Clinical follow-up of chitosan dressings in transradial coronary intervention

WANG Jian-long, ZHOU Yu-jie, LIU Yu-yang, NIE bin, YANG Qing, CHENG Wan-jun

12th ward, Beijing Anzhen hospital, Capital Medical University, Beijing 100029, China

[Abstract] Objectives: To evaluate the hemostatic properties and efficacy of chitosan dressings hemostatic properties in patients undergoing transradial coronary intervention. **Methods:** From Aug to Oct 2010, 220 patients with coronary artery disease were enrolled in the study and divided into chitosan dressings compression group and control group. There were 110 patients in each group. In-hospital vascular related complication was the prima study endpoint. The secondary endpoint included: compression time and the comfort feeling of patients. **Results:** The overall incidence of vascular related complication in the chitosan group was fewer than in the control group (3.6% v.s 11.8%, P=0.023). In chitosan group the compression time condition was superior to the control group (222±46.1min v.s. 291±45.6min), P<0.001 **Conclusion:** The application of chitosan dressings in transradial coronary intervention can reduce the risk of complications, remarkably shorten compression time and improve comfort feeling of the patients.

[Key words]: Angioplasty, transluminal, percutaneous coronary; Radial artery; Vascular complication

Since Campeau et al. successfully completed the first case of transradial artery coronary arteriography in 1989 [1] and Kiemenij successfully conducted the first case of transradial artery coronary artery coronary stent implantation in 1993 [2], and with the continuing progress in intervention techniques and devices, transradial coronary intervention (TRI) has become one of the common approaches of intervention for coronary artery disease.

Due to the anatomical features of the radial artery, the transradial coronary intervention, compared with transfemoral coronary interventions (TFI), has the advantages of low incidence of vascular puncture complications, early mobilization, few hemorrhagic events, and easy acceptance by patients, thus TRI therapy has obtained widespread popularity [3,4]. It was found in practical applications that

although vascular complications after radial artery intervention rarely occur, if postoperative treatment is not carried out in a timely manner, it can still cause serious consequences, even maiming the patient. Now the postoperative hemostasis treatment of TRI applies conventional elastic bandage to compress and stop bleeding or dedicated radial artery hemostatic devices, both of which are pure physical compressing hemostasis. Chitosan is a natural biological material, with hemostatic and antibacterial effect [5, 6] .Studies suggested that it can safely and effectively reduce the puncture hemorrhage in vein penetration after hemodialysis, as well as the use of occlusion compression bandages [7]. It has been proved in animal tests that the application of chitosan hemostatic dressings in femoral artery hemostasis can provide better hemostatic effects than conventional gauze pressing [8].

This study, as a single-center prospective randomized controlled study, is designed to understand the clinical application effects of chitosan hemostatic dressing in the postoperative hemostasis of transradial coronary intervention therapy and in the prevention of vascular puncture complications.

Materials and Methods

1. Subjects: the patients consecutively enrolled in the 12th ward of Beijing Anzhen Hospital for TRI treatment. Inclusive criteria: positive in the Allen test; the radial artery undergoing TRI surgery is applied for the first time; 6Fr radial artery sheath is successfully inserted. Exclusive criteria: acute myocardial infarction; cardiogenic shock; predetermined radial artery puncture kit is replaced; forearm arterial injury or perforation confirmed by angiography unrelated to sheath insertion occurs during TRI surgery; the radial artery sheath unable to send the guide wire or catheter after insertion; allergic to adhesive bandages; existence of contraindications of anti-platelet medication; age > 80 years; uncontrolled hypertension; severe electrolyte imbalance; serious liver and kidney dysfunction; participated in other studies within three months; mental disorders; researchers believe unsuitable; undergone similar surgery within a month; allergic constitution - allergic to seafood, shrimp and crab carapace. The enrolled patients were randomly divided into the chitosan group (Daxon Biomedical(Suzhou Co., Ltd/AnsCare Chitosan hemostatic dressings to stop bleeding) and the control group (specialized radial artery hemostat / Japan Zeon Xemex hemostat group) with the ratio of 1:1.

2. Operation of transradial coronary intervention therapy: All of the enrolled patients were routinely administered the loading dose - 300 mg of aspirin, 300 mg of clopidogrel before surgery, and 100 mg -300 mg / day of aspirin and 75 mg / day of clopidogrel after surgery. Administered the dual antiplatelet drug is for at least 12

months. The patients was conducted local anesthesia with routine 1% lidocaine at the radial artery puncture and uniformly applied the 6 Fr Terumo radial artery puncture kit (20G trocar, 0.025 inch of straight guide wire, 16 cm of radial artery sheath) with Seldinger technique to conduct radial arterial puncture. Routinely injected 3000 U of common heparin through the sheath sidewall after the insertion of the radial artery sheath; added common heparin to 8000-10000 U when conducting interventional therapy. The 5Fr Terumo shared catheter is preferred in the coronary angiography; interventional therapy shall select 6Fr guiding catheter, using 260 cm of Terumo to lead the guide wire.

3. Removal of radial artery sheath and application of hemostasis device: Retreat the radial artery sheath of both groups for 2 cm - 3 cm before hemostasis. The Chitosan group: first put a piece of 2 cm × 3 cm of chitosan hemostatic dressing along its long axis in the place where the artery sheath gets into the skin, making the skin puncture site at the center of the hemostatic dressings; then withdraw the radial artery sheath, and compress for hemostasis for 3 minutes; then roll the folded 16 layers of 7.5 cm × 7.5 cm medical gauze to approximately 3.3 cm x 1.7 cm gauze pad and place it on the dressing with its long axis and the long axis of the hemostatic dressings overlapping, ensuring that the distal edge of the gauze pad exceeds the skin puncture for 2 mm -3 mm, and then compress to wrap with the self-adhesive elastic bandage. The control group: place the hemostatic board oppression pad at the skin puncture site, with the distal edge of the oppression pad exceeding the skin puncture site for 2 mm -3 mm, and then withdraw the radial artery sheath and fix the elastic bandage of the hemostat, maintaining the proper pressure.

4. Postoperative maintenance and removal of the radial artery hemostasis device: reduce the compression on the radial artery routinely 10 minutes after surgery to ensure that the proximal and distal ends of the hemostatic dressings or hemostat touch the fluctuations of the radial artery; from two hours after surgery, conduct radial artery decompression for one hour each and observe for two minutes whether the puncture site is bleeding; the bandage device can be removed if there is no bleeding.

5. Endpoint of the study: The complications at the puncture site of the vessel during TRI postoperative hospitalization is the primary endpoint of the study. Vascular complications include: forearm hematoma, radial artery occlusion, persistent bleeding, delayed type hemorrhage after removal of the bandage or device and myofascial syndrome. Repeatedly count if the patient is simultaneously with two or more complications. In the study, the time of removing the hemostatic device shall be recorded, and the degrees of comfort be judged according to the patient's feelings of postoperative compression hemostasis. The degrees of comfort of the patients are divided into three levels: level 1 is defined as the swelling of the forearm and palm;

level 2 is defined as tolerable swelling and pain in the forearm and palm; level 3 is defined as intolerable swelling and pain. Radial artery occlusion is defined as postoperative disappearance of radial artery pulse and confirmed by Doppler ultrasound test. If the radial artery is still occluded in the Doppler ultrasound recheck one month later, the diagnosis is established.

6. Statistical methods: Measurement data are presented as mean ± standard deviation, numeration data are presented by frequency. Conduct normal distribution test, t test or one-way ANOVA analysis for group measurement data; numeration data are compared by chi-square test or Fisher exact probability test. Select SPSS 13.0 software to process the data; when $P < 0.05$, the difference has statistical significance.

Results

1. Characteristics of clinical data of patients: From August 2010 to October 2010, 220 patients underwent radial coronary interventional therapy and were randomly divided into the hemostatic dressing group and the control group. The two groups of patients had the similar clinical baseline data characteristics and related surgical data, with no statistically significant differences (see Table 1).

Table 1 Characteristics of clinical baseline and surgical data of the two groups of patients

	Chitosan group (n = 110)	Control group (n = 110)	P Value
Age (years)	60.1±14.5	60.1±10.8	0.739
Male, n (%)	78 (70.9)	82 (74.5)	0.545
Smoking, n (%)	53 (48.2)	55 (50.0)	0.787
Height (cm)	168.4±7.3	167.9±7.5	0.605
Weight (kg)	72.1±10.1	72.5±9.9	0.767
Tirofiban n (%)	50 (45.5)	44 (40.0)	0.414
Hypertension, n (%)	67 (60.9)	76 (69.1)	0.203
Hyperlipidemia, n (%)	45 (40.9)	53 (48.2)	0.278
Diabetes, n (%)	25 (22.7)	26 (23.6)	0.873
Baseline serum creatinine (mmol / L)	81.6±14.4	83.0±15.6	0.484

2. Vascular complications of radial artery: The enrolled patients were observed for vascular complications of radial artery puncture during the follow-up. The study

showed that a total of 4 cases of vascular complications of radial artery puncture occurred in the chitosan group (3.6%), which had a lower incidence compared with 13 cases in the control group (11.8%) (P = 0.023). A comparative analysis of the individual events of vascular complications of radial artery indicated that the cases with forearm hematoma in the chitosan group (4 patients, 3.6%) were fewer than those in the control group (10 cases, 9.1%), but there was no statistical difference. Other individual events between the two groups were found to have no significant differences (see Table 2).

Table 2 Analysis of the vascular complications of radial artery in the two groups of post-operative haemostasis

	Chitosan group (n = 110)	Control group (n = 110)	P Value
Forearm hematoma, n (%)	4 (3.6)	10 (9.1)	0.097
Radial artery occlusion, n (%)	0	1 (0.9)	..
Persistent bleeding, n (%)	0	1 (0.9)	..
Delayed type hemorrhage after removing the bandage or device, n (%)	0	1 (0.9)	..
Myofascial syndrome	0	0	..
Total, n (%)	4 (3.6)	13 (11.8)	0.023

4. The post-operative hemostasis time of radial artery intervention: Compare the hemostasis times of both methods. Results showed that the hemostasis time of the chitosan group (222 ± 46.1 min) was significantly reduced compared with that of the control group (291 ± 45.6 min) (P < 0.001).

5. The comparison of the degree of comfort after applying the radial artery hemostatic device: Summarize the degree of comfort of patients for the two hemostatic methods after surgery. Results showed that the chitosan group was superior to the control group (see Table 3).

Table 3 Comparison of the degree of comfort between the two radial artery haemostasis methods

Degree of comfort	Level 1	Level 2	Level 3	P Value
Chitosan group, n (%)	70 (63.6)	29 (26.4)	11 (10.0)	

Control group, n (%)	55 (50.0)	32 (29.1)	23 (20.9)	0.045

Discussion

This study analyzed the clinical effects of hemostasis and the prevention of vascular puncture complications of the chitosan hemostatic compressing dressings in patients undergoing transradial coronary intervention (TRI).

Compared with the traditional femoral artery approach, the biggest advantages of transradial coronary intervention are fewer vascular complications and patients had a better quality of life, which have been proved by ACCESS, TEMPURA and other clinical studies [3, 4]. The MORTAL registration study further confirmed that, compared with the femoral artery approach, the mortality 30 days and 1 year after surgery of the radial artery approach was significantly decreased [9]; the main reason for this advantage is fewer hemorrhagic events after the TRI. Nevertheless, the TRI post-operative puncture related complications are not uncommon in clinical practice. The lack of experience or untimely treatment can still lead to serious complications, even mutilation, such as myofascial syndrome or hand ischemic necrosis. What physicians still need to be concerned with is how to avoid or reduce the occurrence of TRI post-operative vascular complications, to reduce post-operative hemostasis time and to improve the degree of comfort of the patients.

Now the commonly used TRI post-operative hemostatic treatments include the traditional elastic bandage compression, dedicated plate or balloon radial artery hemostatic device, which are all purely physical mechanical compressing hemostasis. The three types of hemostasis are similar in the incidence of puncture related complications, but the dedicated plate or balloon radial artery hemostatic device is superior to the traditional elastic bandage compression in terms of the total hemostasis time [10]. A number of studies have suggested that chitosan has a good hemostatic effect [5, 7, 8]. In this study, by the prospective randomized controlled method, we discussed the clinical effect of hemostasis and the prevention of vascular puncture complications of the chitosan hemostatic compressing dressings in patients undergoing transradial coronary intervention (TRI). Results suggest that the incidence of primary endpoint events (vascular complications of the radial artery) of the chitosan group was lower than that of the control group (3.6% vs. 11.8%, $P = 0.023$). The total hemostasis time of the chitosan group was shorter (222 ± 46.1min vs. 29 ± 45.6min, $P < 0.001$). In the hemostasis process after the radial artery intervention, special attention shall be paid to the key points of the operation; hemostatic compressing points shall be made clear and accurately compressed; closely observe

any symptoms during the compressing period to detect hemostasis-related complications as early as possible, and treat it in a timely manner to prevent further developments. These are the basis of good clinical effect.

In this study the degree of comfort of patients between the chitosan group and the control group has a statistical difference; the distribution of the degree of comfort suggested that in the chitosan group the number of patients in the level 1 degree of comfort was large and that in level 3 was small. The increase in the patients' degree of comfort may be related to that in the chitosan group in that the total compressing hemostasis time was shorter and hemostatic related complications were few.

Results from this study showed that the application of chitosan hemostatic dressings to conduct compressing hemostasis at the puncture point after transradial coronary intervention can significantly shorten the hemostatic operation time. At the same time, it also reduced the incidence of complications such as hemorrhaging or hematoma. It not only achieved the purpose of effective hemostasis but also met the comfort needs of the patients.

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