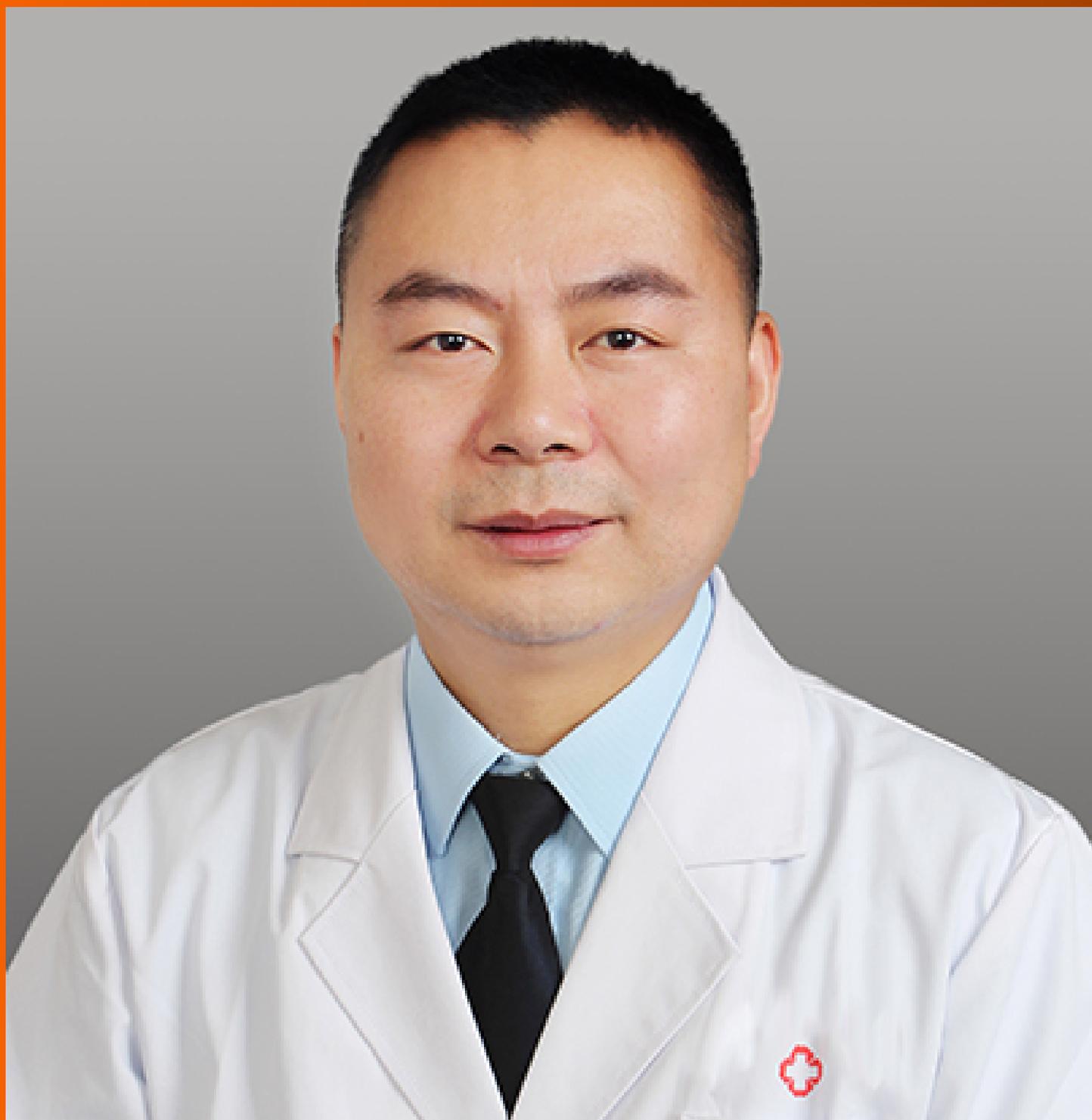


# World Journal of *Cardiology*

*World J Cardiol* 2023 October 26; 15(10): 469-552



**MINIREVIEWS**

- 469 Candida endocarditis: Update on management considerations  
*Jamil Y, Akinleye A, Mirzaei M, Lempel M, Farhat K, Pan S*
- 479 Related mechanisms and research progress in straight back syndrome  
*Kong MW, Pei ZY, Zhang X, Du QJ, Tang Q, Li J, He GX*
- 487 Value of cardiac magnetic resonance on the risk stratification of cardiomyopathies  
*Vidal-Perez R, Brandão M, Zaher W, Casado-Arroyo R, Bouzas-Mosquera A, Fontes-Carvalho R, Vazquez-Rodriguez JM*

**ORIGINAL ARTICLE****Retrospective Study**

- 500 Integrated analysis of comorbidity, pregnant outcomes, and amniotic fluid cytogenetics of fetuses with persistent left superior vena cava  
*Yang X, Su XH, Zeng Z, Fan Y, Wu Y, Guo LL, Xu XY*
- 508 Establishment of a prediction model for prehospital return of spontaneous circulation in out-of-hospital patients with cardiac arrest  
*Wang JJ, Zhou Q, Huang ZH, Han Y, Qin CZ, Chen ZQ, Xiao XY, Deng Z*

**SYSTEMATIC REVIEWS**

- 518 Cardiovascular complications following medical termination of pregnancy: An updated review  
*Singh T, Mishra AK, Vojjala N, John KJ, George AA, Jha A, Hadley M*

**META-ANALYSIS**

- 531 Do cardiopulmonary resuscitation real-time audiovisual feedback devices improve patient outcomes? A systematic review and meta-analysis  
*Sood N, Sangari A, Goyal A, Sun C, Horinek M, Hauger JA, Perry L*

**CASE REPORT**

- 542 Systemic right ventricle complications in levo-transposition of the great arteries: A case report and review of literature  
*Almajed MR, Almajed A, Khan N, Obri MS, Ananthasubramaniam K*

**ABOUT COVER**

Editorial board member of *World Journal of Cardiology*, Hai-Long Dai, MD, PhD, Chief Physician, Professor, Department of Cardiology, Yan'an Affiliated Hospital of Kunming Medical University, Kunming 650051, Yunnan Province, China. dhlkm@qq.com

**AIMS AND SCOPE**

The primary aim of *World Journal of Cardiology (WJC, World J Cardiol)* is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

*WJC* mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

**INDEXING/ABSTRACTING**

The *WJC* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJC* as 1.9; IF without journal self cites: 1.8; 5-year IF: 2.3; Journal Citation Indicator: 0.33. The *WJC*'s CiteScore for 2022 is 1.9 and Scopus CiteScore rank 2022: Cardiology and cardiovascular medicine is 226/354.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Yun-Xiaojuan Wu*.

**NAME OF JOURNAL**

*World Journal of Cardiology*

**ISSN**

ISSN 1949-8462 (online)

**LAUNCH DATE**

December 31, 2009

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone, Pal Pacher

**EDITORIAL BOARD MEMBERS**

<https://www.wjnet.com/1949-8462/editorialboard.htm>

**PUBLICATION DATE**

October 26, 2023

**COPYRIGHT**

© 2023 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Retrospective Study

## Integrated analysis of comorbidity, pregnant outcomes, and amniotic fluid cytogenetics of fetuses with persistent left superior vena cava

Xin Yang, Xin-Hui Su, Zhen Zeng, Yao Fan, Yuan Wu, Li-Li Guo, Xiao-Yan Xu

**Specialty type:** Cardiac and cardiovascular systems**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): 0  
Grade D (Fair): 0  
Grade E (Poor): 0**P-Reviewer:** Rotondo JC, Italy**Received:** July 9, 2023**Peer-review started:** July 9, 2023**First decision:** August 17, 2023**Revised:** August 29, 2023**Accepted:** September 28, 2023**Article in press:** September 28, 2023**Published online:** October 26, 2023

Xin Yang, Xin-Hui Su, Zhen Zeng, Yao Fan, Yuan Wu, Li-Li Guo, Xiao-Yan Xu, Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei Province, China

**Corresponding author:** Xiao-Yan Xu, PhD, Doctor, Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095 Jiefang Avenue, Wuhan 430030, Hubei Province, China. [xuxiaoyan@tjh.tjmu.edu.cn](mailto:xuxiaoyan@tjh.tjmu.edu.cn)

**Abstract****BACKGROUND**

Persistent left superior vena cava (PLSVC) is the most common venous system variant. The clinical characteristics and amniotic fluid cytogenetics of fetuses with PLSVC remain to be further explored.

**AIM**

To develop reliable prenatal diagnostic recommendations through integrated analysis of the clinical characteristics of fetuses with PLSVC.

**METHODS**

Cases of PLSVC diagnosed using prenatal ultrasonography between September 2019 and November 2022 were retrospectively studied. The clinical characteristics of the pregnant women, ultrasonic imaging information, gestational age at diagnosis, pregnancy outcomes, and amniocentesis results were summarized and analyzed using categorical statistics and the chi-square test or Fisher's exact test.

**RESULTS**

Of the 97 cases diagnosed by prenatal ultrasound, 49 (50.5%) had isolated PLSVC and 48 (49.5%) had other structural abnormalities. The differences in pregnancy outcomes and amniocentesis conditions between the two groups were statistically significant ( $P < 0.05$ ). No significant differences were identified between the two groups in terms of advanced maternal age and gestational age ( $P > 0.05$ ). According to the results of the classification statistics, the most common intracardiac abnormality was a ventricular septal defect and the most common extracardiac abnormality was a single umbilical artery. In the subgroup analysis, the concurrent combination of intra- and extracardiac structural abnormalities was a risk factor for adverse pregnancy outcomes (odds ratio  $> 1$ ,  $P < 0.05$ ). Additionally, all abnormal cytogenetic findings on amniocentesis were observed in the comorbidity group. One case was diagnosed with 21-trisomy and six cases was

diagnosed with chromosome segment duplication.

## CONCLUSION

Examination for other structural abnormalities is strongly recommended when PLSVC is diagnosed. Poorer pregnancy outcomes and increased amniocentesis were observed in PLSVC cases with other structural abnormalities. Amniotic fluid cytogenetics of fetuses is recommended for PLSVC with other structural abnormalities.

**Key Words:** Persistent left superior vena cava; Prenatal diagnosis; Amniotic fluid cytogenetics; Pregnancy outcome; Integrated analysis; Comorbidity

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Our study was performed for providing reliable prenatal diagnostic advice through integrated analysis of the clinical characteristics of fetuses with persistent left superior vena cava (PLSVC). We retrospectively studied 97 cases of PLSVC diagnosed using prenatal ultrasonography. Of the 97 cases diagnosed by prenatal ultrasound, 49 (50.5%) had isolated PLSVC and 48 (49.5%) had other structural abnormalities. We found that PLSVC is associated with a certain percentage of other combined structural abnormalities. Examination for other structural abnormalities is strongly recommended when PLSVC is diagnosed. Poorer pregnancy outcomes and increased amniocentesis were observed in PLSVC cases with other structural abnormalities.

**Citation:** Yang X, Su XH, Zeng Z, Fan Y, Wu Y, Guo LL, Xu XY. Integrated analysis of comorbidity, pregnant outcomes, and amniotic fluid cytogenetics of fetuses with persistent left superior vena cava. *World J Cardiol* 2023; 15(10): 500-507

**URL:** <https://www.wjgnet.com/1949-8462/full/v15/i10/500.htm>

**DOI:** <https://dx.doi.org/10.4330/wjc.v15.i10.500>

## INTRODUCTION

Persistent left superior vena cava (PLSVC) is the most common venous system variant. The incidence rate of PLSVC in congenital heart disease is approximately 5%-6%, whereas it is only 0.3%-0.5% in the normal population[1,2]. Previous research has shown that the probability of adverse pregnancy outcomes in isolated PLSVC is lower, and the risk of adverse pregnancy outcomes is significantly increased when combined with other malformations[3]. With improvements in genetic examination technology, some studies have reported that the proportion of fetal chromosomal abnormalities among PLSVC fetuses has significantly increased, which is different from the classic opinion of this disease[4,5].

Since fetal ultrasound examinations are unaffected by pulmonary gases, the prenatal period is the best time to perform vascular examinations[6,7]. Previous studies on PLSVC have focused on a few aspects, some only on the types of comorbidities and others only on pregnancy outcomes. There is a lack of comprehensive studies that provide reliable conclusions for patients and clinicians.

Our study retrospectively collected the clinical data, including the age of the pregnant women, ultrasonic imaging information, pregnancy outcomes, and amniocentesis results, from 97 cases of fetal PLSVC. We integrated clinical information, imaging features, and molecular-level results to provide reliable advice to patients and clinicians in multiple dimensions. Fetal PLSVC cannot be viewed as a purely vascular anatomical variant, and this disease is associated with a certain percentage of other combined structural abnormalities. Therefore, examination for other structural abnormalities should be performed when PLSVC is diagnosed.

## MATERIALS AND METHODS

### Study population

Ninety-seven patients with PLSVC diagnosed using prenatal ultrasonography at Tongji Hospital between September 2019 and November 2022 were retrospectively studied. Clinical characteristics included maternal age, gestational weeks, prenatal ultrasound images, specific types of combined intra- and extracardiac abnormalities, pregnancy outcomes, amniocentesis conditions, and results. The range of maternal age was 22 to 39 years, with a mean age of  $30.36 \pm 3.94$  years. The weeks of gestation at which PLSVC was diagnosed in our hospital was 18 to 34 wk, and the average weeks of gestation was  $24.72 \pm 3.99$  wk. There were 87 single pregnancies (89.7%) and 10 twin pregnancies (10.3%), including two double chorionic villi and double amniotic sac twin fetuses (20.0%) and eight cases of single chorionic villi and double amniotic sac twin fetuses (80%). This study was approved by the Ethics Committee of Tongji Hospital.

### **Inclusion and exclusion criteria**

The inclusion criteria were as follows: (1) Pregnancy at 12 to 34 wk of gestation; (2) complete clinical data; and (3) standard and clear cardiac ultrasound images.

The exclusion criteria were as follows: (1) Pregnancy with three or more fetuses; (2) frequent fetal movement leading to poor-quality echocardiography; and (3) incomplete clinical data.

### **Ultrasound instruments and examinations**

Using the color Doppler ultrasound instruments GE VOLUSON E8 and VOLUSON E10 (GE, Milwaukee, WI, United States) with a probe frequency of 2 to 5 MHz, after determining the fetal orientation and the relationship between the viscera and heart position, the fetal heart examination conditions were selected. The fetal heart segmental analysis method was used to determine the heart, blood vessel structure, and connection relationship. The focus was on four-chamber heart, three-vessel, and three-vessel trachea sections, combined with color Doppler observation of the blood flow direction and vascular morphology[8,9]. According to prenatal screening guidelines, a comprehensive ultrasound examination was performed on fetuses diagnosed with PLSVC to determine whether there are any concomitant intracardiac or extracardiac abnormalities[10,11].

### **Statistical analysis**

Statistical software (SPSS 26.0, IBM Corp., Armonk, NY, United States) was used for the data analysis. The measurement data conforming to a normal distribution are expressed as the mean  $\pm$  SD. The independent samples *t*-test was used for comparison between groups, and the paired sample *t*-test was used for comparison within groups. Count data are expressed as cases (%), and the  $\chi^2$  test or Fisher's exact probability method was used for comparison between groups. Statistical significance was set at  $P < 0.05$ .

## **RESULTS**

### **Comparison of clinical characteristics between the group with isolated PLSVC and the group with additional malformations**

Ninety-seven cases diagnosed using prenatal ultrasound were included in our study, including 49 cases (50.5%) with isolated PLSVC and 48 (49.5%) with other structural abnormalities. The mean age in the isolated PLSVC group was  $30.39 \pm 4.04$  years, and the mean age of those having PLSVC with other malformations was  $30.46 \pm 3.89$  years. There was no statistically significant difference in gestational age between the two groups. The clinical characteristics of the patients are shown in Table 1. We summarized the maternal age, number of fetuses, gestational weeks at first diagnosis, pregnancy outcomes, and amniocentesis conditions. After statistical analysis, we found significant differences in pregnancy outcomes and amniocentesis conditions between the two groups ( $P < 0.05$ ). No statistical differences were found between the two groups in terms of maternal age, number of fetuses, and gestational weeks at first diagnosis. These observations demonstrate that PLSVC with other structural abnormalities may be associated with more adverse pregnancy outcomes. Pregnant women were more likely to be recommended for amniocentesis diagnosis.

### **Types of intracardiac structural abnormalities in PLSVC fetuses**

After summarizing the clinical features, we found that a considerable proportion of PLSVC cases had other structural abnormalities. We summarized the specific types of abnormalities observed with PLSVC to provide a reference for improving the accuracy of ultrasound screening.

Among the included cases, 22 presented with cardiovascular system abnormalities, including 11 with both intracardiac and extracardiac abnormalities. The specific types and number of cases are listed in Table 2. Among these, interventricular septum defects were the most common, followed by aortic coarctation. These results indicate that when a PLSVC is found, scanning of the interventricular septum and aortic arch should be performed.

### **Types of extracardiac structural abnormalities in PLSVC fetuses**

In addition to the cardiovascular system, the types of combined abnormalities of other systems in PLSVC were relatively complex, with 37 cases of abnormalities in extracardiac structures, including 11 combined with both intracardiac and extracardiac abnormalities. The specific types and numbers of cases are listed in Table 3. Among them, a single umbilical artery was observed in the largest number of cases, followed by persistent right umbilical vein and urinary system abnormalities. These results indicate that when PLSVC is found, scanning of the umbilical vascular structure and urinary system should be performed.

### **Subgroup analysis of combined intra- and extracardiac abnormalities**

Based on the above observations, we found that the number of patients with PLSVC combined with intra- and extracardiac abnormalities was not consistent. Therefore, we further investigated how intra- and extracardiac structural abnormalities affect pregnancy outcomes through subgroup analysis. In our case series, 13 (13.4%) patients with PLSVC terminated their pregnancy, and 84 (86.6%) continued their pregnancy. Among the 13 terminated pregnancy cases, 12 (92.3%) had other structural abnormalities and seven (53.8%) had both intracardiac and extracardiac structural abnormalities. We found that patients with PLSVC with extracardiac abnormalities had the highest sustained pregnancy

**Table 1 Clinical characteristics in the isolated persistent left superior vena cava group and the persistent left superior vena cava with other malformations group, *n* (%)**

	Isolated PLSVC ( <i>n</i> = 49)	PLSVC with other malformations ( <i>n</i> = 48)	$\chi^2$	<i>P</i> value
Age				
< 35 years old	42 (85.7)	39 (81.3)	0.35	0.55
≥ 35 years old	7 (14.3)	9 (18.7)		
Number of fetuses				
Singleton	43 (87.8)	44 (91.7)	0.40	0.53
Twins	6 (12.2)	4 (8.3)		
Gestational age at initial diagnosis				
Before 28 wk	46 (93.9)	45 (93.8)	0.001	0.97
After 28 wk	3 (6.1)	3 (6.2)		
Pregnancy outcome				
Persistent pregnancy	48 (98.0)	36 (75.0)	11.01	0.001
Terminated pregnancy	1 (2.0)	12 (25.0)		
Amniocentesis status				
No apparent abnormalities	5 (10.2)	14 (29.2)	15.33	< 0.001
Abnormal results	0 (0.0)	7 (14.6)		
No amniocentesis performed	44 (89.8)	27 (56.2)		

PLSVC: Persistent left superior vena cava.

**Table 2 Specific types of intracardiac structural abnormalities in 97 cases of persistent left superior vena cava, *n* (%)**

Type of intracardiac structural abnormalities	<i>n</i> (%)
Ventricular septal defect	7 (31.8)
Aortic coarctation	5 (22.7)
Tetralogy of Fallot	3 (13.6)
Right-sided aortic arch	3 (13.6)
Left pulmonary artery originating from the right pulmonary artery	1 (4.5)
Single atrium with complete endocardial cushion defect	1 (4.5)
Midline heart with ventricular wall hypertrophy	1 (4.5)
Absence of right superior vena cava	1 (4.5)
Total	22 (100)

rates. Using statistical methods, we compared the other subgroups with this group to identify risk factors. In terms of sustained pregnancy rate, the presence of simultaneous abnormal cardiac and extracardiac structures was a risk factor affecting sustained pregnancy rate (odds ratio > 1, *P* < 0.05). Specific data are presented in [Table 4](#).

### **Amniotic fluid cytogenetics of fetuses with PLSVC**

Amniotic fluid cytogenetics enables further investigation of cases with imaging abnormalities and plays an irreplaceable role in clarifying the etiology. In our case series, 26 pregnant women chose amniocentesis, including five isolated PLSVC cases and 21 PLSVC cases with other abnormalities. No obvious abnormalities were observed in the amniocentesis results of the isolated PLSVC group. However, amniocentesis results in the group with combined intracardiac and extracardiac abnormalities displayed a certain proportion of anomalies, including one case with 21-trisomy and six cases with abnormal copy number variations (CNVs). Despite the limited research data on CNVs in PLSVC cases, specific types of analysis can still provide effective information for clinical practice. Six cases of abnormal CNVs were identified as repetitions of chromosomal regions, including two cases classified as potentially benign, three cases classified as variants of uncertain significance, and one as potentially pathogenic. The results are presented in [Table 5](#). These observations

**Table 3 Specific types of extracardiac structural abnormalities in 97 cases of persistent left superior vena cava, n (%)**

Type of extracardiac structural abnormalities	n (%)
Single umbilical artery	9 (24.3)
Persistent right umbilical vein	6 (16.2)
urinary system abnormalities	6 (16.2)
Neurological system abnormalities	3 (8.1)
Pleural effusion	2 (5.4)
Pulmonary cystadenoma	2 (5.4)
Absence of nasal bone	2 (5.4)
Gallbladder abnormalities	2 (5.4)
Situs inversus	1 (2.7)
Scoliosis	1 (2.7)
Multiple malformations	3 (8.1)
Total	37 (100)

**Table 4 Analysis of pregnancy outcomes in persistent left superior vena cava with intracardiac and extracardiac abnormalities**

Type	Persistent pregnancy, n (%)	OR	95%CI	P value
PLSVC only with extracardiac abnormalities	24 (92.3)			
PLSVC only with intracardiac abnormalities	8 (72.7)	4.5	0.63-31.95	0.12
PLSVC with intracardiac and extracardiac abnormalities	4 (36.3)	21.0	3.16-139.67	0.001

PLSVC: Persistent left superior vena cava.

**Table 5 Six cases with abnormal copy number variation sequencing results in persistent left superior vena cava**

	Chromosomal location	Variation type	Fragment size	Clinical significance
1	Chromosome 15	Repetition	0.4 Mb	Potentially benign
2	Chromosome 2	Repetition	0.5 Mb	Potentially benign
3	Chromosome 11	Repetition	3.9 Mb	VUS
4	Chromosome 19	Repetition	187.4 Kb	VUS
5	Chromosome 1	Repetition	2.3 Mb	VUS
6	Chromosome 1	Repetition	> 10 Mb	Potential pathogenicity

VUS: Variants of uncertain significance.

imply that CNVs may be associated with PLSVC combined with other abnormalities. When PLSVC cases with other abnormalities are detected, amniocentesis may contribute to the prenatal diagnosis and clinical decision-making.

## DISCUSSION

PLSVC is the most common venous system variant. However, the risk of adverse pregnancy outcomes is significantly increased when PLSVC is combined with other malformations. Our study was performed to provide reliable prenatal diagnostic recommendations through integrated analysis of the clinical characteristics of fetuses with PLSVC.

Fetal ultrasound examination is not affected by pulmonary gases; therefore, ultrasound can comprehensively observe the superior vena cava, and prenatal screening is the best time for PLSVC[7]. Several case reports have demonstrated difficulties in the diagnosis of PLSVC in adults, and certain patients require special examination methods[12,13]. PLSVC has typical sonographic features, with a cross-sectional view of the PLSVC visible on the left side of the pulmonary artery

in a three-vessel tracheal section[14]. In cases of PLSVC, approximately 90% enter the right atrium through the coronary sinus and approximately 10% directly enter the left atrium. In patients presenting with the left superior vena cava entering the right atrium through the coronary sinus, a dilated coronary sinus is observed on a four-chamber view[15,16]. Some cases in this study were not detected in the mid-trimester systematic screening, and most missed cases were twins. The limitations associated with scanning due to mutual fetal occlusion may be the main reason for missed diagnoses. This study integrates clinical factors, imaging information, and amniotic fluid cytogenetic information. As such, it is innovative compared to previous studies, showing that PLSVC is not just a simple anatomical variant, but is also associated with a higher rate of other structural abnormalities. In cases of PLSVC combined with other structural abnormalities, there are differences in pregnancy outcomes and amniocentesis.

This study classified and summarized the types and proportions of intra- and extracardiac abnormalities associated with PLSVC. These types of intracardiac and extracardiac abnormalities are consistent with previous research findings, both domestic and international[17-20]. A previous case report indicated that PLSVC can occur with anorectal malformation, an abnormality that we did not observe[21]. However, in this study, the proportion of patients with concurrent intracardiac and extracardiac abnormalities ( $n = 11$ ) was slightly higher than that in similar studies from China[22]. Our results indicate that when a PLSVC is detected, scanning of the interventricular septum, aortic arch, umbilical vascular structure, and urinary system should be performed. These findings may help clinicians reduce the incidence of missed diagnoses.

Pregnancy is a dynamic process, and the composition of fetal peripheral blood also varies with gestational age[23,24]. Amniotic fluid cytogenetics maintains a relatively stable state and greatly improves the accuracy of prenatal diagnoses, especially in cases with imaging abnormalities. Chromosome karyotype analysis is the gold standard for diagnosing chromosomal-related diseases; however, traditional chromosome karyotype analysis cannot detect chromosomal microdeletions or microduplications below 5-10 Mb.

Genomic copy number variant sequencing (CNV-seq) is a second-generation sequencing-based test that can be used to identify CNVs as an aid to prenatal diagnosis when a pregnant woman has an indication for interventional prenatal diagnosis and provides informed consent. Studies have found that the proportion of PLSVC fetuses with chromosomal-related abnormalities is 12.5%, and in isolated PLSVC cases, the proportion of chromosomal-related abnormalities can reach 7%[4]. Du *et al*[5] also demonstrated that in PLSVC cases, especially in cases of combined intracardiac and extracardiac abnormalities, the proportion of chromosomal abnormalities significantly increases. Most previous studies in China focused on chromosomal abnormalities, such as permanent left superior vena cava combined with trisomy 21 and trisomy 18, lacked a summary of the classification of abnormal results of PLSVC combined with CNVs[22,25].

In this study, a total of 26 pregnant women chose amniocentesis for diagnosis, including one case with 21-trisomy and six cases with abnormal CNVs results, all of which showed duplication of chromosomal regions, of which five cases were microduplications of less than 10 Mb.

This study had some limitations. Because the PLSVC incidence rate is only 0.3%-0.5% in the normal population[26], the number of included cases was small, which means that the credibility of the study needs to be further improved. In addition, no significant pathogenic abnormalities were found in the isolated PLSVC group, and in seven cases, abnormalities were found in the amniocentesis results of the group with other abnormalities. The risks of abnormal karyotypes and CNVs may increase in the presence of comorbidities. However, because amniocentesis is an invasive test with some risks[27], the comorbidity group chose to undergo amniocentesis more often, leading to confounding factors in the analysis. However, this study innovatively integrated and analyzed data at clinical, imaging, and genetic molecular levels, which can provide reliable prenatal diagnostic recommendations.

## CONCLUSION

In conclusion, examination for other structural abnormalities should be performed when PLSVC is diagnosed. Poor pregnancy outcomes and increased amniocentesis were observed in PLSVC cases with other structural abnormalities. Amniotic fluid cytogenetics of fetuses is recommended for PLSVC with other structural abnormalities.

## ARTICLE HIGHLIGHTS

### Research background

Persistent left superior vena cava (PLSVC) is the most common venous system variant. Previous research has shown that the probability of adverse pregnancy outcomes in isolated PLSVC is lower, and the risk of adverse pregnancy outcomes is significantly increased when combined with other malformations. In recent years, some studies have reported that the proportion of fetal chromosomal abnormalities among PLSVC fetuses has significantly increased, which is different from the classic opinion on this disease. There is a lack of comprehensive studies that provide reliable conclusions for patients and clinicians.

### Research motivation

In recent years, the advancement of prenatal diagnostic technology has overturned traditional concepts of some diseases.

### Research objectives

We integrated clinical information, imaging features, and molecular-level results to provide reliable advice to patients and clinicians in multiple dimensions.

### Research methods

We retrospectively collected cases of PLSVC diagnosed using prenatal ultrasonography between September 2019 and November 2022. The clinical characteristics of the pregnant women, ultrasonic imaging information, gestational age at diagnosis, pregnancy outcomes, and amniocentesis results were summarized and analyzed.

### Research results

The differences in pregnancy outcomes and amniocentesis conditions between the two groups were statistically significant ( $P < 0.05$ ). According to the results of the classification statistics, the most common intracardiac abnormality was a ventricular septal defect and the most common extracardiac abnormality was a single umbilical artery. Additionally, all abnormal cytogenetic findings on amniocentesis were observed in the comorbidity group.

### Research conclusions

PLSVC is associated with a certain percentage of other combined structural abnormalities. Examination for other structural abnormalities is strongly recommended when PLSVC is diagnosed. Poorer pregnancy outcomes and increased amniocentesis were observed in PLSVC cases with other structural abnormalities. Integrated analysis of multiple levels could provide more information.

### Research perspectives

In future studies, researchers should collect more amniotic fluid cytological data and follow-up prognosis of related fetuses.

---

## FOOTNOTES

**Author contributions:** Yang X and Su XH performed the conception and design; Zeng Z and Guo LL performed the development of methodology; Fan Y and Wu Y contributed to the analysis and interpretation of data; Yang X and Su XH contributed to the writing and review of the manuscript; Xu XY performed the study supervision; Yang X and Su XH contributed equally to this work; all authors had final approval of the submitted versions.

**Supported by** Key Research and Development Plan Projects in Hubei Province, No. 2022BCA041; and National Natural Science Foundation of China, No. 82101277.

**Institutional review board statement:** The study was reviewed and approved by the Institutional Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (No. TJ-IRB20230736).

**Informed consent statement:** All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

**Conflict-of-interest statement:** The authors declare no conflict of interest for this article.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** China

**ORCID number:** Xin Yang 0000-0001-9753-4241; Xin-Hui Su 0009-0002-0317-288X; Zhen Zeng 0000-0002-2816-2939; Yao Fan 0000-0002-5214-6146; Yuan Wu 0009-0002-4727-2903; Li-Li Guo 0009-0008-3454-1581; Xiao-Yan Xu 0000-0002-0996-6819.

**S-Editor:** Fan JR

**L-Editor:** Wang TQ

**P-Editor:** Yuan YY

---

## REFERENCES

- 1 Chao YJ, Chen MR, Hung WL, Yeh SJ, Lin SM. Impact of Persistent Left Superior Vena Cava Detection in a Normal Neonatal Population through Echocardiography. *Acta Cardiol Sin* 2019; **35**: 600-604 [PMID: 31879511 DOI: 10.6151/ACS.201911\_35(6).20190704A]

- 2 **Keleş A**, Yılmaz O, Dağdeviren G, Çelik ÖY, Yücel A, Şahin D. Persistent Left Superior Vena Cava: Why is Prenatal Diagnosis Important? *Fetal Pediatr Pathol* 2022; **41**: 592-602 [PMID: 34106033 DOI: 10.1080/15513815.2021.1933662]
- 3 **Galindo A**, Gutiérrez-Larraya F, Escribano D, Arbues J, Velasco JM. Clinical significance of persistent left superior vena cava diagnosed in fetal life. *Ultrasound Obstet Gynecol* 2007; **30**: 152-161 [PMID: 17616965 DOI: 10.1002/uog.4045]
- 4 **Gustapane S**, Leombroni M, Khalil A, Giacci F, Marrone L, Bascietto F, Rizzo G, Acharya G, Liberati M, D'Antonio F. Systematic review and meta-analysis of persistent left superior vena cava on prenatal ultrasound: associated anomalies, diagnostic accuracy and postnatal outcome. *Ultrasound Obstet Gynecol* 2016; **48**: 701-708 [PMID: 26970258 DOI: 10.1002/uog.15914]
- 5 **Du L**, Xie HN, Zhu YX, Li LJ, Peng R, Zheng J. Fetal persistent left superior vena cava in cases with and without chromosomal anomalies. *Prenat Diagn* 2014; **34**: 797-802 [PMID: 24711103 DOI: 10.1002/pd.4380]
- 6 **Huang W**, Xia LF, Zheng DC, Li X, Zheng YJ. Prenatal echocardiographic diagnosis of fetal permanent left superior vena cava. *Zhonghua linchuangyixue Yingxiangxue Zazhi* 2011; **3**: 193-194
- 7 **Azizova A**, Onder O, Arslan S, Ardali S, Hazirolan T. Persistent left superior vena cava: clinical importance and differential diagnoses. *Insights Imaging* 2020; **11**: 110 [PMID: 33057803 DOI: 10.1186/s13244-020-00906-2]
- 8 **Ergani SY**, Yılmaz O. Step-By-Step Segmental Analysis of the Fetal Heart with an Uncommon Situs Anomaly. *Z Geburtshilfe Neonatol* 2022; **226**: 136-138 [PMID: 35172369 DOI: 10.1055/a-1730-6127]
- 9 **Carvalho JS**, Axt-Fliedner R, Chaoui R, Copel JA, Cuneo BF, Goff D, Gordin Kopylov L, Hecher K, Lee W, Moon-Grady AJ, Mousa HA, Munoz H, Paladini D, Prefumo F, Quarello E, Rychik J, Tutschek B, Wiechec M, Yagel S. ISUOG Practice Guidelines (updated): fetal cardiac screening. *Ultrasound Obstet Gynecol* 2023; **61**: 788-803 [PMID: 37267096 DOI: 10.1002/uog.26224]
- 10 **Salomon LJ**, Alfrevic Z, Berghella V, Bilardo CM, Chalouhi GE, Da Silva Costa F, Hernandez-Andrade E, Malinger G, Munoz H, Paladini D, Prefumo F, Sotiriadis A, Toi A, Lee W. ISUOG Practice Guidelines (updated): performance of the routine mid-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol* 2022; **59**: 840-856 [PMID: 35592929 DOI: 10.1002/uog.24888]
- 11 **Salomon LJ**, Alfrevic Z, Da Silva Costa F, Deter RL, Figueras F, Ghi T, Glanc P, Khalil A, Lee W, Napolitano R, Papageorgiou A, Sotiriadis A, Stirnemann J, Toi A, Yeo G. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth. *Ultrasound Obstet Gynecol* 2019; **53**: 715-723 [PMID: 31169958 DOI: 10.1002/uog.20272]
- 12 **Tyrak KW**, Holda J, Holda MK, Koziej M, Piatek K, Klimek-Piotrowska W. Persistent left superior vena cava. *Cardiovasc J Afr* 2017; **28**: e1-e4 [PMID: 28759082 DOI: 10.5830/CVJA-2016-084]
- 13 **Laasri K**, El Graini S, Zahi H, Halfi IM, Bachri H, Massri EA, Zebbar S, Soufiani A, Fellat N, Bendagha N, Fellat R, Nassar I, Billah NM. Persistent left superior vena cava: Case report. *Radiol Case Rep* 2023; **18**: 79-85 [PMID: 36324842 DOI: 10.1016/j.radcr.2022.09.076]
- 14 **Lopes KRM**, Bartsota M, Doughty V, Carvalho JS. Single left superior vena cava: antenatal diagnosis, associated anomalies and outcomes. *Ultrasound Obstet Gynecol* 2022; **60**: 640-645 [PMID: 35656845 DOI: 10.1002/uog.24966]
- 15 **Hornberger LK**. Re: Cardiac axis shift within the cardiac cycle of normal fetuses and fetuses with congenital heart defect. Y. Zhao, S. Abuhamad, E. Sinkovskaya, M. Mlynarczyk, L. Romary and A. Abuhamad. *Ultrasound Obstet Gynecol* 2015; **46**: 558-563. *Ultrasound Obstet Gynecol* 2015; **46**: 518-519 [PMID: 26525500 DOI: 10.1002/uog.15779]
- 16 **Chaoui R**, Heling KS, Kalache KD. Caliber of the coronary sinus in fetuses with cardiac defects with and without left persistent superior vena cava and in growth-restricted fetuses with heart-sparing effect. *Prenat Diagn* 2003; **23**: 552-557 [PMID: 12868081 DOI: 10.1002/pd.626]
- 17 **Li XJ**, Zhang R, Bian Y, Feng J, Zeng J. Diagnosis and Prognosis Analysis of 72 Fetal Persistent Left Superior vena cava. *Baiqiuen Yixuezazhi* 2016; **6**: 744-745+810
- 18 **Li J**, Jing CL, Chen CM. Prenatal ultrasound diagnosis and clinical analysis of persistent left superior vena cava in 71 cases of fetuses. *Dalian Yikedaxue Xuebao* 2016; **3**: 279-284
- 19 **Durand I**, Hazelzet T, Gillibert A, Parrod C, David N, El Youssef F, Brehin AC, Barre E. Outcomes following prenatal diagnosis of isolated persistent left superior vena cava. *Arch Cardiovasc Dis* 2022; **115**: 335-347 [PMID: 35660361 DOI: 10.1016/j.acvd.2022.03.005]
- 20 **Esin D**, Aslan Çetin B, Şenol G, Selçuki NFT, Gedik Özköse Z, Acar Z, Yüksel MA. Clinical significance of prenatally diagnosed persistent left superior vena cava. *J Gynecol Obstet Hum Reprod* 2022; **51**: 102332 [PMID: 35123124 DOI: 10.1016/j.jogoh.2022.102332]
- 21 **Aihole JS**. Persistent Left Superior Vena Cava: A Rare Association. *Glob Pediatr Health* 2021; **8**: 2333794X211015527 [PMID: 34104691 DOI: 10.1177/2333794X211015527]
- 22 **Wu XL**, Zhou WN. Value of ultrasound detection of persistent left superior vena cava in screening fetal cardiac and extracardiac anomaly. *Yixueyanjiu Yu Jiaoyu* 2016; **2**: 31-35
- 23 **Rotondo JC**, Oton-Gonzalez L, Selvatici R, Rizzo P, Pavasini R, Campo GC, Lanzillotti C, Mazziotta C, De Mattei M, Tognon M, Martini F. SERPINA1 Gene Promoter Is Differentially Methylated in Peripheral Blood Mononuclear Cells of Pregnant Women. *Front Cell Dev Biol* 2020; **8**: 550543 [PMID: 33015055 DOI: 10.3389/fcell.2020.550543]
- 24 **Kirkegaard I**, Henriksen TB, Ulbjerg N. Early fetal growth, PAPP-A and free  $\beta$ -hCG in relation to risk of delivering a small-for-gestational age infant. *Ultrasound Obstet Gynecol* 2011; **37**: 341-347 [PMID: 20737455 DOI: 10.1002/uog.8808]
- 25 **Lian M**, Zhong XH, Zhou SL, Ma Li. Analysis of the causes of misdiagnosis by prenatal ultrasound and merge expectations in fetuses with persistent left superior vena cava. *Zhonguo Chaosheng Yixue Zazhi* 2022; **10**: 1138-1141
- 26 **Poenaru MO**, Hamoud BH, Sima RM, Valcea ID, Chicea R, Ples L. Persistent Left Superior Vena Cava Significance in Prenatal Diagnosis-Case Series. *J Clin Med* 2022; **11** [PMID: 35887792 DOI: 10.3390/jcm11144020]
- 27 **Jummaat F**, Ahmad S, Mohamed Ismail NA. 5-Year review on amniocentesis and its maternal fetal complications. *Horm Mol Biol Clin Investig* 2019; **40** [PMID: 31539354 DOI: 10.1515/hmbci-2019-0006]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

