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CTO Recanalization by Intraocclusion Injection of Contrast: The Microchannel Technique

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Objectives: To assess the utilization of microinjection of contrast for the recanalization of chronic total occlusions (CTO). **Background:** Microchannels in CTOs have been considered important conduits for CTO crossing, utilizing dedicated guidewires. We postulated that microinjection of contrast immediately distal to the proximal cap of the CTO could identify and enlarge these microvessels, creating a passage for crossing the CTO with a floppy guidewire. **Methods:** A total of 32 patients with a CTO were treated with this technique. Following few millimetres penetration of the proximal fibrous cap of the occlusion with a dedicated CTO guidewire, the over-the-wire balloon was advanced into the proximal portion of the occlusion, and 50–100 μg of nitroglycerine followed by 1 ml of contrast was gently injected into the occluded segment. Technical success of the microchannel technique was defined as the ability to visualize the distal true lumen with microinjection of contrast and thereafter cross the CTO with a floppy guidewire in the absence of any dissection. **Results:** Overall, technical success of the microchannel technique was obtained in 20 (63%) with angiographic success in 19. In 12 (37%) cases there was a technical failure because of dissection, and we obtained recanalization of the artery in 7 of these 12 cases with another technique. There was only one case of periprocedural myocardial infarction in an unsuccessful procedure and no major adverse cardiac events or subacute stent thromboses were observed. **Conclusions:** Microinjection of contrast immediately distal to the proximal fibrous cap of a CTO may be an additional technique to facilitate recanalization of CTO.

Key words: chronic total occlusion; microchannel; coronary; percutaneous coronary intervention

INTRODUCTION

Numerous approaches and novel devices have been developed to cross chronic total occlusions (CTO), nevertheless there is still a high number of unsuccessful procedures with the commonest reason being failure to cross the lesion with the guidewire [1–3]. CTOs differ in their anatomic characteristics (i.e., site, length, age, blunt, or tapered morphology) and in their pathological composition compared to standard stenosis. A CTO often starts as a ruptured plaque with bidirectional thrombus formation. With time, the thrombus and lipid are replaced at first by collagen and later also by calcium. The fibrous tissue is particularly dense at the proximal and distal ends of the lesion, creating fibrous caps surrounding a softer core of organized thrombus and lipid [4,5].

Histological examination of CTOs has identified that the majority have intraluminal microchannels which can vary in size from 100–500 μm [5,6]. Strauss et al. have proposed that these intraocclusion microvessels may provide a pathway for guidewire crossing of a CTO [7]. We postulated that by contrast injection immediately distal to the proximal cap of the CTO we could identify and enlarge these microvessels creating a passage for crossing the CTO with a guidewire. In this study, we report our initial experience with this technique.

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MATERIALS AND METHODS

Patient and Lesion Selection

All CTOs attempted by a single operator (MC) between October 2006 and May 2007 were evaluated for this prospective observational study. The inclusion criteria were a CTO of greater than 3 months in duration in a patient with persistent angina on optimal medical therapy and documented ischemia in the territory of the occluded segment. The exclusion criteria were very short occlusions (<5 mm), very long occlusions (>50 mm), unfavorable angle (≤90°) of take-off of the occlusion, and occlusive in-stent restenosis. Among 45 patients satisfying the inclusion criteria, 13 of them had the following exclusion criteria: very short occlusion length in 5, long occlusions in 4, an unfavorable angle in 3, and occlusive in-stent restenosis in 1. All patients provided informed consent for the procedure and subsequent data collection and analysis for research purposes. Glycoprotein IIb/IIIa receptor inhibitors, when required, were only given after successful recanalization of CTO and exclusion of coronary perforation.

Description of Technique

An example of this technique is illustrated in Fig. 1A–E.

1. Selection of an appropriate guide catheter providing excellent backup and support.
2. A 1.5-mm over-the-wire (OTW) balloon with a floppy wire was advanced to the site of the occlusion abutting the proximal fibrous cap and the CTO was probed with the floppy wire to exclude a subtotal occlusion.
3. The floppy wire was exchanged for a dedicated CTO wire (Conquest/Confianza or Miracle family; Asahi Intecc, Nagoya, Japan/Abbott Vascular Devices, Redwood City, CA).
4. The proximal fibrous cap was penetrated centrally with the dedicated CTO wire for only 1–3 mm (Fig. 1B).
5. The OTW balloon was then advanced into the proximal portion of the occlusion simultaneously removing the wire.
6. About 50–100 μg of nitroglycerine was injected via the OTW balloon to dilate the microchannels.
7. At this stage 1 ml of undiluted contrast (using a 2.5-ml syringe) was gently injected via the OTW balloon while taking cine images of the occluded segment.

There were three possible outcomes after the microinjection (Fig. 2):

1. Contrast passed through microchannels and there was distal visualization of the true lumen (Fig. 1C). In those cases we were usually able to successfully pass a floppy wire across the occlusion.
2. It was impossible to inject contrast due to high resistance. In those cases we advanced the dedicated wire 2–3 mm further into the occlusion and repeated steps 5–7.
3. Microinjection revealed a dissection. Depending on the characteristics of the dissection, the operator may have decided to either stop the procedure at this stage or complete recanalization of the CTO with another technique.

Clinical Definitions and End-Points

A CTO lesion was defined as an obstruction of a coronary artery with thrombolysis in myocardial infarction (TIMI) flow grade 0 with an estimated duration of at least 3 months. We defined severe calcification as radiopacities noted without cardiac motion before contrast injection generally compromising both sides of the arterial lumen [8]. Technical, angiographic, and clinical success rates were examined as well as procedural complications. Technical success of the microchannel technique was defined as the ability to cross the CTO with a floppy wire, in the absence of a dissection, with distal guidewire placement in the true lumen after intraocclusion microinjection of contrast. Angiographic success was defined as a residual stenosis <20% and a final TIMI flow grade 2 or higher. Procedural success was defined as angiographic success and freedom from major adverse cardiac events (MACE) defined as death, myocardial infarction (MI), elective or emergency bypass surgery, or repeat percutaneous coronary intervention (PCI) during index hospitalization. Composite 30-day MACE rate reflects the safety of the procedure and was defined as death, MI, and target lesion revascularization (CABG or repeat PCI). MI was defined as an increase in total CK to two times the upper limit of normal in conjunction with a two times elevation in the CK-MB. In all patients CK were evaluated every 6 hr for three times following the procedure and until normalization if they were elevated; CK-MB were obtained in every patient showing elevated total CK more than two times normal values.

Statistical Analysis

Continuous variables are presented as means ± standard deviation and categorical variables as frequencies (%). Continuous variables were compared using independent sample Student *t* test. Categorical varia-

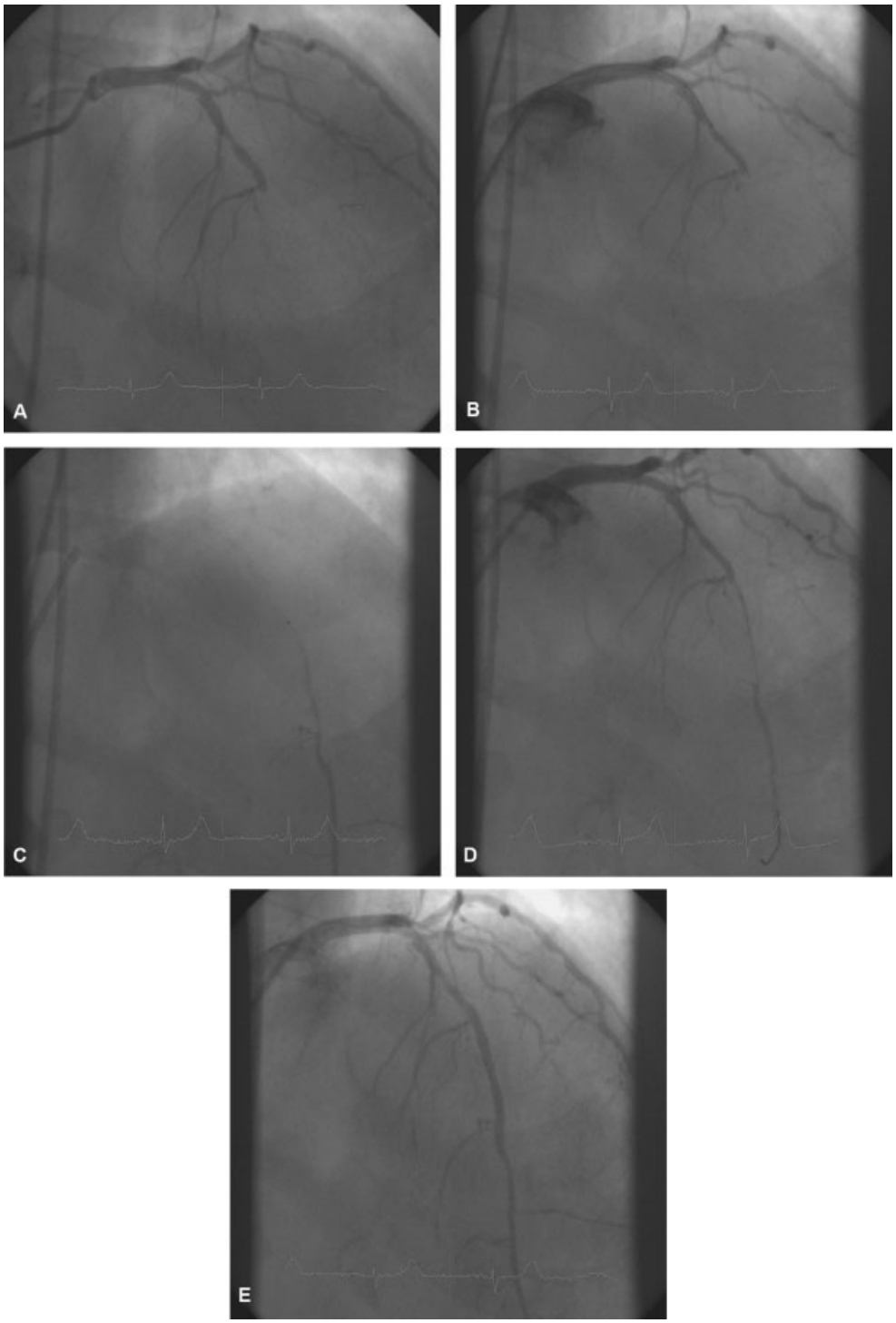

Fig. 1. Demonstration of the microchannel technique utilized to recanalize a CTO of the mid-LAD. (A) Baseline angiogram showing a blunt occlusion of the mid-LAD with a side branch at the site of the occlusion; (B) A Conquest guidewire mounted on an OTW balloon penetrating the proximal fibrous cap by only a few millimetres; (C) Intraocclusion microinjection of contrast revealing the distal true lumen; (D) Length of occlusion after angioplasty with a 1.5 × 15 mm OTW balloon at 10 atm; (E) Final result after stenting with Taxus 2.75 × 28 mm and 2.5 × 12 mm in series.

bles were compared with χ^2 statistic or Fisher's exact test where appropriate. Fisher's exact test was employed when the parametric assumptions underlying χ^2 did not hold (conventionally when the number of events in one or more classes is less then 5). A *P*-value of <0.05 was considered to be statistically significant and all reported *P*-values are two-sided. Statistical analysis was performed using SPSS 11.5 (SPSS, Chicago, IL).

RESULTS

Between October 2006 and May 2007, 32 patients underwent an attempt to recanalize a CTO with this technique as the primary strategy. The baseline patient and lesion characteristics are presented in Tables I and II. The median age of occlusion was 9 ± 6 years and the mean occlusion length was 23.7 ± 14.7 mm. The target vessel was the left anterior descending artery in seven patients (22%), the circumflex or obtuse marginal artery in eight (25%), and right coronary artery in 17 (53%). All vessels with a target CTO had collaterals supplying the distal vessel, including bridging collaterals in 15 vessels (47%) and ipsilateral or contralateral retrograde collaterals in the remainder. The majority of the lesions had a blunt morphology (78%) and were located in the ostial or proximal part of the vessel (68%).

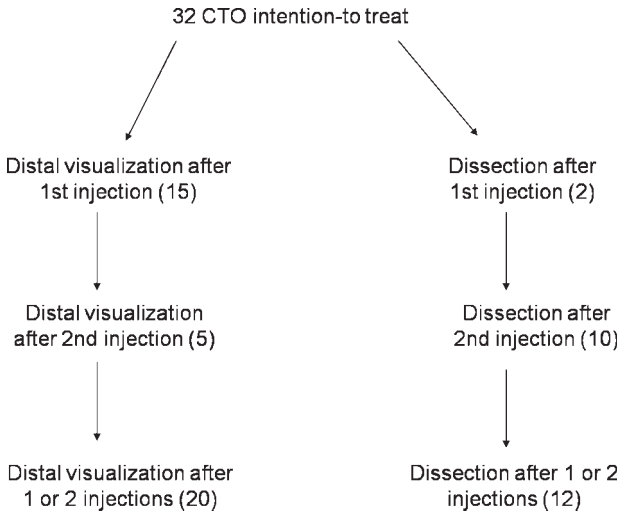

Fig. 2. A flow diagram demonstrating results after the first and subsequent microinjections in this cohort.

The outcome and complications of the cohort treated with the microinjection technique is presented in Fig. 2 and Table III. Overall technical success of microchannel injection was obtained in 20 (63%) with angiographic success in 19 (95%) of these 20. In one case, despite being able to cross the lesion with the guidewire, it was impossible to advance a balloon through the occlusion. In the remaining 12 cases there was a technical failure. Severe calcifications, side branch at the occlusion site, and occlusion length were associated with failure (Table II). In two (17%) cases there was a linear dissection with a tubular configuration after the first injection. In the other 10 (83%) cases, there was no visualization of microchannels, further advancement of the wire and OTW balloon into the occlusion and a second injection resulted in dissection. In seven (58%) of these 12 cases, we obtained a recanalization and final angiographic success by performing the subintimal tracking and re-entry technique (STAR technique) [9]. During all the procedures there were no cases of coronary perforation or rupture.

TABLE I. Baseline Clinical Characteristics

Variables	Total pts (n = 32)	Microchannel Success (n = 20)	Microchannel Failure (n = 12)	P value
Age	62.7 ± 9.7	62.7 ± 10	62.7 ± 9	0.1
Male sex	31 (96.9%)	20 (100%)	11 (91.7%)	0.3
LVEF	51 ± 8	50 ± 9	52 ± 7	0.6
Diabetes	17 (53%)	11 (55%)	6 (50%)	0.5
Hypertension	24 (75%)	15 (75%)	9 (75%)	0.6
Hyperlipidemia	23 (72%)	14 (70%)	9 (75%)	0.5
Current smoking	5 (15.6%)	3 (15%)	2 (16.7%)	0.5
Unstable Angina	1 (3)	1 (5)	0	0.6
Chronic stable angina	27 (84%)	16 (80%)	11 (91.7%)	0.3
Previous MI	20 (62.5%)	13 (65%)	7 (58%)	0.4
Previous PCI	17 (53%)	11 (55%)	6 (50%)	0.5
Previous CABG	15 (47%)	8 (40%)	7 (58%)	0.2
Prior attempt at CTO recanalization	6 (18.8%)	4 (20%)	2 (16.7%)	0.6

Values are presented as numbers (%) or mean ± standard deviation. LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary artery intervention; CABG, coronary artery bypass grafting; CTO, chronic total occlusion.

TABLE II. Lesion Characteristics

Variables	Total pts (n = 32)	Microchannel Success (n = 20)	Microchannel Failure (n = 12)	P value
Vessel				
LAD/diagonal	7 (22%)	7 (35%)	0	0.02
CX/OM	8 (25%)	4 (20%)	4 (33%)	0.3
RCA	17 (53%)	9 (45%)	8 (66.7%)	0.2
Calcified lesion	29 (90%)	18 (90%)	11 (91.7%)	0.6
Severe calcification	7 (22%)	1 (5%)	6 (50%)	0.006
Bridging collaterals	15 (47%)	10 (50%)	5 (41.7%)	0.4
Side branch at occlusion	22 (68%)	11 (55%)	11 (91.7%)	0.03
Ipsilateral collaterals	16 (50%)	8 (40%)	8 (66.7%)	0.1
Controlateral collaterals	15 (47%)	9 (45%)	6 (50%)	0.5
Morphology				
Blunt	25 (78%)	15 (75%)	10 (83%)	0.4
Age of occlusion (yrs)	9 ± 6	8.7 ± 6.8	10 ± 5.8	0.6
Unfavourable angle (≤90°)	4 (12.5%)	1 (5%)	3 (25%)	0.09
Occlusion length (mm)	23.7 ± 14.7	18.5 ± 9.1	33.6 ± 18.5	0.01
Location				
Ostial	3 (9%)	1 (5%)	2 (16.7%)	0.3
Proximal	19 (59%)	12 (60%)	7 (58%)	0.6
Medial	5 (16%)	4 (20%)	1 (8%)	0.3
Distal	5 (16%)	3 (15%)	2 (16.7%)	0.6

Values are presented as numbers (%) or mean ± standard deviation. LAD, left anterior descending coronary artery; CX, left circumflex artery; OM = obtuse marginal artery; RCA, right coronary artery.

TABLE III. Procedural Characteristics, Complications, and Outcomes

Variables	Total pts (n = 32)	Microchannel Success (n = 20)	Microchannel Failure (n = 12)	P value
Procedure time (mins)	132 ± 63	122 ± 65	146 ± 59	0.3
Fluoroscopy time (mins)	49 ± 31	39 ± 26	64 ± 32	0.03
Contrast dose (mls)	447 ± 214	393 ± 188	531 ± 233	0.09
Dissection	12 (37%)	0	12 (100%)	<0.001
Perforation limiting procedure	0	0	0	–
Rupture	0	0	0	–
CTO crossing or attempt time (mins)	45.5 ± 27	33.7 ± 17	68 ± 28	<0.001
Angiographic success	26 (81%)	19 (95%)	7 (58%)	0.01
Clinical Success	25 (78%)	19 (95%)	6 (50%)	0.003

Values are presented as numbers (%) or mean ± standard deviation.

Only one patient (5%), who had a technically unsuccessful procedure, had a periprocedural MI after the STAR procedure. Clinical follow-up was available in all patients at 30 days. During the follow-up period no additional MACE or subacute stent thrombosis occurred in any of the patients.

DISCUSSION

The main findings of this study are: (1) the technical success of microinjection in selected de novo CTO's was 63%; (2) when the microchannel technique failed, procedural success was achieved with a different approach in the majority of cases; and (3) in this initial experience the microchannel technique appears safe with a low risk of complications.

Recanalization of a CTO remains technically challenging with overall success rates between 70 and 80% even with the use of new dedicated wires [1,10]. The commonest reason for a procedural failure is the inability to cross the lesion with a guidewire [1–3]. Contrast injection via an OTW balloon into the distal vessel to confirm that one is in the true lumen has long been accepted as a useful technique in CTO intervention. Our technique developed as an evolution of this approach as we attempted to perform these injections more proximally to identify a roadmap of the obstructed vessel utilizing microchannels. In doing this, we found that in some cases we were clearly identifying preformed microchannels and the contrast not only delineated a roadmap of the occlusion but also provided a new passage across the occlusion that could be crossed by a floppy wire.

Recently innovative imaging techniques (micro-CT) have been used by Strauss et al. to visualize and confirm the presence of these intraocclusional microchannels [7]. These microchannels have already been considered as an important conduit for CTO crossing, either by dedicated tapered guidewires [6] or by the intracoronary infusion of thrombolytics [11]. It has been proposed that these techniques utilize microchannels to facilitate CTO crossing. Our technique uses fluid to identify and possibly dilate these microchannels in a nonaggressive manner. We feel that the contrast follows the path of least resistance in the occlusion, which is likely to be the preformed microscopic spaces of the microchannels. Our hypothesis is that when the balloon tip is in direct contact with the origin or the proximal part of a microchannel, the injection will identify and potentially dilate this channel and facilitate wire crossing. If on the other hand there is no direct contact the injection may cause a new tract to form into the already preformed microchannel.

It would appear from this small cohort that possible unfavorable characteristics for success of this technique include severe calcification, longer occlusions, and an unfavourable angle of take-off of the occlusion. The presence of severe calcification in the occlusion makes it more difficult to penetrate and advance the tip of the OTW balloon into the proximal cap in a precise way. An alternative interpretation is that a CTO with severe calcification has less viable tissue and thus fewer microchannels [6]. We also did not attempt this technique in patients with occlusive restenosis as the pathology of these lesions is different from de novo occlusions as they have greater amounts of fibrous tissue and less neovascularization. The more acute the angle between the proximal vessel and the occluded segment, the greater the difficulty in directing the OTW balloon around the bend and placing it in the proximal cap due to the curve straightening the tip of the balloon. After our initial difficulties in using this technique in occlusions with an unfavorable angle, we started excluding this type of lesion. Bridging collaterals have generally been considered an angiographic predictor of CTO recanalization failure. There appears to be a trend to the presence of more bridging collaterals in the microchannel success group. Bridging collaterals may be evidence that microchannels exist as the same stimulus for neovascularization may stimulate both types of vessels.

In summary we would advise the use of this technique in CTOs according to our inclusion and exclusion criteria. An important aspect for successfully performing this technique is the ability to accurately puncture the central part of the proximal cap with the tip of the guidewire penetrating parallel to the long axis of the occluded segment. The microchannel technique should be attempted as the initial approach rather than a crossover from another technique where subintimal passage of the guidewire may have occurred. In the latter instance, the microinjection technique should be avoided or used with extreme caution as it may result in extension of the dissection. It is important to consider that in this study, a final success was obtained utilizing an extensive subintimal dissection pathway (STAR technique) in seven patients. The operator should be familiar and confident with such an approach before considering to use it as a safe alternative.

Although this report presents the initial results with this technique in only a small group of patients, it is reassuring that this approach was not associated with any serious procedural complication. Even though this technique was not successful in 37% of patients, it did not jeopardize the chance of successful recanalization as most of these patients were successfully recanalized with another technique. In this study we did not use contralateral injections or hydrophillic wire probing in any patient. We cannot deny that the success of this technique may be further enhanced utilizing these additional technical aspects.

CONCLUSIONS

Microinjection of contrast through a balloon catheter immediately distal to the proximal fibrous cap of a CTO may be considered an additional technique to facilitate recanalization of CTO. Further studies are needed to better define the role, the safety and the type of CTO most suitable for this approach.

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