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Improvement of LV functional performance in the chronic total coronary occlusion during the late stage is associated with the extensive collateral development

Yuesong Yang[1*], Bradley Strauss[1], Beiping Qiang[1], Azriel Osherov[1], John J Graham[2], Garry Liu[1], Xiuling Qi[1], Nigel R Munce[1], Michelle Ladouceur-Wodzk[1], Normand Robert[1], Alexander J Dick[3], Graham A Wright[1]

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Purpose

To investigate whether left ventricular (LV) function and regional wall motion improvement are associated with the extent of collateral development in coronary chronic total occlusion (CTO).

Methods

In nine pigs a CTO was created by percutaneously inserting a fibrin plug (AngiosealTM) into the mid-to-distal left anterior descending artery (LAD). Animals were studied six (n=3) or twelve weeks (n=6) later prior to sacrifice. An x-ray angiogram confirmed the LAD CTO at those time points. Cardiac MR (CMR) studies were then conducted on a 1.5T (n=6) or on a 3.0T MRI system (n=3), which included SSFP short axis sections for wall motion and post-gadolinium LGE-MRIs for viability. After sacrifice, both right and left coronary systems were injected with Microfil. X-ray or MSCT angiography of the fixed heart was obtained. A longitudinal cardiac section including the CTO lesion, proximal/distal LAD and the borders of infarction was removed and prepared in gel, then imaged in a micro-CT system at 27 micron resolution. LV functional parameters including wall thickness at end-systole (WTES) and end-diastole (WTED) were measured in border zone, infarct and remote region. Systolic wall thickening (SWT) was calculated using as (WTES-WTED) x100/WTED. CMR and micro-CT data were processed using commercial software. The extent of collaterals on micro-CT images was rated qualitatively using a score from 0 to 3, indicating that no, minimal, moderate, or extensive collaterals were observed. A Student's t-test was used for the statistical significance of differences between measurements at 6 and 12 weeks.

Results

LGE-MRI determined the presence of LV myocardial infarction (MI). Tables 1 and 2 summarize the results of global and regional LV function measurements at both time points. Ejection fraction (LVEF) at 12 weeks was significantly greater than at 6 weeks (39.45±5.38% vs. 26.27±5.77%, P=0.01) although the extent of infarct was similar between these two groups (P=0.16). In border zone the WTES (11.31±1.72 vs. 8.67±0.57mm, P=0.04) and SWT (68.31±11.55% vs. 35.87±19.14%, P=0.01) increased at 12 versus 6 weeks. On the visual scores of collateral development, between 6 and 12 weeks, there was an increase in collateral number (1.33±0.58 vs. 2.83 ±0.41, p<0.003). Figure 1 similarly illustrates increased collateral development at the later time point.

Conclusions

Extensive collateral development during the late stage of myocardial repair after CTO may contribute to LV functional improvement through increased SWT in the border zone. This provides a potential explanation for preserved LV function witnessed in some patients with CTO.

[1]Sunnybrook Health Sciences Centre, Toronto, ON, Canada
Full list of author information is available at the end of the article

Table 1 KV function measurements in coronary CTO pigs

CTO duration	LVEF (%)	EDV (ml)	ESV (ml)	SV (ml)	CO (L)	LVM (g)	LV-MI (g)	% (M/LVM)
6 weeks (n=3, mean±SD)	26.27 ± 5.77	89.64 ± 20.59	65.73 ± 14/47	23.90 ± 8.33	1.61 ± 0.67	71.63 ± 15.39	7.77 ± 2.75	11.45 ± 5.67
12 weeks (n=6, mean±SD)	39.45 ± 5.38	185.90 ± 13.16	113.38 ± 14.51	73.60 ± 9.60	5.71 ± 1.21	129.11 ± 10.06	10.56 ± 2.44	8.21 ± 1.96
P value	0.0115	0.0001	0.0324	0.0001	0.0011	0.0002	0.1637	0.2351

Note: CTO-Chronic total occlusion, LVEF-Left ventricular ejection fraction, EDV-End-diastolic volume, ESV-End-systolic volume, SV-Stroke volume, CO-Cardiac output, LVM-Left ventricular mass at end-diastolic phase, LV-MI-Myocardial infarction mass.

Table 2 Regional LV wall thickness and systolic wall thickening in coronary CTO pigs

CTO duration	B-WTES (mm)	B-WTED (mm)	B-Wall thickening	I-WTES (mm)	I-WTED (mm)	R-WTES (mm)	R-WTED (mm)	R-Wall thickening (%)
6 weeks (n=3, mean ±SD)	8.67 ± 0.57	6.51 ± 1.36	35.87 ± 19.14	3.19 ± 0.49	2.82 ± 0.45	13.54 ± 2.16	8.38 ± 1.55	62.1 ± 5.10
12 weeks (n=6, mean ±SD)	11.31 ± 1.72	6.78 ± 1.31	68.31 ± 11.55	2.43 ± 0.64	2.07 ± 1.02	13.89 ± 3.22	8.72 ± 1.74	58.69 ± 9.58
P value	0.0403	0.7834	0.0142	0.1186	0.2756	0.8710	0.7828	0.5881

Note: CTO-Chronic total occlusion, B-Border zone, I-Infarction segment, R-Remote region, WTES-End-systolic wall thickness, WTED-End-diastolic wall thickness.

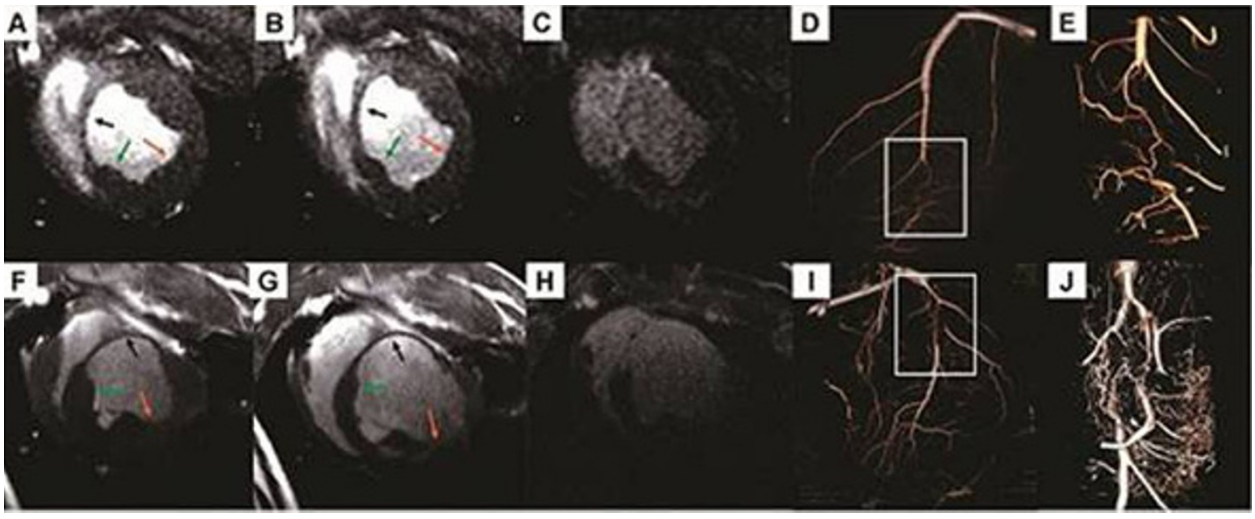

Figure 1 Compared to the minimal collateral formation in the 6 weeks' CTO animal (A-E), extensive collateral development was observed in the 12 weeks' CTO animal (F-J), which is consistent with the increased systolic wall thickening and better LV function performance measured from cine SSFP images in the late stage of CTO. A, F: end-systolic SSFP images; B, G: end-diastolic SSFP images; C, H: LGE-MRI images; D, I: rotational x-ray angiogram; E, J: 3D micro-CT images reconstructed from highlighted box regions of D and I. Black, green and orange arrows indicating infarct, border and remote region.

Author details
[1]Sunnybrook Health Sciences Centre, Toronto, ON, Canada. [2]St.Michael Hospital, Toronto, ON, Canada. [3]Ottawa Heart Institute, Toronto, ON, Canada.

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