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Chronic total coronary occlusion revascularisation positively modifies infarct-related myocardial scar responsible for recurrent ventricular tachycardia

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Running Title

Modulation of scar causing ventricular tachycardia

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Abstract

Aims: Can revascularisation of an infarct-related artery chronic total occlusion (IRA-CTO) have a modulatory effect on myocardial scar composition?

Methods and Results: This is a unique, first-time report of 3 consecutive patients presenting with myocardial scar-related recurrent ventricular tachycardia (rVT) on a background of ischaemic cardiomyopathy. Electro-anatomic mapping of the left ventricular endocardium was performed before and immediately after IRA-CTO percutaneous coronary intervention (PCI) to assess for changes in scar composition and size. There were substantial percentage reductions in the low voltage area of scar compared to baseline after IRA-CTO PCI (Patient 1: -12.8%, Patient 2: -27.0%, and Patient 3: -15.3%). Interval remapping ≥6 months after the index procedure demonstrated extensive net reductions in all areas of myocardial scar (Patient 1: dense scar = -7.5%, border zone scar = -54.9%, low voltage area = -32.7% and Patient 2: dense scar = -38.6%, border zone scar = -59.6%, low voltage area = -51.7%). Patient 3 declined interval remapping but has remained free of rVT at 1-year follow up.

Conclusions: IRA-CTO PCI may positively modify the size and composition of myocardial scar associated with rVT in the context of ischaemic cardiomyopathy.

Classifications

Depressed left ventricular function, prior myocardial infarction, chronic coronary total occlusion, ischaemic cardiomyopathy

Abbreviations

CTO=chronic total occlusion

VA=ventricular arrhythmia

IRA=infarct-related artery

rVT=recurrent ventricular tachycardia

RFA=radiofrequency ablation

CMR=cardiac magnetic resonance

ICD=implantable cardioverter defibrillator

RCA=right coronary artery

LAD=left anterior descending

AVCx=atrioventricular circumflex

MI=myocardial infarction

PCI=percutaneous coronary intervention

Introduction

Coronary chronic total occlusions (CTO) confer a higher risk of ventricular arrhythmia (VA) and mortality (1). Studies also suggest a chronic occlusion of an infarct-related coronary artery (IRA-CTO) is an independent predictor of recurrent ventricular tachycardia (rVT) despite previously successful radiofrequency ablation (RFA) (2). Whether revascularisation of an IRA-CTO in patients with ischaemic cardiomyopathy complicated by rVT has a modulatory effect on myocardial scar is unknown.

Methods

Three consecutive patients presented to our institution with rVT from November 2015 to July 2016. High-density multi-electrode electro-anatomic mapping (EAM) of the left ventricular endocardium was performed before and immediately after IRA-CTO revascularisation, using CARTO® 3 (Biosense-Webster, Diamond Bar, CA, USA) or EnSite™ NavX™ Velocity (St Jude Medical Inc., Milwaukee, WI, USA) mapping systems in conjunction with PentaRay® or Livewire™ catheters. This was performed as a single procedure.

Following an interval period of at least six months, patients were brought back for high density scar remapping prior to planned VT ablation. All patients provided written informed consent for their procedures.

Results

A 60-year-old gentleman with ischaemic cardiomyopathy and an IRA-CTO of his right coronary artery (RCA) presented with rVT. He had had a successful VT ablation and an implantable cardioverter-defibrillator (ICD) in situ from 4 years previously. EAM revealed low voltage scar around the mid and basal aspects of the inferior wall consistent with previous myocardial infarction (MI) and ablation (Online Supplementary Figure 1). Immediately after RCA CTO percutaneous coronary intervention (PCI) (Online Supplementary Figure 2), remapping revealed extensive changes in the composition and dimension of the myocardial scar. After a six-month interval, remapping revealed further changes in scar characteristics (Online Supplementary Table 1). The patient has remained free of significant VT after repeat RFA at one-year follow up.

A 77-year-old gentleman with ischaemic cardiomyopathy presented with rVT. Angiography revealed a left anterior descending (LAD) artery CTO. EAM revealed low voltage scar around the apex, anterior and antero-septal walls, consistent with a previous anterior infarct. The patient proceeded to LAD CTO PCI. Immediate remapping thereafter revealed a substantial reduction in both the low voltage and border zone areas, but no change in the dense scar area. After an eighteen-month interval, EAM revealed considerable net reductions in all areas of scar.

A 56-year-old gentleman presented with rVT. He had had a lateral MI fifteen years previously associated with an atrioventricular circumflex (AVCx) artery CTO. Cardiac magnetic resonance imaging demonstrated severely impaired left ventricular systolic function and a thin, akinetic lateral wall with evidence of viability in the anterior and inferior walls. EAM revealed low voltage scar around the lateral and posterior wall. AVCx CTO PCI was performed during the index admission. Immediate remapping thereafter showed reductions in all zones of the infarct territory. The patient declined the offer of interval remapping prior to VT RFA. He has remained in New York Heart Association class II with no further admissions for rVT.

Discussion

For the first time in the literature IRA-CTO PCI has been shown to induce an immediate reduction in the low voltage area of an infarct territory on EAM, followed by a further reduction after an interval period. There were also substantial reductions to the border zone and dense scar areas in the two patients who had interval remapping at ≥6 months prior to planned VT RFA.

A putative mechanism for the increased susceptibility to VA in post-MI scar is ischaemia. Chronic hypoperfusion circumventing the infarcted necrotic core may adversely impact the border zone by increasing regions of slow conduction, which provide substrate for re-entry. Revascularisation of an IRA-CTO may potentially lead to improved perfusion of the infarcted region thereby reducing ischaemic burden and the extent of the border zone area.

This novel observation could have wide ranging implications for the management of scar-related rVT. Rather than consider revascularisation of an IRA-CTO purely based on viability and the abolition of angina symptoms, our observations suggest there is scope to perform PCI in this lesion subset as a means of attenuating arrhythmogenic substrate. Furthermore IRA-CTO PCI could revolutionise the timing and efficacy of VT RFA. Performing VT RFA in those with ischemic cardiomyopathy and an ICD has been shown to significantly lower the rate of the composite primary outcome of death, VT storm and appropriate ICD therapy when compared to escalation of anti-arrhythmic therapy alone, especially when the patient has already been treated with amiodarone. Eradication of all induced VTs during an ablation can, however, be a long and difficult procedure. In performing PCI for this subset of patients with an IRA-CTO to reduce the border zone area first, we may potentially streamline and enhance the success of subsequent VT RFA by allowing for more targeted ablation.

Limitations

This is a small study so robust conclusions cannot be drawn. Moreover, the use of different mapping systems may have affected the continuity of the results. There is much to learn here and we accept these observations could simply be a play of chance. Hence the need for a prospective proof of concept study to better understand the effects of IRA-CTO revascularisation on scar-related VT substrate; its role in the long-term management of rVT; alongside hospital re-admission rates for VT and the burden of VT as assessed by ICD discharge and anti-tachycardia pacing volume.

Conclusion

Percutaneous revascularisation of an IRA-CTO may positively modify the size and composition of myocardial scar responsible for rVT, signaling a potentially novel indication for CTO PCI in a subset of patients with ischaemic cardiomyopathy.

Impact on Daily Practice

- IRA-CTO PCI may reduce the size and composition of myocardial scar in a subset of patients with ischaemic cardiomyopathy presenting with rVT.
- Further investigation is required but we suggest this observation could represent a novel and innovative indication for CTO PCI over and above the established need to mitigate angina symptoms when viability is demonstrated.
- IRA-CTO PCI could be performed as an adjunct to scar-mediated VT ablation to reduce ICD discharge, recurrent hospitalisation and to help moderate the use of anti-arrhythmic pharmacotherapy.

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Conflicts of Interest

AM, MP and DHS report no conflicts of interest pertaining to the work.

JS reports receiving speaker's fees from St Jude, Biosense and Bayer.

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Online Supplementary Data

Online Supplementary Figure Legends

Online Supplementary Figure 1 Left ventricular endocardial bipolar voltage maps

Online Supplementary Figure 2 Chronic total occlusion percutaneous coronary interventions

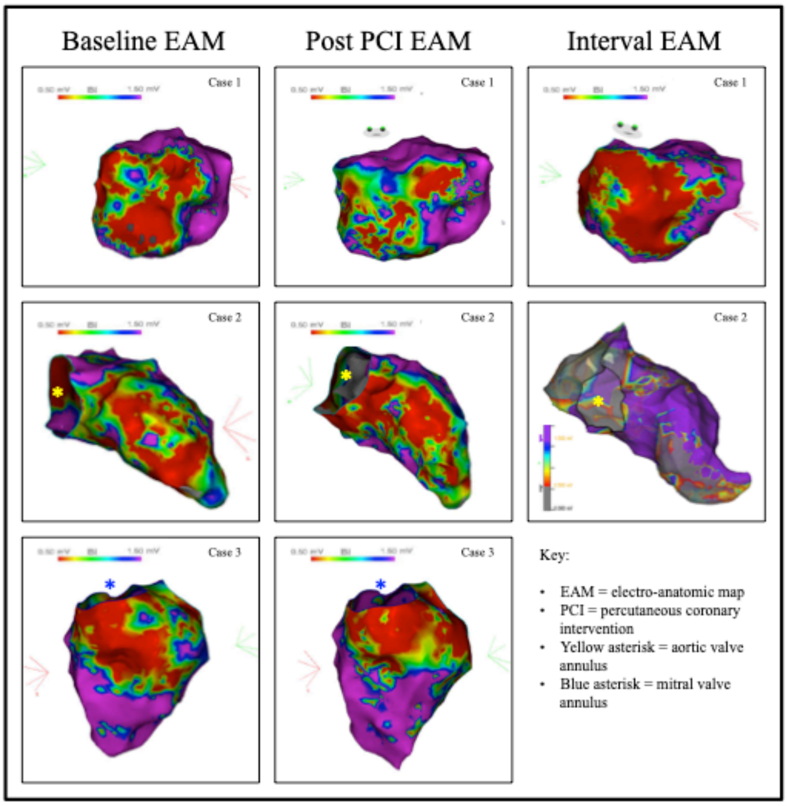
Online Supplementary Figure 1 Left ventricular endocardial bipolar voltage maps

Dense scar, where the isthmus site of a re-entry circuit is thought to be located, was demarcated at a bipolar voltage of <0.5 mV. Re-entry, in which an electrical impulse cycles repeatedly through an area of cardiac tissue, is thought to be the predominant mechanism instigating the generation of scar-related monomorphic VT. The low voltage area, where almost the entire diastolic portion of a re-entry VT circuit is usually found in ischaemic cardiomyopathy, was defined as a bipolar voltage of <1.5 mV. The border zone area, where over half of VT exits are found, was set at a bipolar voltage between 0.5 and 1.5 mV.

Patient 1: There is myocardial scar in the right coronary artery territory (anterior-posterior view) following a previous inferior myocardial infarction. Dense scar (<0.5 mV) can be seen in red, border zone scar (0.5 – 1.5 mV) is indicated by a spectrum of colours from yellow to green and low voltage scar (<1.5 mV) is represented in blue. Magenta signifies normal myocardium. After revascularisation the electro-anatomic map changes with a reduction in the dense scar and low voltage areas (see Table 1). After an interval of 6 months there is an increase in dense scar (although overall there has been a net reduction in size compared to baseline) and a substantial attenuation of the border zone scar and low voltage areas.

Patient 2: There has been an infarct in the left anterior descending artery territory (right anterior oblique view with aortic annulus removed). After coronary intervention, the dense scar area increases but the border zone scar and low voltage area have both decreased. After an 18-month interval there has been a considerable reduction in all the myocardial scar areas.

Patient 3: The scar is in the left circumflex artery territory following a lateral infarct (posterior-anterior view). Remapping immediately after coronary intervention demonstrates a reduction in all areas of the scar.

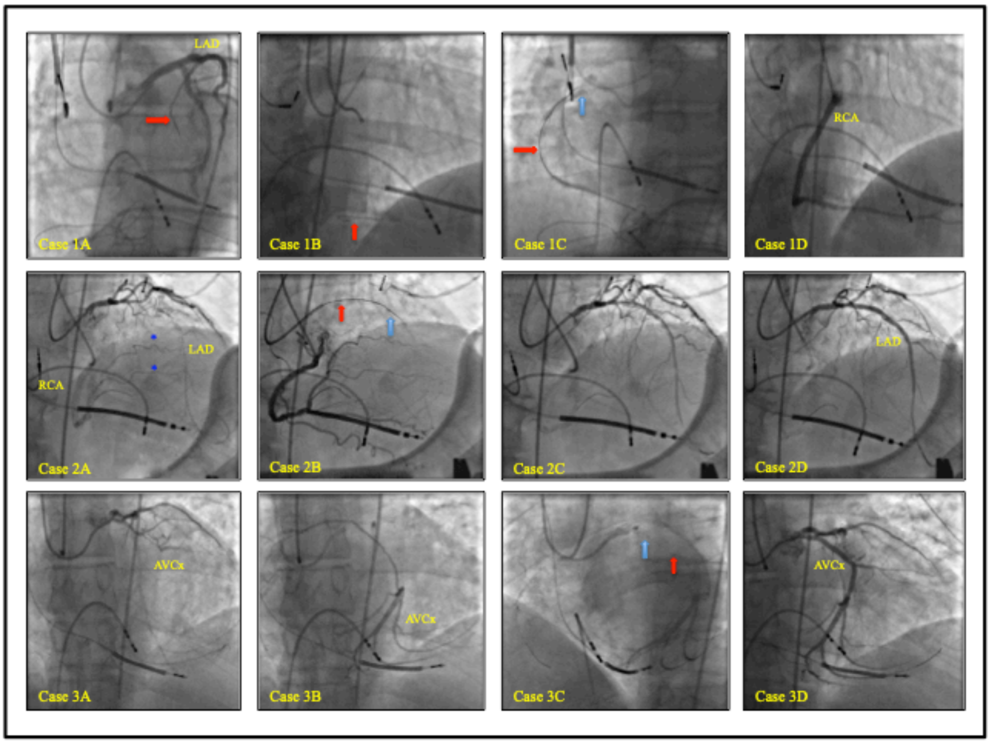


Online Supplementary Figure 2 Chronic total occlusion percutaneous coronary intervention

Patient 1: The occluded right coronary artery (RCA) was reopened using bilateral arterial access from the right radial and right femoral arteries, a retrograde approach via the first septal perforator (**Plate A: red arrow**), and a reverse controlled antegrade and retrograde subintimal tracking (CART) technique using a knuckled Fielder XT (Asahi Intecc, Aichi, Japan) (**Plate B: red arrow**) wire retrogradely, with antegrade rewiring of the retrograde Corsair (Asahi Intecc, Aichi, Japan) catheter (**Plate C: red and blue arrows**).[8] There was an excellent angiographic result (**Plate D**).

Patient 2: Revascularisation of the occluded left anterior descending (LAD) artery using bilateral arterial access from the right radial and right femoral arteries. There was a potential retrograde approach via distal RCA collaterals (**Plate A: blue asterisks**). A Finecross (Terumo Corporation, Tokyo, Japan) microcatheter (**Plate B red arrow**) and an Ultimate Bros 3 (Asahi Intecc, Aichi, Japan) guidewire (**Plate B: blue arrow**) facilitated an antegrade approach. Following balloon pre-dilatation (**Plate C**), three BioMatrix (Biosensors International, Singapore) stents were deployed (**Plate D**).

Patient 3: The occluded atrioventricular circumflex (AVCx) vessel was approached using bilateral arterial radial and femoral access (**Plate A**). The distal AVCx was visualized via collaterals from the RCA (**Plate B**). Using a Finecross microcatheter (**Plate C: red arrow**) and a Runthrough (Terumo Corporation, Tokyo, Japan) wire (**Plate C: blue arrow**), the short occlusion was negotiated via the antegrade approach. Three Orsiro (Biotronik AG, Bulach, Switzerland) stents were deployed (**Plate D**).



Key: LAD=left anterior descending artery; RCA=right coronary artery;

AVCx=atrioventricular circumflex artery.

Online Supplementary Table 1 Changes in myocardial scar geometry after IRA-CTO PCI

*The EnSite NavX Velocity system does not perform volumetric analysis.

Case 1	Baseline	Post IRA-CTO PCI	**Percentage change from baseline**	Interval mapping after 6 months	**Percentage change from baseline**
Dense scar (cm^2)	34.6	17.9	**-48.2%**	32.0	**-7.5%**
Border zone scar (cm^2)	39.5	46.7	**+18.2%**	17.9	**-54.9%**
Low voltage area (cm^2)	74.1	64.6	**-12.8%**	49.9	**-32.7%**
Total surface area (cm^2)	323.5	320.1	**-1%**	230.6	**-28.7%**
LV volume based (ml)	327.2	327.1	**0%**	266	**-18.7%**
Number of points collected in LV	3749	4087	-	5806	**-**
Case 2	Baseline	Post IRA-CTO PCI	**Percentage change from baseline**	Interval mapping after 18 months	**Percentage change from baseline**
Dense scar (cm^2)	21.5	22.3	**+0.04%**	13.2	**-38.6%**
Border zone scar (cm^2)	40.6	26.6	**-34.5%**	16.8	**-59.6%**
Low voltage area (cm^2)	62.1	48.9	**-27.0%**	30.0	**-51.7%**
Total surface area (cm^2)	196.1	197.2	**0%**	199.6	**0%**
LV volume based (ml)	170.7	172.9	**+1%**	N/A*	**N/A***
Number of points collected in LV	907	839	**-**	957	**-**
Case 3	Baseline	Post IRA-CTO PCI	**Percentage change from baseline**		
Dense scar (cm^2)	15.8	13.1	**-17.1%**		

Border zone scar (cm^2)	14.3	12.3	**-14.0%**	
Low voltage area (cm^2)	30.1	25.5	**-15.3%**	
Total surface area (cm^2)	270.6	271.1	**0%**	
LV volume based (ml)	276.7	277.1	**0%**	
Number of points collected in LV	1162	2131	**-**	

Key: IRA-CTO=infarct-related artery chronic total occlusion; PCI=percutaneous coronary intervention; LV=left ventricle.