Extracorporeal Membrane Oxygenation (ECMO): A Promising Option for Treating Adult Down Syndrome Patients?

Dear Editor,

Down syndrome (DS) remains the most common chromosomal disorder with the incidence of 1 in 700 babies in the United States. DS increases the risk of respiratory and congenital heart defects and therefore, increasing the need for extra life support.[1] Without surgery, congenital heart disease is a major source of morbidity and premature death. The life expectancy of patients with DS without any congenital heart defects is 60 to 70 years of age.[2] However, patients with congenital heart defects have 5 times higher risk of death as compared with people without any congenital defects.[3]

We read an article "Extracorporeal membrane oxygenation characteristics and outcomes in adult patients with down syndrome" published by Vicky Duffy et al emphasizing the use of extracorporeal membrane oxygenation in Adult DS patients with heart and respiratory failure which is refractory to all other treatments. The use of an extracorporeal membrane in the pediatric DS population with heart and respiratory failure has been emphasized in previous articles and is also used more often used as a last resort and it showed promising results for cardiac and respiratory support increasing longevity. In this latest article, the use of extracorporeal membrane oxygenation among the DS adult population and its clinical outcomes were evaluated. This study was conducted, using the Extracorporeal Life Support Organization registry database which highlighted the use of extracorporeal membrane oxygenation (ECMO) in 21 adult DS patients with the approximate incidence 0.88/1,000.[4,5] Among 21 DS patients who were studied, 9 patients were alive, and 12 patients were deceased. This study compared the differences in the characteristics among deceased and alive DS patients who used ECMO and the author did not find any significant difference except fewer incidences of mechanical and neurological changes among deceased DS patients who used ECMO. Also, the mortality rate was similar when compared with non-DS patients who were placed on ECMO. There were no remarkable outcome differences in ECMO using alive and deceased DS patients with regards to age, weight, gender, initial pH, initial pO2, duration of the extracorporeal membrane, oxygenation run, ventilator or extracorporeal membrane oxygenation mode, and nitric oxide use.

We would like to share our views as this study has some shortcomings due to the small sample size of adult patients, and not including other important variables. Pediatric DS patients are usually diagnosed early, treated appropriately, and they rarely require ECMO in adulthood. Therefore, in the literature, we have scarce data availability for adult DS patients using ECMO. Further data and more trials are necessary to clarify the actual role of ECMO before expanding its indications. Nevertheless, ECMO should be used in adult DS patients requiring critical life support with heart and respiratory failure which is refractory to all other treatments. It has the potential to alter the current paradigms for refractory cardiac and respiratory failure.

Disclosures

The authors has no conflicts of interest to disclose.

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Clinical Outcomes of Nonagenarians After Transcatheter Aortic Valve Implantation

Stehli et al conducted a follow-up study to evaluate the short- and mid-term outcomes of 71 nonagenarians after transcatheter aortic valve implantation (TAVI).[1] At 1 year, odds ratio (OR) (95% confidence interval [CI]) of nonagenarians against <90-year-old patients for living in an aged-care facility was 5.99 (2.62 to 13.67). I have some concerns regarding their study.

Goudzwaard et al investigated the association between frailty, delirium, and 1-year mortality in 213 older patients with TAVI.[2] Frailty was present in 61 patients (28.6%) and adjusted OR (95% CI) of frailty for delirium was 3.3 (1.55 to 7.10), and adjusted hazard ratio (HR) (95% CI) of frailty for 1-year mortality was 2.1 (1.01 to 4.52). These data presents that physical and mental illness in the elderly is also useful to evaluate the prognosis of nonagenarians.

Regarding to the first query, Anand et al conducted a meta-analysis to evaluate the association between frailty and clinical outcomes after TAVI.[3] Pooled HRs (95% CIs) of frailty for mortality ≤30 days and >30 days after TAVI were 2.35 (1.78 to 3.09) and 1.63 (1.34 to 1.97), respectively. In addition, pooled HRs (95% CIs) of subjective and objective assessment of frailty for mortality >30 days after TAVI were 1.42 (1.28 to 1.59) and 2.63 (1.87 to 3.70), respectively. Prognosis in nonagenarians after TAVI should also be evaluated by frail indicators to prevent subsequent mortality risk.

Second, Stehli et al presented wide range of 95% CI of OR. Although I cannot confirm that the authors conducted multivate adjustment, Peduzzi et al evaluated the effect of events per independent variable in logistic regression analysis, and events per independent variable value ≥10 are recommneded for stable estimates.[4] Anyway, limited number of events should be paid with caution.

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Interatrial Block: Thromboembolism Risk in the Absence of Atrial Fibrillation

Smietana et al presented a very good review on the possible mechanisms of cardiogenic thromboembolism in the absence of clinical atrial fibrillation (AF).[1] They succinctly highlighted the potential mechanisms including subclinical AF (incidentally detected by monitoring devices), atrial cardiomyopathy (collagen deposition and/or atrial myocardial fibrosis), left atrial appendage mechanical dysfunction (decreased appendage flow velocities, contractility dysfunction such as atrial standstill and/or variation in appendage morphology) and embolism from other sources (such as aortic atheroma or paradoxical embolism across interatrial septal defects).

The authors surprisingly did not even mention about interatrial block (IAB) or Bayes' syndrome in their review which in fact is a well-recognized risk factor for thromboembolism. IAB refers to a P-wave duration of >120 ms on surface electrocardiogram, while advanced IAB denotes a prolonged P-duration in association with biphasic P-morphology in the inferior leads representing caudocranial activation.[2–4] IAB has been shown to be a significant risk factor for stroke and other thromboembolic conditions including mesenteric ischemia.[2,5–7] Although IAB is a known precursor for atrial arrhythmogenesis, IAB can predispose to thromboembolism in the absence of atrial arrhythmias.[2–4] IAB, although may often accompany left atrial enlargement, is indeed a representative of left atrial electromechanical dysfunction, which may either precede or occur without the presence of left atrial enlargement and atrial arrhythmias.[2,3] IAB-induced electromechanical dysfunction causes a sluggishly contractile left atrium which may serve as a nidus for thrombi or microthrombi, and may increase the risk for thromboembolic events.[2,3,6,7] The propensity for thromboembolism, especially in advanced IAB appears independent of the associated atrial arrhythmias.[3] In smaller observational and retrospective studies, IAB has previously been shown to be associated with embolic stroke and systemic thromboembolism in patients without a history of known AF.[8] There has been a significant body of literature to also suggest that many patients develop systemic thromboembolism just by the virtue of an increased cardiac risk profile (such as the one estimated by the presence of a higher CHADS score, an acronym for congestive heart failure, hypertension, age >65 years, diabetes mellitus, and stroke), even without the presence of clinical AF.[3,9,10] The prospective Asymptomatic Stroke and Atrial Fibrillation Evaluation in Pacemaker Patients study demonstrated a sequential increase in the risk of cerebrovascular attack (CVA) with increase in CHADS score in all patients without clinical AF.[9] The results from another large prospective registry also demonstrated that the CHADS and CHADS-Vasc scores predicted CVA with fair accuracy in patients without AF and suggested a potential role for antithrombotic therapy in such patients based on their CHADS risk score.[10]

In fact, IAB may be an electrocardiographic hallmark which may either precede or even represent an underlying microstructural atrial cardiomyopathy. Some studies have debated that patients with high CHA2DS2-VASc and advanced IAB, even without known AF may be at high risk for stroke and may potentially benefit from anticoagulation.[3,4] Thus, IAB as a risk factor for thromboembolism should not be ignored by clinicians. IAB's specific risk contribution toward thromboembolism and its clinical application should be further investigated in the future in large randomized investigations.

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