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**Titolo:** Biomarkers, genetics and epigenomics in pediatric VAD Patients

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**Lingua:** inglese

**Abstract:** Objective: Ventricular assist device (VAD) utilization is increasing in children with heart failure (HF) unresponsive to medical therapy, allowing for bridge to transplantation. The use of circulating biomarkers is crucial for the management of adult patients with HF, but their role in pediatric setting is unknown. In this study we assessed the effects of VAD implant on plasma levels of inflammatory and cardiac biomarkers as well as of circulating micro RNAs (miRNAs) in pediatric patients with HF. Methods: Blood samples were collected from 12 HF pediatric patients [73.91±27.94 (mean±SD) months, 6 males, 19±3.8 LVEF%, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles 1/2] before and at 4 hrs, 1, 3, 7, 14 and 30 days after VAD implant. Indications for support was idiopathic dilated (9 patients), non compaction (2 patients) and hypertrophic cardiomyopathy (1 patient). Inflammatory and cardiac biomarkers (Figure 1A) were measured in frozen plasma through the use of immunoassay tests. The circulating miRNAs were extracted from serum samples and miRNA profile was determined by NGS. and validated by real-time PCR. Results: Inflammatory and cardiac biomarker levels during time-course were reported in Figure 1A. Cytokines increased significantly up to 4 hrs after VAD implant, while cardiac biomarkers up to 1 day. Only NT-proBNP decreased significantly up to 1 month of VAD implant compared to pre-VAD values. After sequencing, a total of 169 miRNAs were detected in serum samples. Among them, 13 miRNAs were simultaneously modulated at 1 month after VAD implant compared to pre-VAD levels, i.e. 9 miRNAs decrease and 4 increase (Figure 1B). Real-time PCR validation confirmed a reduction for miR-409-3p and miR-432-5p. Finally, significant correlations with bio-humoral markers were observed for these miRNAs (Figure 1 C). Conclusions: VAD implant induced modifications in circulating levels of cytokine, cardiac biomarkers and miRNAs. NT-proBNP levels and miRNAs significantly decreased after 1 month compared to the values pre-VAD, suggesting the involvement of these biomarkers in molecular mechanisms triggered by VAD implant in children.

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