News and Views

Clinical Outcomes in ARDS Patients with Diabetes

Acute respiratory distress syndrome (ARDS) patients with diabetes have adverse clinical outcomes evident as lower survival rate, longer lengths of stay in the hospital and intensive care unit (ICU) and higher levels of inflammation compared with those who did not have diabetes. These findings from a secondary analysis of data from the Fluids and Catheters Treatment Trial (FACTT) were published in the March 2024 issue of the journal *Respiratory Medicine*[1].

Researchers from the University of Georgia in Augusta, Georgia, USA conducted this secondary analysis of data from the FACTT, which compared two fluid management strategies (conservative and liberal) in patients with ARDS.

For the present study, 173 people with known diabetes and 794 without diabetes from the FACTT were enrolled and outcomes such hospital and ICU stays, days on ventilator till independent breathing and death at 90 days were examined. In-hospital mortality at 90 days was the primary end point of the study. The aim of the study was to investigate the impact of diabetes mellitus on critical care outcomes and explore potential biomarkers associated with these outcomes.

Participants with pre-existing diabetes had a poorer survival rate (61.3%) compared to those without diabetes (72.3%), which was statistically significant ($p = 0.006$). Diabetic subjects also had markedly longer duration of hospitalizations (24.5 vs. 19.7 days; $p = 0.008$) and longer stays in the ICU (14.8 vs. 12.4 days; $p = 0.029$). Between the two groups, there was no discernible difference in the number of ventilator days until unaided breathing (11.7 vs. 10 days; $p = 0.1$).

The study also evaluated plasma chemokines and cytokines using a multiplex test based on human magnetic beads. Analyses showed a nonsignificant trend toward raised levels in diabetic patients compared to nondiabetic patients on both days 0 and 1. Specifically, cytokines tumor necrosis factor alpha (TNF-α), interleukin (IL)-10, and IL-6, and chemokines C-reactive protein (CRP) and monocyte chemoattractant protein-1 (MCP-1) showed elevated levels in participants with diabetes. Of note, levels of lipopolysaccharide-binding protein (LBP) were significantly higher in patients with diabetes versus those without diabetes.

These findings show worse clinical outcomes in ARDS patients with pre-existing diabetes compared to those with no diabetes suggesting a negative impact of diabetes on lung function. Hence, respiratory functions of these patients should be carefully monitored. Further studies, according to the authors, can provide greater insights into the specific mechanisms by which diabetes influences respiratory functions in ARDS and validate this association.

Reference

1. Alanazi AH, et al. Secondary Analysis of Fluids and Catheters Treatment Trial (FACTT) data reveal poor clinical outcomes in acute respiratory distress syndrome patients with diabetes. Respir Med. 2024;223:107540.

Foot Complications in Patients with Diabetic Polyneuropathy and Chronic Kidney Disease

Patients with diabetic polyneuropathy (DPN) and chronic kidney disease (CKD) are at higher risk of developing major adverse foot events (MAFEs) and functional mobility deficits, suggests a study published in the journal *Metabolism and Target Organ Damage*[1]. The risks were evident even in the early stages of CKD and increased further as CKD progressed.

The aim of this study was to ascertain the risk ratios (RR) for MAFEs as well as moderate and severe functional mobility deficits by analyzing medical records of 284 patients with DPN across various stages of CKD.

Foot X-ray reports in the medical records of 152 participants were used to collate data on MAFEs, such as foot fractures, ulcerations, Charcot neuropathic arthropathy, osteomyelitis, and any minor foot amputations (partial/complete toe amputation, partial/complete ray amputation, or transmetatarsal amputation); the modified physical performance test (mPPT) was used to evaluate functional mobility deficits in 132 participants. mPPT scores <22 were defined as severe mobility deficit, while scores ranging from 22 to 29 were considered as moderate mobility deficit. Every stage of CKD was evaluated for both unadjusted and adjusted (age, body weight, race, and glycated hemoglobin [HbA1c]) RR calculations, with stage 1 CKD serving as the reference group.

Across all CKD stages, the RR for diabetic foot ulceration, Charcot neuropathic arthropathy, and neuropathic foot fracture stayed constant. Unlike foot fracture and

Charcot neuropathic arthropathy, instances of ulceration, osteomyelitis, and minor foot amputation were more common in patients with DPN and stages 3, 4, and 5 diabetic kidney diseases. In stage 1 CKD, the frequency of foot ulceration was 6%, whereas it rose to 20% in stage 4 CKD and 24% in stage 5 CKD. Sixteen percent patients with stage 4 CKD had foot osteomyelitis, while 24% with stage 5 CKD had foot osteomyelitis. There was a higher risk of minor amputation in stages 4 and 5 of CKD. The RR of moderate mobility deficit was 7-times higher in CKD stages 3, which increased 12 stimes in Stage 5 CKD. The RR of severe mobility deficit increased fivefold in stage 3, 10-fold in stage 4 and rose steeply by 30-fold in stage 5. Across all CKD stages, an inverse correlation between mPPT scores and MAFE prevalence was found.

According to the authors, this is the first study to determine the risk of MAFEs and functional mobility deficits in patients with DPN and CKD. These findings highlight the importance of proactive foot care and functional mobility assessment in these patients, even in the early stages of CKD (stages 2 and 3) when preventive interventions are possible. As functional mobility decreased, as indicated by lower mPPT scores, the prevalence of MAFEs increased, regardless of CKD stage.

Early detection followed by timely intervention and targeted management strategies may help minimize the risk of foot complications and functional mobility deficits in this population, which, if left untreated, may lead to lower extremity amputation. These findings also call for educating patients about the risks for MAFEs and accompanying functional mobility deficits, which may further aid early recognition of foot complications.

Reference

1. Sinacore DR, Kline PW. Major adverse foot events and functional mobility deficits associated with diabetic neuropathy and nephropathy. Metab Target Organ Damage. 2024;4:15.

Fetal Nuchal Translucency Measurements Cut-offs: Time for a Rethink?

Fetuses with nuchal translucency measurements as low as 2.0 mm have a higher probability of chromosomal abnormalities, suggest a recent study published in *JAMA Network Open*[1]. Fetuses with nuchal translucency measurements of 3.0 to <3.5 mm were 20 times more at risk of having abnormalities versus those with measurements <2.0 mm. The risk was sixfold higher in fetuses with measurements of 2.5-3 mm and more than doubled when the nuchal transparency measurement ranged between 2 and 2.5 mm.

Kara Bellai-Dussault from the School of Epidemiology and Public Health, University of Ottawa, Canada and coauthors conducted this retrospective cohort study to explore how different nuchal translucency measurements correlate with the likelihood of specific cytogenetic outcomes in singleton pregnancies. For this, they used data of all singleton pregnancies with an estimated delivery dates between September 2016 and March 2021 from the Better Outcomes Registry & Network, which serves as the perinatal registry for Ontario, Canada. The reference group for comparison consisted of pregnancies with a nuchal translucency measurement <2.0 mm. Chromosomal anomalies such as Down syndrome, Edwards syndrome, and Patau syndrome were identified through prenatal and postnatal cytogenetic tests conducted in Ontario laboratories. The results of cell-free DNA (cfDNA) screening and clinical assessment at birth were added to the data from cytogenetic testing to identify pregnancies free of chromosomal abnormalities.

Analysis of data revealed that a nuchal translucency of <2.0 mm was present in the majority of the study group (86.9%; n = 3,59,807) out of the 4,14,268 pregnancies that were included in the study. The mean maternal age at the predicted delivery date was 31.5 years. Chromosomal abnormalities were present in 0.5% of this group.

As the nuchal translucency measurement increased, the risk of chromosomal abnormalities increased. For pregnancies with nuchal translucency measurements of 3.0 to <3.5 mm, the adjusted risk ratio (aRR) was 20.33 and the adjusted risk difference (ARD) was 9.94%. When limited to chromosomal abnormalities outside the widely screened aneuploidies (excluding trisomies 21, 18, and 13 and sex chromosome aneuploidies), the aRR was 4.97 and the ARD was 1.40%.

The findings from this cohort study suggest a clear association between higher nuchal translucency measurements and the elevated risk of chromosomal anomalies. Those with nuchal translucency measurements <2.0 mm were at the least risk. The study further indicates that even after excluding the commonly screened chromosomal anomalies, there remains a significantly increased risk of anomalies not frequently checked for by many prenatal genetic screening programs associated with higher nuchal translucency measurements. Overall, this study underscores the importance of nuchal translucency measurements as

a valuable screening tool in prenatal care. Even slight increases in nuchal translucency can potentially signal an elevated risk of chromosomal abnormalities.

A cut-off of 3.0 mm or greater or above the 99th percentile for the crown-rump length in the first trimester has been proposed by the American College of Obstetricians and Gynecologists (ACOG) for further diagnostic testing such as prenatal cfDNA screening or cytogenetic testing[2].

This study, by suggesting that pregnancies with nuchal translucency measurements lower than the 3.0 mm threshold were associated with risk of chromosomal anomalies, may have practice changing implications for prenatal genetic screening.

References

1. Bellai-Dussault K, et al. Ultrasonographic fetal nuchal translucency measurements and cytogenetic outcomes. JAMA Netw Open. 2024;7(3):e243689.
2. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstet Gynecol. 2020;136(4):e48-e69.

Childhood Atopic Dermatitis and Risk of Inflammatory Bowel Disease

Children with atopic dermatitis are at risk of developing inflammatory bowel disease (IBD). However, no such association was noted for other atopic manifestations. These findings were recently published March 21, 2024, in *The Journal of Pediatrics*[1].

This study focused on investigating potential associations between early childhood allergic conditions and the subsequent development of IBD. The study analyzed data from two large, prospective cohort studies in Scandinavia: 9,041 children from the All Babies in Southeast Sweden (1997-1999) and 74,270 from the Norwegian Mother, Father, and Child Cohort Study (2000-2009) who were followed up from birth until 2021 or a diagnosis of IBD. Data on any atopy such as asthma, food allergy, atopic dermatitis and allergic rhinitis by the age of 3 years was obtained from parents through questionnaires. Two or more diagnostic records in the national health registries were used to identify IBD. The adjusted hazard ratio (aHR) for several confounders including parental history of IBD, atopy, educational level, smoking habits, and national origin.

During a follow-up period of over 1,174,756 person-years, a total of 301 patients received the diagnosis of IBD. By the age of 3 years, 31,671 children (38%) developed an atopic manifestation. After adjusting for confounding variables, children with atopic dermatitis at the age of 3 years were more likely to develop IBD (pooled aHR 1.46), ulcerative colitis (pooled aHR 1.78), and Crohn's disease (pooled aHR 1.53). In contrast, neither analyses that explicitly examined early-life food-related allergic symptoms, asthma, or allergic rhinitis were linked to subsequent risk for IBD (pooled aHR 1.20) nor were any atopic manifestations by the age of 3.

This study suggests that although atopic symptoms in early infancy were not generally linked to IBD, children with atopic dermatitis in particular were more likely to develop IBD, indicating that there may be potential common etiological characteristics between atopic dermatitis and IBD. According to the authors, "a deeper understanding could significantly benefit the development of novel treatment approaches capable of effectively addressing both conditions, consequently enhancing patient outcomes". Atopic dermatitis may thus be an indicator of children at risk for developing IBD. Hence, clinicians managing children with atopic dermatitis should be aware of this association and closely monitor them for early recognition of IBD and timely intervention, if required.

Reference

1. Lerchova T, et al. Atopic dermatitis in early childhood and risk of inflammatory bowel disease: a Scandinavian birth cohort study. J Pediatr. 2024:114027.

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