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Comparison of coronary artery bypass grafting and percutaneous coronary intervention for syphilitic coronary artery ostial lesions

A 4-year retrospective study

Junyu Han, MS[a], Wuyang Zheng, MS[a], Weihua Li, MD[a], Qiang Xie, MD[a], Zhengrong Huang, MD[a], Shuyu Yang, MD[b,*]

Abstract

This study investigated the efficacy of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in treatment of patients with syphilitic coronary artery ostial lesions (SCAOL).

Sixty SCAOL patients were divided into two groups according to the different treatments: the CABG group (n = 32) and the PCI group (n = 28). We determined serum levels of β-type natriuretic peptide (BNP) and cardiac function, and evaluated treatment efficacy such as the rates of restenosis, patency, and major adverse cardiovascular events (MACEs) during hospital stay and the effects of antisyphilis and different types of CABG on restenosis during the 6-month follow-up period.

There were no statistical differences in demographic or baseline clinical characteristics, BNP levels, left ventricular end-diastolic diameter (LVDd), or ejection fraction (EF) between the CABG and PCI groups at 1 week after surgery, However, after 6-month of follow-up, the CABG group had a significantly lower rate of coronary artery restenosis, lower incidence of MACEs, and better cardiac function than the PCI group. Within the CABG group, the left internal mammary artery (LIMA) subgroup had a lower restenosis rate than the saphenous vein graft (SVG) subgroup. In addition, patients who had received anti-syphilis therapy had a significantly lower restenosis rate than those without anti-syphilis therapy at 6-month post-surgery.

Compared with patients who received PCI, patients who received CABG had better prognoses. LIMA has a better therapeutic efficacy than SVG in terms of the restenosis rate, and anti-syphilis treatment significantly reduces the restenosis rate, compared with non-anti-syphilis treatment.

Abbreviations: BNP = β-type natriuretic peptide, CABG = coronary artery bypass grafting, CAG = coronary angiography, CCTA = coronary computed tomography angiography, EF = ejection fraction, IVUS = intravascular ultrasonography, LIMA = left internal mammary artery, LVDd = left ventricular end-diastolic diameter, MACEs = major adverse cardiovascular events, PCI = percutaneous coronary intervention, SCAOL = syphilitic coronary artery ostial lesions, SVG = saphenous vein graft.

Keywords: coronary artery bypass grafting, percutaneous coronary intervention, syphilis coronary artery ostial lesions

1. Introduction

Syphilis is a chronic and systemic sexually transmitted disease caused by Treponema pallidum. Clinically, syphilis can be divided into four stages based on disease progression: primary, secondary, latent, and tertiary.[1] As the disease progresses, syphilis not only affects the skin and mucous membranes, but also involves almost all tissues and organs of the body. In particular, at the late stage, syphilis affects the cardiovascular system, that is, cardiovascular syphilis, which can eventually lead to death.[2] Syphilitic coronary

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[a] Department of Cardiology, [b] Xiamen Diabetes Institute, The First Affiliated Hospital of Xiamen University, 55 Zhenhai Road, Xiamen, Fujian, China.

[*] Correspondence: Shuyu Yang, Xiamen Diabetes Institute, The First Affiliated Hospital of Xiamen University, 55 Zhenhai Road, Xiamen, Fujian 361003, China (e-mail: ysyxmu@163.com).

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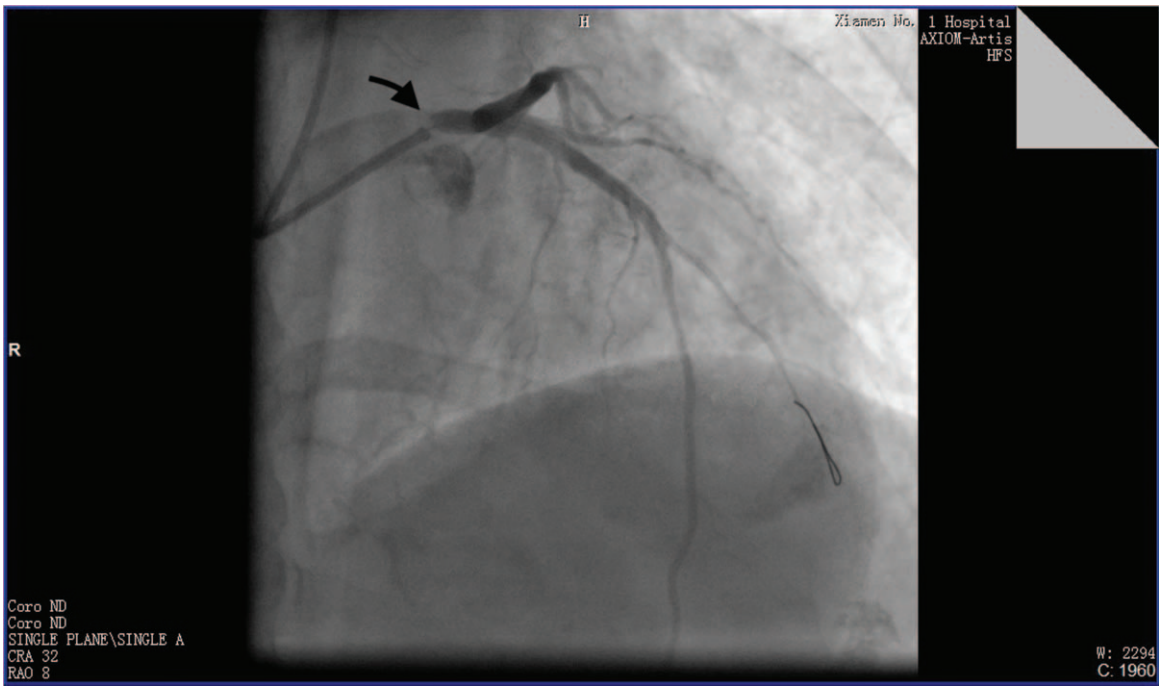

Figure 1. CAG of SCAOL. The arrow points to the position of coronary artery opening stenosis during CAG, which is ~95%.

artery ostial lesions (SCAOL) are cardiovascular syphilis lesions associated with a high rate of disability and mortality.[3] Therefore, how to improve the long-term survival rate and quality of life in SCAOL patients has been an active area of research in the field.

Currently, there are two major treatments for SCAOL: coronary bypass grafting (CABG), which includes the left internal mammary artery (LIMA) and saphenous vein graft (SVG),[4] and percutaneous coronary intervention (PCI).[5] However, which treatment is more efficient in the treatment of SCAOL has not been clear. The purpose of this study was to compare the efficacy of CABG and PCI in the treatment of SCAOL patients. We also compared LIMA and SVG in terms of efficacy, and compared the efficacy of anti-syphilis vs non-anti-syphilis therapies in the treatment of SCAOL.

2. Materials and methods

2.1. Subject selection

This retrospective study included a total of 60 patients who were admitted to our hospital between October 2015 and October 2019 with SCAOL, including 32 males and 28 females with an average age of 50.2 ± 7.5 years. Patients who met the following criteria were included in this study:

1. clinical manifestation as angina pectoris, often with emotional agitation, fatigue, excessive exercise, and mental tension;
2. on electrocardiography, a decreased ST segment, inverted T-wave, and ST segment elevation in an aVR lead. Myocardial infarction occurred occasionally;
3. hematological examination of syphilis was strongly positive;
4. coronary angiography (CAG) revealed severe stenosis of left main artery ostial lesions, and/or severe stenosis of right coronary artery ostial lesions.

Severe stenosis was defined as having a lumen area stenosis rate >50 and/or minimum lumen area of the left main artery $<6\,mm^2$, as revealed by intravascular ultrasonography (IVUS) and quantitatively determined by CAG three-dimensional (3D) reconstruction quantitative analysis (Figs. 1 and 2).

All patients were given standard treatment for coronary heart disease: aspirin 0.1 g once a day, tegrilol 90 mg twice a day, and atorvastatin 20 mg before bed. Drugs for underlying diseases such as diabetes and hypertension were continuously administered.

Patients who had one of the following were excluded from this study: history of autoimmune disease, history of other infectious diseases, history of recent acute infectious disease, other cardiovascular disease, or tumor. This report was approved by the Ethics Committee of The First Affiliated Hospital of Xiamen University. Written informed consent was obtained from the patient.

2.2. Data collection

Demographic characteristics including age, gender, and body mass index (BMI) were collected through the hospital's database. Smoking was defined as having more than 10 years of smoking, at least 20 cigarettes/day. Diabetes was defined as having a: fasting blood glucose level ≥7.0 mmol/L or having a blood glucose level ≥11.1 mmol/L 2 h after a meal.

Hyperlipidemia was defined as having a total cholesterol concentration >5.7 mmol/L and/or a low-density cholesterol concentration >3.3 mmol/L.

Syphilis was diagnosed when the results of the toluidine red unheated serological test (TRUST) and the treponema pallidum particle agglutination (TPPA) test were positive.

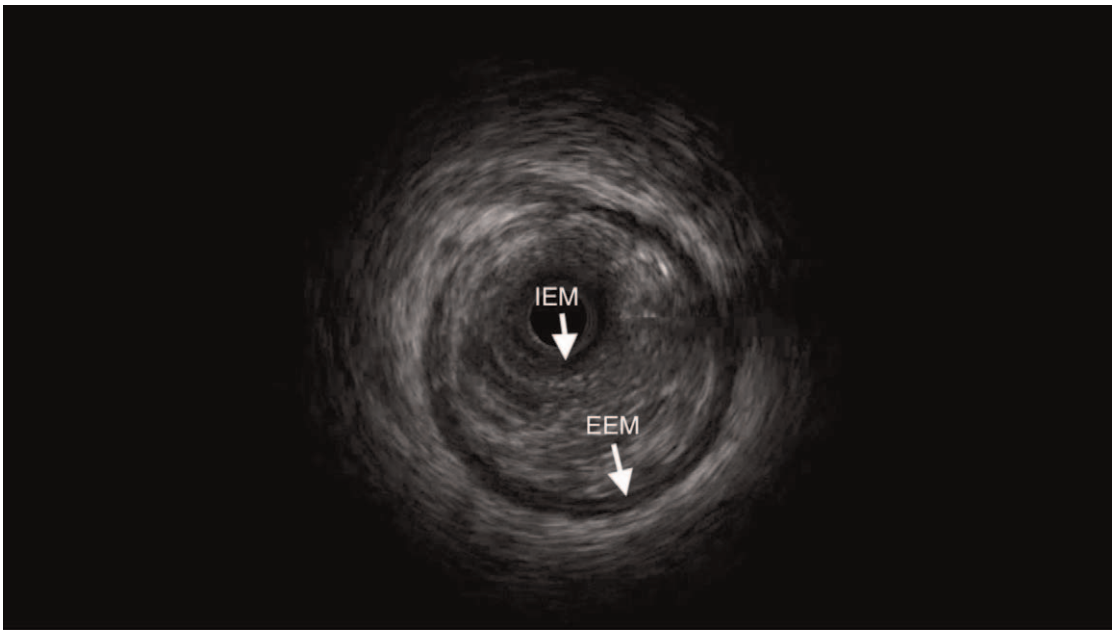

Figure 2. IVUS of SCAOL. The two arrows point to the internal elastic membrane (IEM) and extra-elastic membrane (EEM) of the coronary artery, respectively. The two elastic membranes represent the plaques between them, and the plaque load is ~90%.

2.3. Clinical examination

All patients underwent the following examinations: blood tests for hematologic evidence of syphilis, BNP, electrocardiography, and echocardiography before surgery. CAG was performed to identify coronary artery ostial lesions without contraindications. A diagnosis of SCAOL required positive results on a syphilis test (TPPA and TRUST, stenosis of coronary artery ostial lesions (QCA determination of lumen area stenosis rate and/or minimum lumen area of the left main by IVUS). Patients were divided into two treatment groups: the CABG group (n = 32) and the PCI group (n = 28), according to the different treatments. One week after surgery, BNP, left ventricular end-diastolic diameter (LVDd), and ejection fraction (EF) were measured. After 6 months, the coronary stent restenosis rate was determined by QCA and/or IVUS with PCI. Patients with CABG were evaluated with coronary computed tomography angiography (CCTA; QCA determination of lumen area stenosis rate >50% and/or degree of vascular stenosis >50% is defined as restenosis; Fig. 3). We also measured BNP, EF, LVDd, and the incidence of major adverse cardiovascular events (MACEs). The MACES included the recurrence of angina pectoris, heart failure, myocardial infarction, and cardiac death. CABG was performed with two different methods: the left internal mammary artery (LIMA) approach and saphenous vein graft (SVG) approach. After surgery, patients were assigned to one of two groups based on whether they had received anti-syphilis treatment: an anti-syphilis treatment group and a non-anti-syphilis treatment group. The anti-syphilis treatment was standard: an intramuscular injection of benzathine penicillin G (2.4 million units, 3 times/week).

2.4. Statistical analysis

All data were analyzed and processed with SPSS 23.0 statistical software. Statistical significance was determined by chi-square test and t test. $P < .05$ was considered statistically significant.

3. Results

3.1. Comparison of demographic and preoperative clinical characteristics between the CABG and PCI groups

There were no significant differences between the CABG and PCI groups in terms of age, gender, history of smoking, diabetes, BMI, hyperlipidemia, mean systolic blood pressure, mean diastolic blood pressure, degree of coronary stenosis (as determined by intravascular ultrasound), BNP, LVDd, and EF ($P > .05$, Table 1).

3.2. Comparison of clinical characteristics between CABG and PCI groups 1 week after surgery

Measurements of serum BNP levels, LVDd, and EF of all patients obtained 1 week after the operation revealed no significant difference between groups ($P > .05$, Table 2).

3.3. Comparison of clinical characteristics between CABG and PCI groups 6 months after surgery

The incidence of stent restenosis and bridging restenosis, serum BNP levels, LVDd, EF, and MACEs were determined in all patients at 6 months after surgery. As shown in Table 3, the CABG group had significantly greater improvement in all aforementioned indexes, compared with the PCI group ($^{*}P < .05$, Table 3).

We also compared the restenosis rates after LIMA vs SVG in the CABG group. The results showed that the LIMA group had a significantly lower restenosis rate than the SVG group ($^{*}P < .05$, Table 4).

3.4. Comparison of restenosis rate between anti-syphilis treatment and non-anti-syphilis treatment at 6 months

The anti-syphilis treatment group had a significantly lower restenosis rate than the non-anti-syphilis treatment group ($^{*}P < .05$, Table 5).

Figure 3. CCTA of restenosis after CABG. The arrow points to the stenosis of the opening of SVG in the wall of the aorta after CABG. The stenosis is ~90%.

4. Discussion and conclusions

There are no reports on the incidence of SCAOL. However, some epidemiological data show that the incidence of syphilis is ~45 out of 100,000 cases, and that 25% to 35% of cases have lesions extending to the mouth of the coronary artery, resulting in narrowing of the coronary artery mouth. The incidence also varies across geographic areas, with higher incidence observed in areas with more developed economies.[1,2]

The major findings from this study were that:

1. CABG-treated SCAOL patients had better short-term outcomes than PCI-treated patients;
2. LIMA-treated SCAOL patients had a lower restenosis rate than SVG-treated patients;
3. SCAOL patients who received anti-syphilis therapy had better outcomes than patients who did not receive anti-syphilis therapy.

It has been well documented that syphilis spirochetes can enter lymph nodes and other organs through the lymphatic system, causing damage to various systems throughout the body.[6–8] For the cardiovascular system, at the beginning, syphilis spirochetes enter the nutrient vessels of the aortic root from the lymphatic tissue of the mediastinum hilum.[9] Because the ascending aorta is rich in lymphatics and nutrient vessels, syphilis easily causes aortitis, which may affect bilateral coronary artery openings, but is limited to the area 1.5 to 2.0 cm from the openings.[10] These pathological changes result in endarteritis, stenosis, and/or the occlusion of coronary arteries, and lead to severe clinical manifestations,[11,12] which are different from the manifestations of coronary heart disease caused by atherosclerosis. In patients with cardiovascular syphilis, coronary artery stenosis may occur.[8] When syphilis is accompanied by coronary artery opening stenosis, patients are diagnosed with SCAOL, while

Table 1

Comparison of demographic and preoperative clinical characteristics between the CABG and PCI groups.

Clinical characteristics	CABG	PCI
Age (years)	50.5 ± 8.8	50.1 ± 9.1
Gender		
Male	19	16
Female	13	12
Smoking	6	6
Diabetes	3	3
Body mass index. Over 30	5	4
Hyperlipidemia	4	4
Mean systolic blood pressure	118.3 ± 8.1	117.9 ± 8.6
Mean diastolic blood pressure	70.1 ± 4 .8	69.8 ± 5.1
BNP (ng/mL)	252.5 ± 16.3	249.3 ± 18.1
LVDd (mm)	56.3 ± 7.1.	55.7 ± 8.2
EF (%)	46.1 ± 5.9	46.5 ± 5.4
Degree of coronary stenosis (%)	85.6 ± 6.8	86.3 ± 6.4

Table 2

Comparison of patient characteristics between the CABG and PCI groups at 1 wk after surgery.

Clinical characteristics	CABG	PCI
n	32	28
BNP (ng/mL)	152.1 ± 10.9	149.5 ± 9.9
LVDd (mm)	53.3 ± 6.5	52.8 ± 6.2
EF (%)	48.3 ± 6.8	49.1 ± 6.5

Table 3

Comparison of clinical characteristics between the CABG and PCI groups at 6 month after surgery.

Clinical index	CABG	PCI
n	32	28
BNP (ng/mL)	72.5±8.5	90.5±8.9*
LVDd (mm)	45.5±4.8	50.1±4.7*
LVEF (%)	56.9±6.8.	51.2±6.3*
Number of restenosis	4	10*
MACE/case	2	8*

* $P < .05$ vs CABG group.

patients with concurrent coronary artery ostial stenosis are more likely to be diagnosed with coronary atherosclerotic heart disease.[13,14] In this study, all patients were diagnosed with SCAOL rather than traditional coronary artery atherosclerotic heart disease by coronary angiography. This approach was elected because:

1. these patients were syphilis-test positive and
2. did not have increased stenosis below the coronary artery ostial lesions, which is characteristic of SCAOL.[15,16]

In our study, we compared the efficacy of two therapies, CABG and PCI, in the treatment of SCAOL patients. We found that there were no significant differences in outcomes between these two groups at 1 week after surgery. However, at the 6-month follow-up, patients in the CABG group were found to have better cardiac function, a lower restenosis rate, and fewer MACEs than those in the PCI group.

As mentioned above, SCAOL should be considered distinct from atherosclerotic coronary artery disease, which is a lesion of the aorta rather than a problem of the coronary artery itself.[17] Endarteritis of the aorta leads to endovascular necrosis and the destruction of elastic tissue. Therefore, coronary stent implantation is often ineffective, and the smooth muscle of the aorta is often unable to fully expand after stenting, which increases the risk for restenosis.[18] The aorta has substantial muscle mass, which facilitates stent restenosis. We concluded that CABG-treated SCOAL patients had better prognoses than PCI-treated patients, at least within the 6-month period post-surgery, as reported previously.[18]

CABG may be performed via the LIMA or SVG approach. Because persistent infection of the ascending aorta can lead to proximal anastomotic restenosis, syphilis-induced arteritis does not usually involve the main branch of the aortic arch.[19] Therefore, restenosis often occurs at the proximal anastomosis of the great saphenous vein transplantation, and LIMA is superior to SVG in the treatment of this condition.[20,21] In accordance with the above findings, in the present study, we also compared the efficacy of two CABG treatments, LIMA and SVG, in managing SCAOL. The results showed that LIMA was better than SVG, as evidenced by the significantly lower restenosis rate in the LIMA group, compared with the SVG group. Thus, our observations support the notion that LIMA is more effective than SVG in the treatment of SCAOL patients.

Table 4

Comparison of restenosis rates between LIMA and SVG groups at 6 month after surgery.

Group	Restenosis	No-restenosis	Total	Restenosis rate (%)
LIMA	1	22	23	4.55*
SVG	3	6	9	33.3
Total	4	28.	32.	14.29

* $P < .05$ vs SVG.

Table 5

Comparison of restenosis rates between patients who received anti-syphilis treatment and those who did not at 6 month after the operation.

Group	Restenosis	No-restenosis	Total restenosis	Rate (%)
Anti-syphilis	6	29	35	17.1*
Non-anti-syphilis	8	7	15	53.3
Total	12	38.	50.	24

* $P < .05$ vs non-anti-syphilis.

In our study, we also compared outcomes between SCAOL patients who received anti-syphilis treatment and those who did not. We showed that patients in the anti-syphilis treatment group had a significantly lower restenosis rate than those in the non-anti-syphilis treatment group. These findings suggest that anti-syphilis treatment for SCAOL patients is important and can benefit SCAOL patients, at least with respect to the restenosis rate. These findings also confirmed that the diagnosis of SCAOL was correct.

Some limitations of this study should be acknowledged. For example, this study was a single-center retrospective study with a small sample size. Therefore, our findings need to be further corroborated by multi-center randomized double-blind controlled studies that include large cohorts. Also, the follow-up period of this study was short, and thus a long term follow-up will be needed in future studies.

In conclusion, the short-term outcomes observed in our study population demonstrate that CABG is more efficient than PCI in the treatment of SCAOL. LIMA can also significantly reduce the incidence of restenosis, compared with SVG. Finally, anti-syphilis treatment is important for improving prognosis in SCAOL patients.

Author contributions

Data curation: Weihua Li, Qiang Xie.
Formal analysis: Junyu Han, Zhengrong Huang.
Investigation: Wuyang Zheng, Weihua Li.
Supervision: Shuyu Yang.
Writing – original draft: Junyu Han, Wuyang Zheng
Writing – review & editing: Shuyu Yang.

References

[1] Hook EW3rd. Syphilis. Lancet 2017;389:1550–7.
[2] Singh AE, Romanowski B. Syphilis: review with emphasis on clinical, epidemiologic, and some biologic features. Clin Microbiol Rev 1999; 12:187–209.
[3] Shankarappa RK, Moorthy N, Panneerselvam A, et al. Bilateral coronary ostial lesions in cardiovascular syphilis treated by means of percutaneous coronary stenting. Tex Heart Inst J 2013;40:630–2.
[4] Wolfe JA. The coronary artery bypass conduit: II. Assessment of the quality of the distal anastomosis. Ann Thorac Surg 2001;72:S2253–2258. discussion S2258–2259, S2267–2270.

[5] Kim SM, Lee SY, Lee JH, et al. Repeated isolated bilateral coronary ostial stenosis related to the syphilitic aortitis. Korean J Intern Med 2017; 32:747–9.
[6] Workowski KA, Bolan AG. 2015 Sexually transmitted diseases treatment guidelines. Morb Mort Wkly Rep 2015;64:
[7] Roberts WC, Ko JM, Vowels TJ. Natural history of syphilitic aortitis. Am J Cardiol 2009;104:1578–87.
[8] Treglia G, Taralli S, Maggi F, et al. Usefulness of (18)F-FDG PET/CT in disease extent and treatment response assessment in a patient with syphilitic aortitis. Clin Nucl Med 2013;38:e185–7.
[9] Lafond RE, Lukehart SA. Biological basis for syphilis. Clin Microbiol Rev 2006;19:29–49.
[10] Ghazy T, Matschke K, Kappert U. A monstrous aneurysm of the descending aorta as a sole manifestation of tertiary syphilis treated endovascularly. Eur Heart J 2011;32:2411.
[11] Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541–619.
[12] Morshed MG, Singh AE. Recent trends in the serologic diagnosis of syphilis. Clin Vaccine Immunol 2015;22:137–47.
[13] Gugssa SA, Johnston JC. Syphilitic aortic aneurysm with spastic paraparesis: a novel presentation and review of the literature. J Neurol Sci 2012;323:241–4.
[14] Simonenko VB, Popov AV, Siuch NI, et al. Syphilitic mesaortitis. Klin Med (Mosk) 2012;90:77–9.
[15] Balink H, Spoorenberg A, Houtman PM, et al. Early recognition of aortitis of the aorta ascendens with (1)(8)F-FDG PET/CT: syphilitic? Clin Rheumatol 2013;32:705–9.
[16] Bouvier E, Tabet JY, Malergue MC, et al. Syphilitic aortic regurgitation and ostial coronary occlusion. J Am Coll Cardiol 2011;57:e375.
[17] Nakazone MA, Machado MN, Barbosa RB, et al. Syphilitic coronary artery ostial stenosis resulting in acute myocardial infarction treated by percutaneous coronary intervention. Case Rep Med 2010;2010:830583.
[18] Choon Ta N, Chee Tang C, Chi Keong C. Syphilitic coronary artery ostial stenosis presenting with acute myocardial infarction. Heart 2013;99:290.
[19] Gornik HL, Creager MA. Aortitis. Circulation 2008;117:3039–51.
[20] Calafiore AM, Contini M, Vitolla G, et al. Bilateral internal thoracic artery grafting: long-term clinical and angiographic results of in situ versus Y grafts. J Thorac Cardiovasc Surg 2000;120:990–6.
[21] Ochi M, Hatori N, Bessho R, et al. Adequacy of flow capacity of bilateral internal thoracic artery T graft. Ann Thorac Surg 2001;72:2008–11. discussion 2012.