MULTI-CENTERED CLINICAL TRIAL·

Therapeutic Effect of Affinity™ Coronary Stent in the Treatment of Coronary Artery Disease and Clinical Follow-up

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[Abstract] Objective: to evaluated the safety and therapeutic effect of USA made Affinity™ coronary stent in the treatment of coronary artery disease. **Method:** Retrospective analysis was performed on 1352 patients with coronary artery disease who were treated by insertion of Affinity™ coronary stent in 21 heart centers. Cardiac death, myocardial infarction, target vessel remodeling rate, main adverse cardiac event (MACE) and incidence of in-stent thrombogenesis within 1 year were observed. **Results:** Affinity™ stents were inserted into 1869 lesions in 1352 patients, among whom 23.3% were diabetic, 90.49% were with acute coronary syndrome. Type C lesion accounted for 30.98%, branch lesion accounted for 11.13%, and chronic complete occlusive lesion accounted for 7.81%. Average length of target lesion vessel was 21.99±10.57, average stenosis was 88.18%±10.93%, reference vessel diameter was 3.17±1.81, and maximum dilation pressure was 13.77±3.01 atm. Lesion that needed pre-balloon dilation was 78.12% while lesion that needed after-balloon dilation was 25.79%. The results of follow-up showed that accumulated incidence of cardiac death, myocardial infarction, target vessel remodeling, MACE within 12 months was 0.52%, 0.96%, 2.14% and 3.62% respectively, all within acceptable range. One-year accumulated incidence of thrombus (0.66%) was similar with the results of other studies. **Conclusion:** The results of one-year follow-up indicated that Affinity™ coronary stent had good safety and efficacy.

Currently, coronary artery stenting has become the preferred method for interventional therapy of coronary artery disease. Several large-scale clinical trials have demonstrated that Sirolimus drug-eluting stent can significantly decrease revascularization rate of target lesion and it has good safety. Affinity™ stent is a Sirolimus drug-eluting stent that has been approved by State Food and Drug Administration. It has been widely applied clinically since its marketing in the end of 2005. However, there has been no large-sample clinical investigation on its efficacy and safety up to now. The present study performed a retrospective analysis on the information about patients treated with Affinity™ stent insertion in 21 domestic hospitals, so as to provide preliminary data on efficacy and safety of Sirolimus drug-eluting stent.

Information and methods

1. Case information

1352 patients who were treated by Affinity™ stent in 21 heart centers (the list was shown in appendix) from January, 2006 to September, 2006 were included, meanwhile those who were treated by coronary stents of other brands were excluded.

2. Methods

2.1 Collection of baseline information: Read medical record of the patients and record their general demographic characteristics, medical history and clinical diagnosis.

2.2 Recording of the results of coronary arteriongraphy and course of surgery: Read surgery record of the patients and record type and characteristics of the coronary artery disease, number and size of the inserted stent, and immediate outcome of the surgery.

2.3 Follow-up: According to different durations after stent insertion, inquire and record the occurrence of main endpoint event by consulting medical record, out-patient clinic follow-up or telephone follow-up. The collection of all clinical information was completed on 31st, December, 2007. 6-month and 12-month accumulated incidence of endpoint event was calculated.

2.4 Main endpoint: incidence of major adverse cardiac events (MACE, including cardiac death, nonlethal myocardial infarction and revascularization of target vessel)

2.5 Statistical method: All data were analyzed using SAS software. Measurement data were expressed with mean±SD ($\bar{x}$ ±s), while numeration data were expressed with percentage.

Results:

1. Baseline information of the patients: A total of 1352 patients were included and 1869 lesions were treated (table 1). Average age of included patients was 62.33±10.94 years old and 72.78% were males. As far as previous medical history was concerned, diabetes accounted for 23.30% and acute coronary syndrome accounted for 90.49%. Among 1352 patients, triple

vessel disease accounted for 30.10%. Among 1869 lesions, type C lesion accounted for 30.98%, left main stem lesion accounted for 1.5%, branch lesion accounted for 11.13%, and chronic complete occlusive lesion accounted for 7.81%.

2. Immediate surgery outcome: Immediate surgery success rate was 100% and there was no stent drop-out during the surgery. Average vessel length of target lesion was 21.99±10.57 mm, average stenosis was 88.18%±10.93%, reference vessel diameter was 3.17±1.81mm, and maximum dilation pressure of lesion was 13.77±3.01 atm. Among 1869 lesions, 78.12% needed pre-balloon dilation, while 25.79% needed post-balloon dilation. Lesions that treated by insertion of overlapped stents accounted for 10.33%, while branch lesions that successfully treated by kissing balloon technique accounted for 7.93% (table 2).

3. Results of clinical follow-up: MACE was defined as the sum of incidence of cardiac death, nonlethal myocardial infarction, target vessel revascularization (TvR). 6-month and 12-month accumulated incidence of MACE was 0.89% and 3.62%, respectively (table 3).

6 month: Cardiac death occurred in 6 patients (0.44%). Myocardial infarction occurred in 4 patients, 2 were related with target vessel (0.15%) and 2 were related with stent thrombus(0.15%). Target vessel revascularization was performed in 2 patients. There were 12 MACE (0.89%) all together.

Table 1. General characteristics of 1352 subjects

Items	Value
Age (years old x±s)	62.33±10.94
Male	984 (72.78%)
Previous myocardial infarction	380 (28.11%)
Previous CABG	5 (0.37%)
Previous PCI	99 (7.32%)
Diabetes	315 (23.30%)
Hypertension	884 (65.38%)
Hyperlipoidemia	593 (43.86%)
Family history of coronary artery disease	97 (7.17%)
Smoker	727 (53.77%)
Clinical diagnosis	
Silent ischemia	29 (2.14%)
Stable angina	96 (7.10%)
Unstable angina	736 (54.44%)
None-sT-elevation myocardial infarction	46 (3.40%)
sT-elevation myocardial infarction	445 (32.91%)
Disease type	
Type A lesion	182 (9.74%)
Type B1 lesion	548 (29.32%)
Type B2 lesion	536 (28.68%)
Type C lesion	579 (30.98%)
Chronic complete occlusive lesion	146 (7.81%)
Branch lesion	208 (11.13%)
Multi-branch lesion	780 (59.17%)
Lesion characteristics	
Average number of target lesion	1.38
Average length of target lesion (mm, x±s)	21.99±10.57
(mm, $\bar{x}$ ±s) Reference vessel diameter (mm, x±s)	3.17±1.81
Average stenosis (%,mm, x±s)	88.18±10.93

Table 2. Immediate surgery outcome of 1352 patients

Items	Value
Per capita number of inserted stents	1.38
Average stent length (mm, x±s)	26.65±12.64
Pre-balloon dilation	1460 (78.12%)
Post-balloon dilation	482 (25.79%)
Kissing balloon dilation	79 (7.93%)
Average maximum dilation pressure (atm, x±s)	13.77±3.01
Insertion of overlapped stents	193 (10.33%)
Average maximum dilation pressure (atm, x±s)	13.77±3.01
Visual measurement of residual stenosis	
0%	1643 (87.91%)
0%～10%	128 (6.85%)
>10%	15 (0.80%)

Note: 1 atm=101.325 kPa

Table 3. Results of clinical follow-up (n=1352)

Time of follow-up (month)	6	12
Cardiac death	6 (0.44%)	7 (0.52%)
Nonlethal myocardial infarction	4 (0.30%)	13 (0.96%)
Target lesion revascularization	2 (0.15%)	22 (1.63%)
Target vessel revascularization (non target lesion)	0	7 (0.51%)
Main adverse cardiac event	12 (0.89%)	49 (3.62%)

6-12month**:** There were 1 case of cardiac death, 9 cases of myocardial infarction (7 were related with target vessel), 20 cases of TLR (7 were related with target vessel revascularization in non target lesion). During this period, there were 37 cases of MACEs.

There were 2 cases (0.15%) of acute thrombus (0-24h), 1 case (0.07) of subactue thrombus (1-30days), and cases of advanced stage thrombus (31-365days). 1 year accumulated incidence of thrombus was 0.66%.

Discussion

Retrospective analysis on the present study showed that Affinity™ Coronary Stent System had a good clinical effect

during its application in "real world". For analysis in all of 1352 patients with the stent, immediate surgery success rate reached 100%. 6-month and 12-month incidence of MACE was 0.89% and 3.62%, respectively. The design of this study belonged to multi-centered registration study, and its result was better than that of other first generation drug-eluting stents (Sirolimus-eluting stent Cypher, Paclitaxel-eluting stent raxus). SIRIUS study showed that the 1 year incidence of MACE for Cypher was 8.3% [1].TAXUS IV study showed that the 1 year incidence of MACE for Taxus was 10.6% [2,3].

Affinity™ Sirolimus-eluting stent is a novel stent that independently designed by our country. Its platform adopted double coiled spiral structure to offer good supporting force and adherence ability. For Affinity™ Sirolimus-eluting stent, Sirolimus is loaded on PBMA/PEVA polymer coating in a concentration of 120μg/cm^2. A top coating is coated on the outer surface to control the rate of drug release.

The aim of the present was to evaluate the safety and efficacy of Affinity™ stent in clinical application. From the perspective of clinical diagnosis, patients with diabetes accounted for 23% and patients with acute coronary syndrome accounted for more than 90%. In the study, type B and type C lesion accounted for 89%, multi-branch disease accounted for almost 60%, chronic completed occlusive lesion accounted for 7.8%, and branch lesion accounted for 11%, so the lesions were rather complicated. The average length of lesion was relatively long (21.99±10.57mm).

1 year accumulated incidence of thrombus for Affinity™ stent was 0.66%. In SPIRIT III clinical trial, the 1 year accumulated incidence of thrombus for XIENCE and Taxus was 0.9% and 0.6%, respectively [4].Iakovou[5] et al. reported that 9-month incidence of thrombosis in "real world" for Cypher and Taxus was 1.3% and 1.7%, respectively, which was similar with that for Affinity™ stent in the present study. Occurrence of advanced stage thrombus may be related with delayed endothelialization of the stent [6]. After being inserted into the vessel, Sirolimus was released to local lesion in an eluting way. Although it can inhibit restenosis, it can also delay healing of the lesion at the same time, which will lead to delayed endothelium regeneration and increase the risk of delayed stent thrombus [7]. All patients were treated with standard anticoagulant and antithrombotic therapy. However, there was still thrombosis, which was a problem that should to be paid attention to in clinical application of drug-eluting stent.

In summary, the present study confirmed tentatively that Affinity™ stent was safe and effective in clinical treatment of coronary artery disease. Its therapeutic effect was as excellent as that of import stent. Its relatively low price made it more attractive in domestic clinical application.

(Note: The clinical centers and main investigators involved were Huo Yong, Chen Ming, and Li Jianping from First Hospital of Peking University, Li zhanquan from the People's Hospital of Liaoning Province, He Ben from Shanghai Renji Hospital, Chen Shaoliang from Nanjing First Hospital, Yu Bo from Second Affiliated Hospital of Harbin, Li Kang from Beiing Xuanwu hospital, Wang Dongqi from Affiliated Hospital of Xian Jiaotong University, Fu Guosheng from Zhejiang Shaoyifu Hospital, Wang Ningfu from Hangzhou First Hospital, Ma Genshan from Jiangsu Zhongda Hospital, Yang Zhijian from the People's Hospital of Jiangsu Province, Wang Jianan from the Second Affiliated Hospital of Zhejiang University, Shen Xiangqian from the Second Affiliated Hospital of Hunan Xiangya Medical College, Qi Guoxian and Jia Dalin from the First Affiliated Hospital of Chinese Medical University, Qu Peng from the Second Hospital of Dalian Medical University, Cao Xuebin and Mu Xianyou from the 252 Military Hospital, Ma Yitong from the First Affiliated Hospital of Xinjiang Medical University, Li Bao from Shanxi institute of cardiovascular diseases, Zheng Qiangsun from Tangdu Hospital of the Forth Military Medical University, Deng Pingshuan from the First Affiliated Hospital of Henan Technology University, Cai Shanglang from Qingdao Medical College Affiliated Hospital).