

Brucella endocarditis: epidemiology and clinical features of 23 cases from 2007 to 2018

Lijuan Zhang

Xinjiang Medical University Affiliated First Hospital

Tao Zhang

Xinjiang Medical University Affiliated First Hospital

Dan Han

Xinjiang Medical University Affiliated First Hospital

Ranran Gao

Xinjiang Medical University Affiliated First Hospital

Jianzhong Yang

Xinjiang Medical University Affiliated First Hospital

Xiaobo Lu (✉ luxbo520@163.com)

Xinjiang Medical University Affiliated Tumor Hospital <https://orcid.org/0000-0001-5270-6249>

Research article

Keywords: brucella endocarditis, Brucella sp., aortic valve

Posted Date: September 20th, 2019

DOI: <https://doi.org/10.21203/rs.2.14687/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background : The data of *Brucella* endocarditis is relatively little. This study was to summarize the characteristics of epidemiology and clinical features of brucella endocarditis. **Methods:** 23 patients with brucella endocarditis collected in our hospital from July 2007 to August 2018 were analyzed. **Results:** Among the patients, 91.3% was male, the age was 42.6 ± 12.4 years old. 69.6% patients had contacted with cattle and sheep. The most common symptom in these patients was chest tightness (60.8%), shortness of breath (60.8%), fever (43.5%) and anemia (43.5%). In the patients with anemia, 50% also had a lower platelet (including one patient had lower leucocyte level). Blood culture before taking antibiotics is easy to find *Brucella* sp. The aortic valve (91.3%) is most commonly involved, followed by mitral valve (17.4%) and tricuspid valve (8.7%). 87.0% of patients followed with complications, including cardiac failure (73.9%), pulmonary infection (43.5%), hydropericardium (34.8%), renal insufficiency (21.7%), multiple organ disfunction (4.3%), bacterial aneurysm rupture (4.3%), paravertebral abscess (4.3%), cerebral infarction (4.3%), pericardial stenosis and adhesion (4.3%). 47.8% of patients exhibited hyperglobulinemia and 80% of patients with renal insufficiency had hyperglobulinemia. 22 patients had suffered antibiotics and surgery treatment and one patient gave up treatment. 2 patients (8.7%) died because of ventricular fibrillation and refractory heart failure. **Conclusion:** *Brucella* endocarditis was a complex disease and could lead to multiple organ disfunction. Cardiac failure was the main reason for death and the mortality was 8.7%.

Background

Infective endocarditis (IE) is a high fatality rate of disease, the incidence of each year for 3-9/100000 cases [1-4]. Gram-positive bacteria were the main etiology of IE [5], while *Brucella* sp. (gram-negative bacteria) is rare. Previous studies about brucella endocarditis were mainly cases report [6-8]. These studies due to the limitation of the number of cases, unable to obtain some important disease information, such as common complications, mortality and the leading cause of death. Therefore, we collected 23 cases of brucella endocarditis to be analyzed in our hospital from July 2007 to August 2018.

Methods

Diagnosis of brucella endocarditis was made with history, clinical findings, echocardiographic images confirming the diagnosis of infective endocarditis, positive agglutination test [9]. Infective endocarditis was defined according to the modified Duke criteria [10].

Results

3.1 Clinical manifestation and complications

Among 23 patients, 21 (91.3%) was male, the age was 42.6 ± 12.4 years old, the hospital stay was 20 (9,27) days. 16 patients had contacted with cattle and sheep, while the other did not find the direct

causes. Blood culture and agglutination test had been performed in all the patients, 6 cases (26.1%) found *Brucella sp.* using blood culture and 18 cases (78.2%) showed a higher serum brucella IgG degrees (> 1:160), only one showed positive of both. The waveform temperature change of 3 patients were showed in the figure 1 before using antibiotics. Blood culture before taking antibiotics found *Brucella sp.* in the 3 patients. The most common symptom in these patients was chest tightness (14 cases; 60.8%), shortness of breath (14 cases; 60.8%), fever (10 cases; 43.5%) and anemia (10 cases; 43.5%), followed by heart murmur (6 cases; 26.1%), the whole body dropsy (4 cases; 17.4%), double leg edemas (2 cases; 8.7%), splenomegaly (1 cases; 4.3%). In the patients with anemia, 5 also had a lower platelet (including 1 had lower leucocyte level). Total 20 (87.0%) patients followed with complications including cardiac failure, pulmonary infection, hydropericardium, renal insufficiency, multiple organ disfunction, bacterial aneurysm rupture, paravertebral abscess, cerebral infarction, pericardial stenosis and adhesion. The results were showed in the table 1.

3.2 Laboratory tests and Cardiac ultrasound

Among these patients, 10 cases exhibited increased erythrocyte sedimentation rate (only 13 patients had this data). The globulin level was (35.1±9.3) g/L and total 11 cases (47.8%) exhibited hyperglobulinemia. 4 of 5 patients with renal insufficiency had hyperglobulinemia. The LDH level was (299.3±156.7) IU/L and total 13 patients (56.5%) had a higher LDH. The other Laboratory tests were showed in the table 1. Cardiac ultrasound showed that all the patients had vegetations. The aortic valve is most commonly involved, followed by mitral valve and tricuspid valve. 21 patients (91.3%) involved aortic valve, including 11 aortic valve, 5 congenital bicuspid aortic valve, 3 aortic valve + mitral valve, 2 aortic valve + tricuspid valve. The data was showed in the table 2 and figure 2. Aortic valve perforation happened in 5 patients.

3.3 Treatment

22 patients had suffered antibiotics and surgery treatment and one patient gave up treatment. 11 patents had suffered antibiotics plus surgery treatment. Treatment data showed in the table 3. 20 patients (87.0%), had improved symptoms after treatment, were released and continued to take antibiotics for at least three months. Two of patients (both involved aortic valve) treated with Quinolone + penicillin died after 3 and 16 days' treatment, respectively. The direct cause of death were ventricular fibrillation and refractory heart failure, respectively. Cardiac failure (IV level) was the only complication in both of the death.

Discussion

The lack of abundant information about brucella endocarditis lead us to collecte the materials of the 23 patients with brucella endocarditis in our hospital from July 2007 to August 2018. These data showed that 91.3% of patients was male, the age was 42.6±12.4 years old. The most common symptom in these patients was chest tightness, shortness of breath, fever and anemia. 43.5% of patients had anemia and 47.8% exhibited hyperglobulinemia. Blood culture before using antibiotics was easier to find *Brucella sp.*

The aortic valve is most commonly involved, followed by mitral valve and tricuspid valve. The common complications were cardiac failure, pulmonary infection, hydropericardium, renal insufficiency. 2 patients died because of ventricular fibrillation and refractory heart failure. Cardiac failure (IV level) was the main reason for death.

Brucella endocarditis seemed to be more inclined to male. Previous studies and our data all showed that above 70% of patients was male [11-12]. A review reporting brucella endocarditis (1966 to 2011) also showed 75.3% of patients were male after analyzing all English and French articles in PubMed, Google and Scopus [13]. The reason for it is still unclear. Interestingly, the research about IE also showed a higher rate of male (69.4%) [14]. Research showed that male gender contributes to the progression of aortic regurgitation [15]. The high rate of endocarditis may due to high rate of damage and degeneration of valve in male.

Isolation of *Brucella sp.* in the blood is important for the diagnosis of brucella endocarditis. However, the positive rate was low in brucella endocarditis. The reason for the low rate may be the using of antibiotics. Our results showed that only 26.1% of patients found *Brucella sp.* in the blood. While blood culture performed before using antibiotics all found *Brucella sp.* The results indicated that it was important to perform blood culture before using antibiotics to find *Brucella sp.*

Koruk ST, et al showed involvement rates of the aortic, mitral and tricuspid valves were 49.1%, 43.4% and 5.7% in *Brucella* endocarditis, respectively [16]. Our results showed that *Brucella* mainly infected aortic valve (91.3%), followed by mitral (17.4%) and tricuspid valve (8.7%). The retrospective research about infection endocarditis cases also showed a higher rate of left native valve [14]. Left native valve seemed to be easier to be involved. A possible reason may be a higher pressure in left ventricle, and thus more susceptible to be damaged than other heart valves. Our results also showed that 21.7% of patients with *Brucella* endocarditis were congenital bicuspid aortic valve. Congenital valvular disorder made *Brucella sp.* easier to settle down in the damage valves.

Hyperglobulinemia was found in 47.8% of patients. Interestingly, 4 of 5 patients with renal insufficiency also exhibited hyperglobulinemia. As we known that immunoglobulin deposition is a important reason leading to chronic kidney disease [17]. Thus, the complication of renal insufficiency may due to hyperglobulinemia. The infections generally induce the formation of immune complexes, and glomerulonephritis occurs after the deposition of immune complexes in the kidney. A case report about *Brucella* glomerulonephritis showed that glomerulonephritis could be managed by only using antibiotic therapy, supporting our hypothesis [18]. The results also indicated that antibiotics treatment was also important to control the complication.

Antibiotics with or without surgery treatment was the main treatment for the *Brucella* endocarditis. Our results showed that Rifampin +tetracycline was an effective treatment for *Brucella* endocarditis. Keshtkar-Jahromi M, et al showed that the mortality of *Brucella* endocarditis was 32.7% in the only medical treatment patients, 6.7% in the combined medical and surgical treatment and total mortality was 10.7% from 1966 to 2011 [13]. While, our recent data showed the mortality in the only medical treatment

patients was 18.2%, no death in combined surgical and medical therapy and the total mortality was 8.7%. Research about showed 50% of death occurred during or early after surgery mostly related to cardiac arrhythmias in Brucella endocarditis from 1991 to 2009 [11]. A more experiential heart valve replacement surgery may lead to low death in patients with combined medical and surgical treatment in our results. Two patients treated with quinolone + penicillin died because of cardiac failure in a short time after admission. Quinolone + penicillin was used because of delayed diagnosis of Brucella endocarditis. These results indicated effective antibiotics application was important to control the progression of Brucella endocarditis. Cardiac failure (IV level) was main reason for death. [Koruk ST](#), et al showed that mortality increased 25-fold after complication with congestive heart failure, supporting our results [16].

Conclusions

We investigated the epidemiology and clinical features of 23 patients with Brucella endocarditis from July 2007 to August 2018. This study is useful for the identification of clinical trends and the predictable distribution of prognostic factors.

Abbreviations

IE, Infective Endocarditis

LDH, Lactate Dehydrogenase

WBC, Leucocyte count

Hb, Haemoglobin

PLT, Platelet count

ALT, Alanine Aminotransferase

AST, Aspartate Aminotransferase

PSA, Pericardial Stenosis and Adhesion

Declarations

Ethics approval and consent to participate

All the participants were enrolled after written informed consent was obtained from the patients or their family members (the death patients) and this study was approval from the Ethics Committee of Xinjiang Medical University according to the Helsinki Declaration (20150402-05).

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing Interest

None to declare for all the authors.

Funding

XL has received grants (2010DS890294) from the Open Topics of Xinjiang Key Laboratory of critical Disease though “ T cell subgroup analysis in Brucella patients” (SKLIB-XJMDR-2014-2).

Authorship contributions

LZ and XL designed the research, collected and analyzed data, and wrote the paper. TZ and JY contributed to data acquisition. DH and RG contributed to analysis of data. All authors had read and approved the Manuscript

Acknowledgements

None.

References

1. Correa de Sa DD, Tleyjeh IM, Anavekar NS, et al. Epidemiological trends of infective endocarditis: a population-based study in Olmsted County, Minnesota. *Mayo Clin Proc.* 2010;85:422-426.
2. Duval X, Delahaye F, Alla F, et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: three successive population-based surveys. *J Am Coll Cardiol.* 2012;59:1968-1976.
3. Federspiel JJ, Stearns SC, Peppercorn AF, et al. Increasing US rates of endocarditis with *Staphylococcus aureus*: 1999-2008. *Arch Intern Med.* 2012;172:363-365.
4. Sy RW, Kritharides L. Health care exposure and age in infective endocarditis: results of a contemporary population-based profile of 1536 patients in Australia. *Eur Heart J.* 2010;31:1890-1897.
5. Valliattu J, Shuhaiber H, Kiwan Y, Araj G, Chugh T. Brucella endocarditis. Report of one case and review of the literature. *J Cardiovasc Surg (Torino).* 1989;30:782-785.
6. Akturk S, Kaya H, Akturk E. An acute myocardial infarction due to Brucella prosthetic valve endocarditis starting shortly after the onset of non-specific symptoms. *BMJ Case Rep* 2015. doi:10.1136/bcr-2014-209001

7. Jia B, Zhang F, Peng P, et al. Brucella endocarditis: clinical features and treatment outcomes of 10 cases from Xinjiang, China. *J Infect.* 2017;74(5):512-514.
8. Oguzhan N, Akgun H, Unal A, et al. Brucella glomerulonephritis and prosthetic valve endocarditis: a case report. *Int Urol Nephrol.* 2012;44(2):643-646.
9. Gurse D, Candemir M, Baltarli A, Demir M. A case of Brucella endocarditis with involvement of mitral and aortic valves: case report. *Turkiye Klinikleri Cardiovasc Sci.* 2009;21:80-83.
10. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J.* 2009; 30:2369-2413.
11. Keshtkar-Jahromi M, Boroumand M, Razavi SM, et al. Brucella endocarditis, a report of 14 cases (1991-2009). *J Infect.* 2010;61(1):89-92.
12. Sasmazel A, Baysal A, Fedakar A, et al. Treatment of Brucella endocarditis: 15 years of clinical and surgical experience. *Ann Thorac Surg.* 2010;89(5):1432-1436.
13. Keshtkar-Jahromi M, Razavi SM, Gholamin S, et al. Medical Versus Medical and Surgical Treatment for Brucella Endocarditis. *Ann Thorac Surg.* 2012;94(6):2141-2146.
14. Zhu Wu, Zhang Q, Zhang J. The changing epidemiology and clinical features of infective endocarditis: A retrospective study of 196 episodes in a teaching hospital in China. *BMC Cardiovasc Disord.* 2017;17(1)113. doi: 10.1186/s12872-017-0548-8.
15. Pereira TM, Nogueira BV, Lima LC, et al. Cardiac and vascular changes in elderly atherosclerotic mice: the influence of gender. *Lipids Health Dis* 2010;9:87.
16. Koruk ST, Erdem H, Koruk I, et al. Management of Brucella endocarditis: results of the Gulhane study. *Int J Antimicrob Agents.* 2012;40(2):145-150.
17. Ying WZ, Li X, Rangarajan S, et al. [Immunoglobulin light chains generate proinflammatory and profibrotic kidney injury.](#) *J Clin Invest.* 2019;130:2792-2806.
18. [Oguzhan N, Akgun H, Unal A, et al. Brucella glomerulonephritis and prosthetic valve endocarditis: a case report.](#) *Int Urol Nephrol.* 2012;44(2):643-646.

Tables

Table 1 the Baseline characteristics and Complication of patients.

Baseline characteristics (n=23)		Complication (n=23)	
Age (years)	42.6±12.4	pulmonary infection (n)	10 [43.5%]
Male (n)	21 (91.3%)	Hydropericardium (n)	8 [34.8%]
WBC (x10 ⁹ /L)	8.5±3.7	Hydrothorax (n)	10
HB (g/L)	109.4±21.6	Cardiac failure (n)	17 [73.9%]
PLT (x10 ¹¹ /L)	1.8±0.9	II	5
Urea (mmol/L)	11.2±8.5	III	4
Creatinine (umol/L)	116.5±83.5	IV	8
AST (IU/L)	30.9 (20.8,68.2)	Renal insufficiency (n)	5 [21.7%]
ALT (IU/L)	24.5 (11.1,69.8)	Multiple Organ Dysfunction (n)	1 [4.3%]
Glb (g/L)	35.1±9.3	Bacterial aneurysm rupture (n)	1
LDH (IU/L)	299.3±156.7	Paravertebral abscess (n)	1
ESR (mm/h) [§]	38 (16,55)	PSA (n)	1
Hospital stays (d)	20 (9,27)	Cerebral infarction (n)	1
Blood culture (+) [*]	6 (26.1%)	Splenomegaly (n)	1
Brucella IgG (+) [#]	18 (78.2%)	Hyperglobulinemia (n)	11 [47.8%]

WBC, leucocyte count; Hb, Haemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PSA, Pericardial stenosis and adhesion; * blood culture found *Brucella sp.*; #serum brucella IgG degrees > 1:160; §only 13 patients had this data.

Table 2 the involved valve in the patients.

The site of neoplasm	n	
aortic valve	11	Fig 2A/B
congenital bicuspid aortic valve	5	Fig 2C
aortic valve + mitral valve	3	Fig 2C
aortic valve + tricuspid valve	2	Fig 2D
mitral valve + Artificial aortic valve	1	Fig 2E
No coronary sinus ruptures in the aorta	1	Fig 2F

Table 3 the treatment of patients.

Treatment	n
Therapy	22
Combined surgical and medical therapy	11
Medical therapy only	11
Antibiotic regimens	
Rifampin + tetracycline	3
Rifampin + tetracycline + aminoglycoside	1
Rifampin + tetracycline + quinolone	5
Rifampin + tetracycline + penicillin	8
Rifampin + tetracycline + ceftriaxone	1
Rifampin + tetracycline + vancomycin	2
Quinolone + penicillin	2
Surgical treatment	
Aortic valve replacement	8
Aortic and mitral valve replacement	1
Aortic and tricuspid valve replacement	1
other	1

Figures

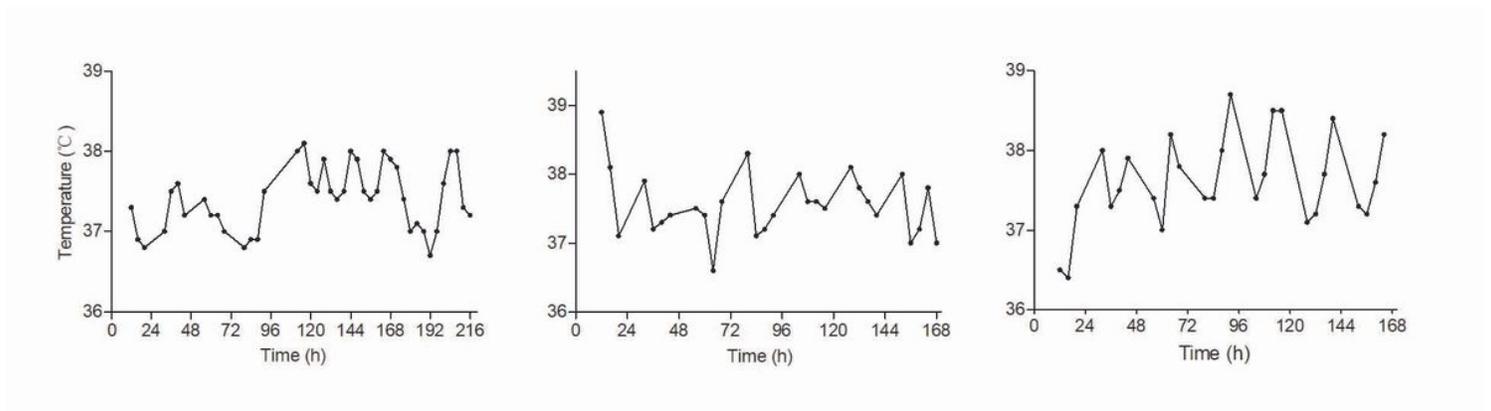


Figure 1

The waveform temperature change of 3 patients whose blood culture was performed before using antibiotic.

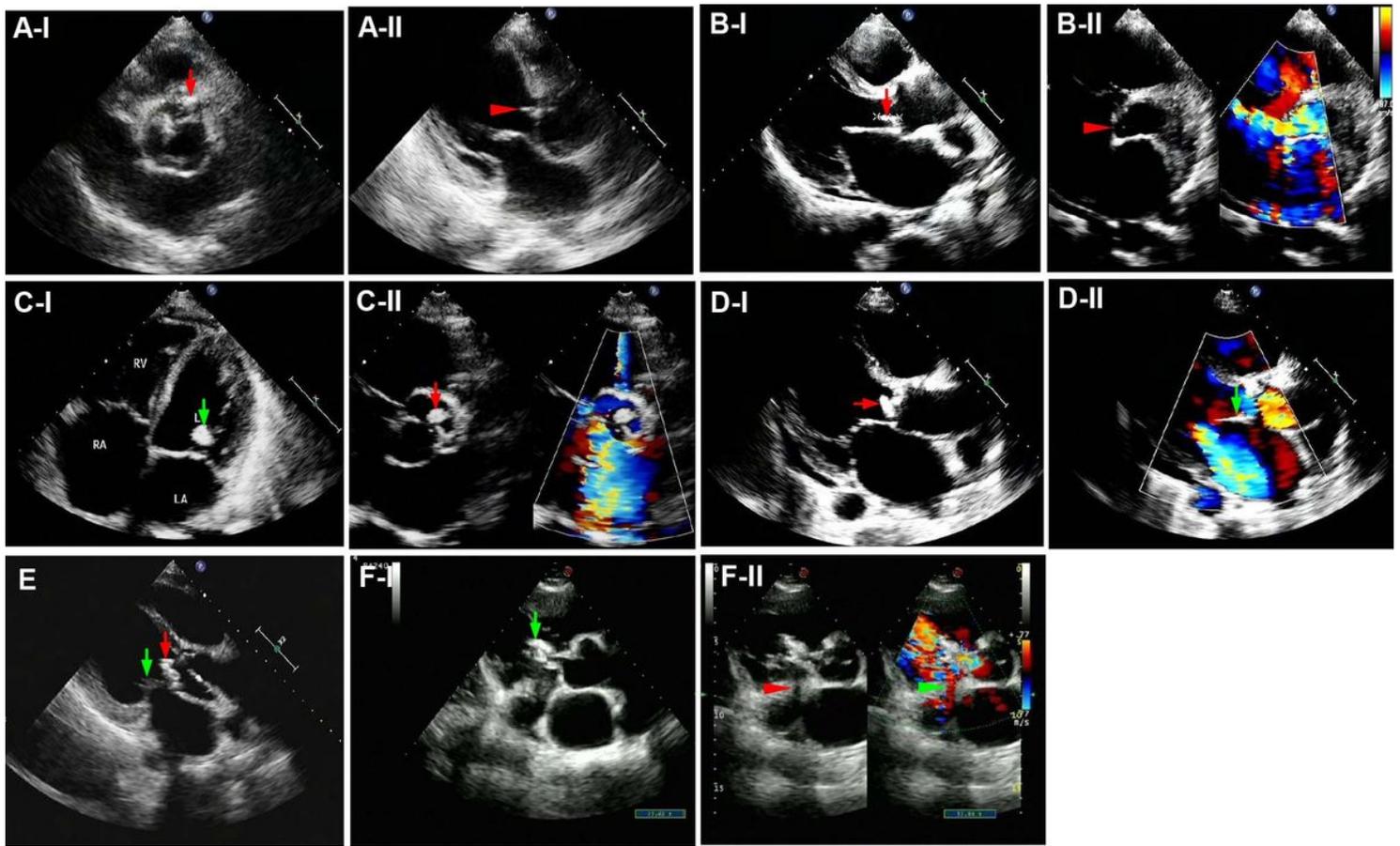


Figure 2

Ultrasonic results of different Brucella endocarditis. The red arrow showed neoplasm in aortic valve (including congenital bicuspid aortic valve and Artificial aortic valve); the green arrow showed neoplasm in mitral valve or tricuspid valve or No coronary sinus. The arrowhead showed perforation of valve (A-II), the right coronary sinus perforating into the right atrium (B-II), No coronary sinus perforating into the right atrium (F-II).