



Micro-RNAs as Biomarkers for Myocardial Damage

after Cardiac Surgery in Children

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 Successful treatment of a disease depends on <u>early detection</u> and <u>appropriate therapy</u>

 The presence of certain disease states can be identified by monitoring the expression levels of biomarkers (DNA, RNA, proteins)

• Biomarkers are an extremely important tool in areas like oncology, virology inflammation and heart disease

Acyanotic heart disease

- Blood is flows from the left side of the heart to the right side of the heart due to a structural defect (hole) in the interventricular septum.
- People with acyanotic heart disease retain normal levels of oxyhemoglobin saturation in systemic circulation.



Cyanotic heart disease

- Group-type of congenital heart defect (CHD)
- Occurs due to deoxygenated blood bypassing the lungs and entering the systemic circulation or a of oxygenated and unoxygenated blood entering the systemic circulation.





Procedure:

Norwood procedure

The Norwood procedure create a new functional systemic circuit in patients with hypoplastic left heart syndrome, or certain types of mitral atresia, or other conditions that result in single ventricle circulation.

Stage 1 : An aortopulmonary shunt is created to connect the aorta to the main pulmonary artery to provide pulmonary blood flow. Stage 2 : Glenn procedure- separation of the systemic and pulmonary circulation

Stage 3 : Fontan procedure



Procedure:

Bidirectional Glenn procedure

- The bidirectional Glenn shunt procedure involves rerouting circulation such that the superior vena cava (SVC) drains into the right pulmonary artery.
- This results in deoxygenated blood returning from the head and upper body directly routed to the pulmonary arteries for oxygenation by the lungs, reducing the ventricular workload.
- The blood passing from the SVC into the pulmonary arterial system flows bidirectionally into both right and left lungs.

Procedure:

Fontan

- The Fontan procedure involves diverting the venous blood from the right atrium to the pulmonary arteries without passing through the right ventricle.
- The venous blood from the IVC goes directly to the pulmonary arteries.







How efficient are the present biomarkers?

Troponin (Tn) and CPK, the present biomarkers, are insufficient as they are not specific enough

- Elevated values of the biomarkers in the absence of clinical evidence of ischemia could also occur as a consequence of other causes of cardiac injury such as: myocarditis, sepsis, cardioversion or ablation
- A major drawback of the contemporary Tn assays is their inadequate sensitivity during the first few hours after heart damage as they are released slowly from damaged cardiomyocytes and do not peak until 6 to 12 h after the onset of symptoms







Development of a diagnostic tool that will improve medical

management and outcome following cardiac damage

Adequate Biomarker should be:

- Stable
 - Rapid release kinetics
 - Specific to the organ we would like to monitor
 - Detectable in a small sample of serum

Micro-RNAs (miRNAs)

- MicroRNAs (miRNAs) are small, RNA molecules encoded in the genomes of plants and animals. They function as regulators of gene expression
- 2. Involved in all biological processes
- 3. <u>Tissue-specific</u> expression pattern
- 4. High biostability when excreted into plasma

Emerged as plasma biomarkers for many pathological states (cancer, diabetes, viral infections)





Our Study – Preliminary Results

- Samples were obtained from 40 pediatric patients with CHD, pre-operatively, 6 hours, 12 hours and 24 hours after the operation
- miRNAs were extracted from serum samples
- The relative amount of the miRNAs in plasma was measured by Quantitative RT-PCR (very sensitive)
- The miRNAs of interest:

miRNA-208a and miRNA-208b which are heart-specific miRNA-499 which is specific for skeletal muscle



Our Study – Clinical Parameters



- 1. <u>Age</u> at the time of operation
- 2. Days at the hospital
- 3. <u>Max. Inotropic score-</u> score for inotropic support (inotropic support include the following drugs: Milrinone, epinephrine, Norepinephrine, Dopamine, Dobutamine, Vasopressin)
- 4. <u>ACC-</u> An Aortic Cross-Clamp is a surgical instrument used in cardiac surgery to clamp the aorta and separate the systemic circulation from the outflow of the heart
- 5. <u>Cardiopulmonary bypass (CPB</u>) is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and the oxygen content of the patient's body
- 6. Lactate: indicating inflammation at 0hr, 6h, 12hr and 24hr
- 7. <u>Aristotle</u>: A score for evaluating the complexity of heart surgery





Results

		СРВ	ACC
MIR_208A_ 6h	Correlation Coefficient	476**	585**
	Sig. (2- tailed)	.004	.000
	Ν	34	33
MIR_208A_ 12h	Correlation Coefficient	347	557**
	Sig. (2- tailed)	.060	.002
	Ν	30	29
mir_208b_6 h	Correlation Coefficient	421*	527**
	Sig. (2- tailed)	.013	.002
	Ν	34	33
mir_208b_1 2h	Correlation Coefficient	245	459*
	Sig. (2- tailed)	.192	.012
	Ν	30	29
mir_499_6h	Correlation Coefficient	316	519**
	Sig. (2- tailed)	.069	.002
	Ν	34	33
mir_499_1 2h	Correlation Coefficient	286	426*
	Sig. (2- tailed)	.112	.017
	Ν	32	31

There is a correlation between: **ACC** and all three miRNAs at 6h and 12h (*p*-Value<0.05) **CPB** and miRNA-208A 6h, miRNA-208B 6h (p-Value<0.05)

Results



Results









Divide the pationts into several groups according to the type of operation and test correlations between the levels of miRNAs an the clinical parameters of each group

Four groups of patients will be considered:







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Thank-you!