AHA-AEPC-JSPCCS-TSPC Joint Symposium

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Current Management of Severe CHF by Mechanical Support and Cardiac Transplant

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所属正式名称：安河内聰(長野県立こども病院循環器センター)、小野稔(東京大学医学部　心臓外科)、Euro Jokinen(Children's Hospital University of Helsinki, Finland)

[AJS-04]Transcoronary infusion of cardiac progenitor cells in hypoplastic left heart syndrome: 3-year follow-up of the TICAP trial

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Backgrounds- Hypoplastic left heart syndrome (HLHS) is one of the severe malformations in congenital heart diseases. Initial results of TICAP phase 1 study (NCT01273857) conducted in our hospital have shown that intracoronary infusion of cardiosphere-derived cells (CDCs) following staged palliation was feasible and safe to treat the patients with HLHS; however, the long-term safety and clinical outcomes remain elusive, as is the question whether any prognostic significance may provide independent information to predict the functional benefits in CDC recipients. **Methods and Design-** This trial is a prospective controlled study. Fourteen consecutive patients with HLHS who are undergoing staged-2 or -3 surgical palliations were enrolled between January 2011, and January 2012. Seven patients assigned to receive intracoronary CDCs infusion 1 month after the cardiac surgery followed by 7 patients allocated to a control group with standard care alone. The primary endpoint was to assess the procedural feasibility and safety and the secondary endpoint was to evaluate the cardiac function and heart failure status from the baseline through long-term follow-up. **Results-** No complications were reported within 30 months after CDC infusion. Endpoint analysis was assessed by echocardiogram and showed that right ventricular ejection fraction (RVEF) in CDC-treated group increased markedly during the follow-up period (baseline: 46.9±4.6 % vs. 30 months: 54.1±2.3%, P=0.0006). Absolute changes in RVEF were greater in the CDC-treated group than in controls at 30 months (+7.2 ± 4.8% vs. +2.7 ± 2.2%, P=0.04). Similarly, fractional area change calculated by echocardiogram was higher in the CDCs than in controls (39.2 ± 2.2% vs. 33.9 ± 4.5%, P=0.02). These cardiac function improvements in long-term resulted in decrease in BNP levels (P=0.02) and lower incidence of unintended coil occlusion for collaterals (P=0.03) at 30 months after CDC transfer compared with controls. In addition, continuous somatic growth (weight-for-age z score: WAZ) was evident in CDC-treated group through 30 months observation rather

than controls (P=0.00004). As independent predictors of treatment responsiveness, absolute changes in RVEF at 30 months were negatively correlated with age, WAZ, and RVEF at CDC infusion (age: r=-0.77, P=0.045; WAZ: r=-0.97, P=0.005; EF: r=-0.88, P=0.008). **Conclusion-** Intracoronary CDC infusion after staged procedure improves RVEF in patients with HLHS and that persists during 30 months of follow-up. This therapeutic strategy may merit somatic growth enhancement and reduce the incidence of heart failure as well as further collateral intervention after palliations. A randomized phase 2 trial (PERSEUS: NCT01829750) is ongoing in our hospital to verify the therapeutic efficacy as to determine the prognostic values and risk stratification in patients with single ventricle physiology.