Extended Abstract

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The Proper Delivery Pressure for Cardioplegic Solution in Neonatal Cardiac Surgery – An Investigation of Biomechanical and Structural Properties in Neonatal and Adult Coronary Arteries

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Introduction: One of the most important issues in pediatric cardiac surgery is myocardial protection to have good outcomes. As it is crucial to ensure an adequate heart function after aortic occlussion and cardiopulmonary bypass, which is needed for the surgical repair of congenital heart diseases, the care must be taken regarding this matter.

As congenital heart diseases are various and most surgical repairs are complex, it is crucial to maintain an adequate myocardial protection, especially when operating on neonates. Besides it has to be remembered that the immature myocardium has structural and functional characteristics varies from those of the adult myocardium. It is widely accepted that the immature heart has a greater tolerance to ischemia than the adult or mature heart, but it is more vulnerable to the increased amount of water, which is a problem for those using the crystalloid cardioplegia.

Cardioplegia is full electromechanical standstill of the heart when cardioplegic solution is injected into coronary arteries with a pump. Tissue preservation is achieved by conserving energy stores through rapid arrest which decreases the ongoing metabolic rate and minimises changes induced by ischemia with specific protective agents. The cardioplegic solution contains high concentration of potassium, which usually goes together with magnesium, procaine and hypothermia to increase the effectiveness. The most important goal of cardioplegia is to protect the heart against ischemic damage of myocardium. When cardioplegic solution is injected into coronary arteries with a pump in order to ensure myocardial protection, it is necessary to determine the correct delivery pressure to avoid damage of the heart. It has to be taken into report that coronary arteries in neonates are immature and much more fragile and simpler to damage. There are many structural, physiologic, biomechanical and metabolic diferences comparing to adults, therefore the myocardium of neonates may be more prone the pressure injury in pediatric than in adult cardiac surgery. Too high perfusion pressure would damage coronary arteries and myocardium. On the other hand, control of intraoperative myocardial affect depends also on the completeness of delivery of cardioplegic solution, therefore the right infusion pressure should be used.

Materials and methods: Eleven samples of neonatal coronary arteries and eight samples of adult coronary artery obtained from autopsies were used as experimental materials. The mean age of neonates was 12.3+/-13.7 days and the mean weight 4.1+/-0.9 kg. The length of the specimens was approximately 4 cm. After resection the specimens were kept in Custodiol Perfusion Solution no longer than 24 hours until the mechanical tests were carried out. A special device was used to estimate the internal pressure, axial force, longitudinal and circumferential deformation of the Coronary artery. A sample of coronary artery was gradually loaded by internal pressure from 0 to 220 mmHg while supporting the length of the sample

constant at $L_{\circ}$, the length in situ. The pressure was elevated gradually in 20-mmHg steps. The diameter was recorded at each pressure level. Structural changes were estimated after conventional sample fixation, embedding and sectioning using standard bright field optics and immunohistochemical En Vision protocols.

Results: We observed that the relationship between pressure and strain, and stress and strain in neonates was non-linear. There was a big difference between neonates and adults in terms of elastic modulus.

There was a rapid increase of strain until the inner pressure reaches 80 – 100 mmHg and not as rapid regarding to the stress in the arterial wall. When the internal pressure exceeds 100 mmHg the strain of the arterial wall increases much slower, but at the same time the wall stress and modulus of elasticity begin to increase rapidly.

The strain in the wall of neonatal coronary artery, when the inner pressure is 80 mmHg, reaches 32.71±6.59%, which is more than twice higher comparing to the adult coronary artery – 15.86±1.45%, . As for stress, it reaches 68.17±10.65 kPa with the same inner pressure in neonatal coronary artery and increases rapidly, when increasing the pressure. When it achieves 120 mmHg, the strain is 107.48±15.05 kPa, which is more than twice higher, comparing to the strain with inner pressure of 80 mmHg. The strain in the wall of adult coronary artery was 53.36 kPa. The stiffness in the wall of neonatal coronary artery increases rapidly comparing to adult, when the inner pressure exceeds 80 mmHg.

Modulus of elasticity of the wall of neonatal coronary artery is 867.08±199.43 kPa, when the inner pressure is 80 mmHg, but when it reaches 100-120 mmHg - 1176±215.42 kPa ($p<0.05$). In adults modulus of elasticity in the same pressure is 781.8±103.66 kPa, which is lower comparing to neonates. When the inner pressure increases from 60 mmHg to 120 mmHg, it increases from 641.42±36.14 to 825.25±108.64 kPa. In neonatal coronary artery it increases from 867.08±199.43 to 1494.49±331.01 kPa. It can indicate the possible damage in the wall of neonatal coronary artery, when the inner pressure exceeds 100–120 mmHg.

Conventional histological examination revealed partial damage and rupture of intimal and medial constituents of the wall of neonatal coronary artery under exposure of 120 mmHg comparing with rather intact vascular wall in adults. Analysis of elastic and contractile properties of the vascular wall assessed by use of appropriate immunohistochemical markers showed that vimentin expression

reflecting supportive strength created by intermediate filaments within the myocyte and pericyte cytoplasm was decreased under experimental conditions in neonates; vimentin-positive cells appeared through the wall demonstrating compactness in media before exposure, and loose distribution in markedly thickened muscular coat after exposure as well as lacking of expression from adventitia. Application of pressure at a rate 60-70 mmHg in neonates demonstrated remarkable disorganization and loosening of distribution of medial myocytes decorated with anti-actin antibody. Microvascular vasa vasorum stained with anti-CD34 demonstrated an universal adventitial expression, and a decrease of it applying pressure. Better preservation of microvascular beds stained for CD34 was noticed in younger adults. Finally, anti-desmin decoration revealed positivity appearing at the medial-adventitial interface of neonates, and lacking of it under exposure and with aging.

Conclusions: Collectively, our results based on examination of biomechanical properties and structural peculiarities of vascular beds suggest that delivering cardioplegic solution in neonatal coronary arteries everyone should be cautious applying pressure higher than 100 mmHg, thus increasing a risk of structural damage of the vascular wall, which, in turn, leads to the injury of myocardium.