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SAFETY DILEMMA OF LONG-TERM PROTECTION OF DEL NIDO / HTK CARDIOPLEGIA IN MINIMALLY INVASIVE VALVE SURGERY: CLINICAL IMPACT ON MICROVASCULAR INTEGRITY CONFIRMED BY CELL CULTURE DATA

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Key Words: Minimally Invasive Surgical Procedures; Valves; Myocardial Protection

**Objective:** Despite the popularity of single-dose cardioplegic techniques especially in minimally invasive surgery, the time window and targeted population for successful reperfusion remain unclear. The endothelial glycocalyx (EG) is fundamentally involved in numerous physiologic and pathophysiologic actions in the circulatory system. The present study aimed to compare plasma levels of syndecan-1, a biomarker of EG integrity, in patients undergoing minimally invasive valve surgery with either Del Nido or HTK cardioplegia verified by cell culture of myocardial cells.

**Methods:** This prospective cohort study included high-risk patients (Euroscore II >5) undergoing primary minimally invasive valve replacement and received different cardioplegia solutions between January 2017 and July 2018: Group 1: St. Thomas- N=35; Group 2: Del Nido- N=42 and Group 3: HTK- N=36.

Serum Syndecan-1 levels were measured by ELISA via arterial line before (T1) and via coronary sinus sample at the end of the cardiopulmonary bypass (CPB) (T2) with a solid-phase monoclonal BB4 antibody against an extracellular domain of human Syndecan-1.

A left ventricular punch biopsy specimen is collected at the end of CPB in each case and processed. Cells were incubated with LPS in combination with Lipopolysaccharide binding protein, IL-1 $\beta$  or with GM6001 in culture medium with 2% FCS until 24 h and were routinely grown to 80%–90% confluence. EG shedding (Syndecan-1, SC-12765) until 24 h was documented in microscopy.

#### Results:

There was not a significant difference among the groups with respect to demographic data, BMI and the change in the troponin-I levels at T1 and T2 (p = 0.162). Early perioperative data demonstrated that all three types or cardioplegia techniques provided effective clinical outcome with similar effects on blood biochemical parameters. Cross clamp time was 72±10 in Group 1, 69.4±10 for Group 2 and 67±12 min for Group 3 (p=0.232). Serum Syndecan-1 concentration is summarized in Table.

Microscopic imaging confirmed quantitative results of Syndecan-1 dying with different confluences (Figure).

#### Conclusion:

Myocardial preservation is a concept without clear and specific clinical signs. Given its importance, protection of the EG is undoubtedly a promising future target in cardiac operations.

Our data underlines the impact of current protection techniques on cellular function. A possible association between elevated syndecan-1 levels and postoperative complications needs to be clarified in larger studies.

### References

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	Serum Syndecan-1 T1 (ng/mL)	Serum Syndecan-1 T2 (ng/mL)	Cell Culture EG Shedding (Relative Fluorescence Units)- 24 h
St Thomas	28.3± 4.6	108.6± 5	16450± 3200
Del Nido	31.1±3.9	98.7±5.6	17450± 3500
НТК	29.2± 4.1	68.4± 5.3*	11650± 3400*

## Table: Quantitative Assessment of EG shedding of study groups

**Figure:** Syndecan-1 staining of LV punch biopsy cell culture of patients received St. Thomas (top), Del Nido (Middle) and HTK (Lower) Cardioplegia





