Table 1
Comparison of the Main Clinical and Echocardiographic Characteristics of the Initial and the Validation Samples

Characteristics	MR ≥ 3 Initial sample[4] N = 177	MR ≥ 3 Validation sample N = 144	*P*
Clinical characteristics			
Age, y	81.3 ± 6.3	80.9 ± 5.2	.713
Male	102 (57.6)	96 (66.7)	.098
STS Score, %	5.1 [3.9-7.8]	4.7 [3.3-7.1]	.342
Logistic EuroSCORE, %	12 [9-18]	11.2 [6.9-16.9]	.441
Hypertension	129 (73.3)	101 (70.1)	.588
Diabetes mellitus	61 (34.7)	52 (36.1)	.758
Chronic kidney disease	44 (25)	35 (24.3)	.910
Prior heart surgery	23 (13.1)	17 (11.8)	.748
Prior atrial fibrillation	58 (33.1)	41 (28.1)	.407
NYHA class III-IV	77 (44)	58 (40.3)	.110
Echocardiographic characteristics			
Aortic valve area, mm^2	0.63 [0.5-0.78]	0.7 [0.4-0.7]	.899
Peak gradient, mmHg	80.9 ± 23.1	83.2 ± 21.3	.789
Mean gradient, mmHg	51.4 ± 15.6	52.4 ± 12.3	.882
Left ventricular ejection fraction, %	60 [49.5-66]	62 [48-68]	.210
SPPA, mmHg	50 [35-60]	47 [33-56]	.103

Values are expressed as No. (%), mean ± standard deviation, or median [25^{th}-75^{th} interquartile range], depending on variable distribution.
MR, mitral regurgitation; NS, nonsignificant; NYHA, New York Heart Association; SPPA, systolic pressure of pulmonary artery; STS, Society of Thoracic Surgeons.

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Available online 02 December 2018

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https://doi.org/10.1016/j.rec.2018.10.007
1885-5857/

Circulating MiRNA Dynamics in ST-Segment Elevation Myocardial Infarction-driven Cardiogenic Shock

Dinámica de microARN circulantes en pacientes con infarto agudo de miocardio con elevación del segmento ST con shock cardiogénico

To the Editor,

Cardiogenic shock (CS) occurs in approximately 5% of acute myocardial infarction cases and, despite improvements over the last few decades, it represents the leading cause of in-hospital mortality, remaining as high as 40%.[1]

MicroRNAs (miRNAs) bind target mRNA and act as posttranscriptional regulators of gene expression. MiRNAs can be detected in the circulation and have been proposed as promising biomarkers due to their robust stability to temperature changes and their resistance to degradation by endogenous RNase activity. More specifically, miR-21 is deregulated under cardiovascular disease conditions such as heart failure. MiR-122 has been reported to play a role in remodeling and fibrosis and in the early identification of ST-segment elevation myocardial infarction (STEMI) patients at higher risk of developing major adverse events after undergoing primary percutaneous coronary intervention (PCI), and has been found to be massively increased in a porcine model of CS.[2,3] MiR-320a and miR-423-5p are highly expressed in the fetal heart.[4] In addition, miR-320a is elevated in patients with chest pain of ischemic origin.[5] MiR-423-5p has been validated in patients with heart failure and its abundance is related to disease severity.[6]

Therefore, in the present study, we sought to assess the expression dynamics of these miRNAs during the first 24 hours

Table 1
Demographic and Clinical Characteristics of the Studied Patients

		No.
Age, years	67.8 ± 13.3	43
Male sex	28 (65)	43
Risk factors		
Smoking current/past	13 (30)/11 (25)	43
Hypertension	27 (63)	43
Diabetes	19 (44)	43
Dyslipidemia	23 (53)	43
Previous MI	3 (7)	43
Previous PCI	5 (12)	43
Presentation		
Anterior STEMI	28 (65)	43
SBP, mmHg	96.8 ± 31.6	43
DBP, mmHg	55.8 ± 17.1	43
HR, bpm	84.5 ± 29.1	43
Primary PCI	41 (95)	43
Time to reperfusion, min	197 [143-291]	41
Number of diseased vessels		
1	12 (29)	41
2	16 (39)	41
3	13 (32)	41
Left main disease	10 (24)	41
LEVF, %	38.6 ± 13.0	43
Lactate, mmol/L (on admission)	9.2 ± 6.0	7
Haemoglobin, g/dL (on admission)	11.7 ± 2.5	43
Creatinine, mg/dL (on admission)	1.7 ± 0.7	43
CK-MB peak, ng/mL	457.4 ± 444.6	43
cTnI peak, ng/mL	212.2 ± 328.0	43
Complications		
Out-of-hospital cardiac arrest	15 (35)	43
Ventricular fibrillation	13 (30)	43
Complete cardiac block	12 (28)	43
Management		
Mechanical ventilation	22 (51)	43
Inotropic drugs	40 (93)	43
Intra-aortic balloon pump	24 (56)	43
Other mechanical circulatory support (Impella)	1 (2)	43
Death at 30 d	19 (44)	43

CK-MB, creatine kinase-MB; cTnI, cardiac troponin I 99th percentile cutoff value for the upper reference limit: 0.5 ng/mL; DBP, diastolic blood pressure; HR, heart rate; LEVF, left ventricular ejection fraction; MI myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; STEMI, ST-segment elevation myocardial infarction.

after patient admission to the unit. This prospective observational study included 51 consecutive patients with STEMI complicated with CS (approximately 4% of 1265 STEMI admitted), treated with primary PCI between February 2011 and March 2015. Six were excluded due to mechanical complications, and 2 did not sign the informed consent form and were not included; finally, 43 patients fulfilled the inclusion criteria. All-cause death at 30 days was 44.2% (n = 19). In particular, inclusion criteria were systolic blood pressure < 90 mmHg (or $>$ 90 mmHg with vasopressors for $>$ 30 minutes), signs of poor peripheral perfusion, signs of pulmonary congestion and lack of rapid resolution after primary PCI. Postdischarge deaths were identified by telephone contacts and from electronic patient records.

Baseline demographics and clinical data were recorded during admission (Table 1). Serum samples were obtained at 3 time points (on admission immediately after primary PCI, at 12 hours, and at 24 hours), and stored at −80 °C until analysis. Total RNA was extracted from 200 μL of serum samples using miRCURY RNA Isolation Kit (Exiqon, Vedbaek, Denmark). A synthetic C elegans miRNA Cel-miR-39 (Qiagen, Hilden, Germany) was spiked in to normalize for extraction efficiency. Reverse transcription was performed with miScript II RT Kit (Qiagen) and quantification was performed using miScript SYBR Green PCR kit (Qiagen) and miRNA-specific miScript primer sets (Qiagen) on Roche LightCycler 480.

The study was approved by the Clinical Investigation Committee at Germans Trias i Pujol University Hospital and all participants, or their closest authorized relative, provided informed consent according to the declaration of Helsinki.

Analysis of the kinetics of the studied miRNAs revealed a significant increase in miR-320a and miR-423-5p at 12 hours

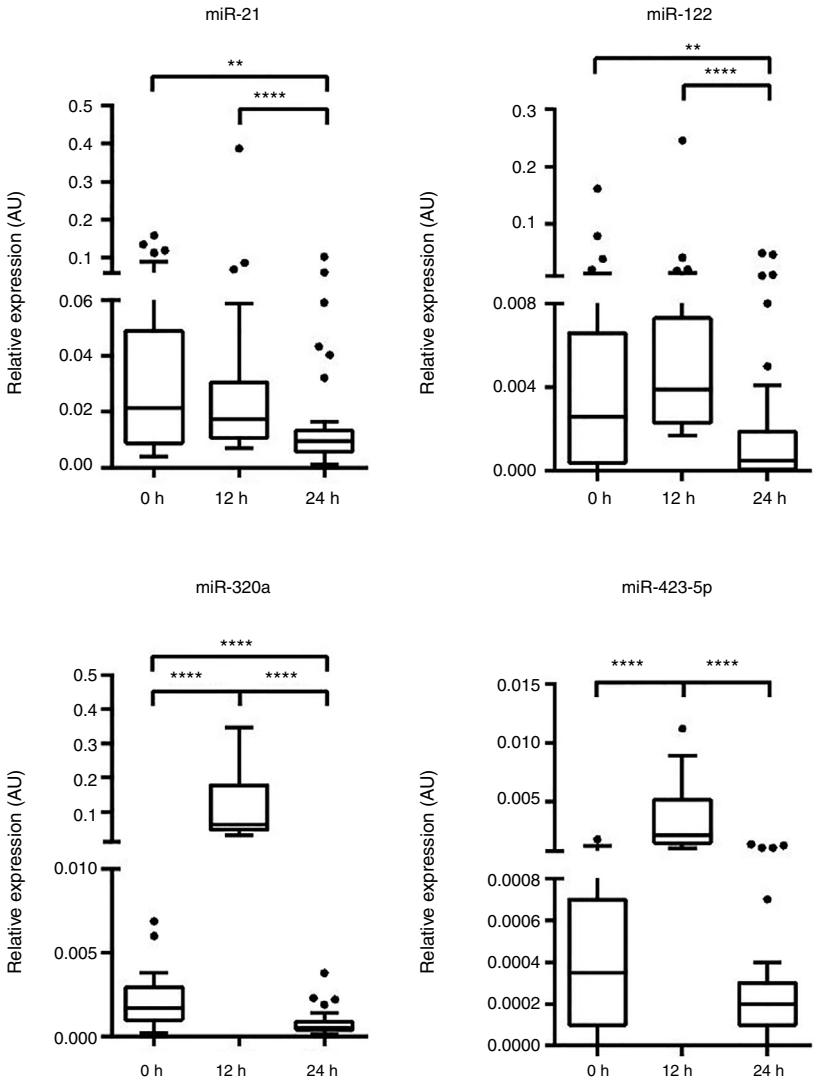

Figure 1. MiRNA dynamics in cardiogenic shock. Data are presented as boxplots with the median depicted and outliers as separate dots. The data account for 43 different patients at 0, 12, and 24 hours. $^{**}P < .01$ and $^{****}P < .001$. AU, arbitrary units.

compared with baseline ($P < .001$). However, all studied miRNAs decreased significantly from 12 to 24 hours ($P < .001$). MiR-21, miR-122, and miR-320a levels decreased significantly to below baseline ($P = .006$, $P = .003$, and $P = .000$, respectively), whereas miR-423-5p levels in the plasma returned to baseline ($P = .09$; Figure 1).

In the presence of the multiorgan damage that characterizes CS, the origin of this boost in miR-320a and miR-423-5p at 12 hours is uncertain. Remarkably, the 4 studied miRNAs returned to baseline (or lower) after 24 hours despite the persistence of CS.

Although interesting, these results should be interpreted with caution. The limitations imposed by the small cohort, the small set of miRNAs under consideration, and the focus on STEMI patients should be taken into account, as other circumstances may reflect differently on these miRNA data.

Circulating miRNAs have generated strong expectations as emerging genetic prognosticators in addition to the current peptide bioarmamentarium. Studying the dynamics of these miRNAs, we have been able to dissect a pattern that could indicate an unknown role in CS.

In conclusion, monitoring of miR-21, miR-122, miR-320a, and miR-423-5p in STEMI patients with CS revealed dynamic behavior during the first 24 hours after patient admission, with a peak at 12 hours.

Acknowledgements

We acknowledge Katariina Immonen for technical assistance.

FUNDING

This work was supported by grants from the *Ministerio de Educación y Ciencia* (SAF2014-59892), *Fundació La MARATÓ de TV3* (201502, 201516), CIBER Cardiovascular (CB16/11/00403), CERCA Programme (Generalitat de Catalunya), the Helsinki-Uusimaa Hospital District, the Finnish Foundation for Laboratory Medicine, and the Liv och Hälsa Foundation.

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Available online 22 November 2018

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1885-5857/

Endovascular Treatment of Recurrent Chylopericardium: In Vivo Demonstration of Chylopericardial Connections

Tratamiento endovascular del quilopericardio recurrente: demostración in vivo *de conexiones quilopericárdicas*

To the Editor,

A 53-year-old Caucasian woman was admitted to hospital for increasing dyspnea on exertion and episodes of near fainting. Echocardiography revealed pericardial effusion with evidence of tamponade. The chylous nature of the fluid was confirmed by the high level of triglycerides and by a cholesterol–triglyceride ratio, which was characteristically less than 1. Cytology demonstrated an abundance of lymphocytes. Surgical pericardial window was performed. Repeat echocardiography revealed recurrent severe effusion, for which a pericardial catheter was kept in place to enable continuous drainage. When the patient was placed on a low fat diet enriched with medium-chain triglycerides, drainage was reduced but was persistent.

The patient underwent extensive evaluation to identify the cause of the chylous pericardium. Routine laboratory tests demonstrated normal blood counts, electrolytes, liver function, lipid profile, serum urea, serum creatinine, serum calcium, and lactate dehydrogenase. There was no sign of systemic inflammatory reaction. Computed tomography (CT) of the chest revealed no obstruction to the thoracic duct. Pericardial fluid cultures were repeatedly negative for a bacterial cause. Tuberculosis was excluded by a negative Mantoux test and by repeat cultures and microscopic examination of specimens from the pericardial effusion.

Unfortunately, severe bilateral pleural effusion developed after withdrawal of the pericardial catheter. After multidisciplinary team discussion, the patient underwent surgical ligation of the thoracic duct. After initial improvement, the patient had persistent bilateral pulmonary effusion and moderate pericardial effusion.

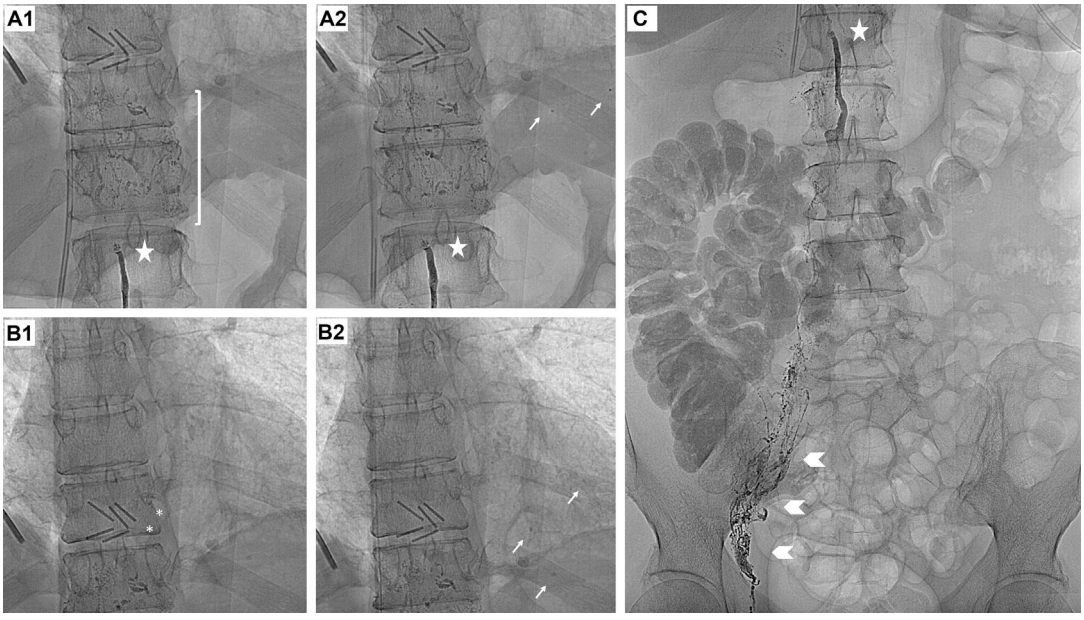

Figure 1. Lymphography showing ligation of the thoracic duct by surgical clips (A-B-C, stars). A2-B2 show spontaneous extravasation from the iodinated drops from the lymphatic system into the pericardium (arrows) by periiliac and pericava retroperitoneal injection of lymphatic contrast (ethiodized oil; C: arrowheads).