



Physician connect

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you '**Physician connect**' which contains latest and interesting news in the field of Medicine.

This issue contains

- Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in COVID-19
- A Randomized Trial of a Multifactorial Strategy to Prevent Serious Fall Injuries: STRIDE Trial
- First-Trimester Maternal Folic Acid Supplementation and Congenital Heart Diseases: A Large Case-Control Study

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

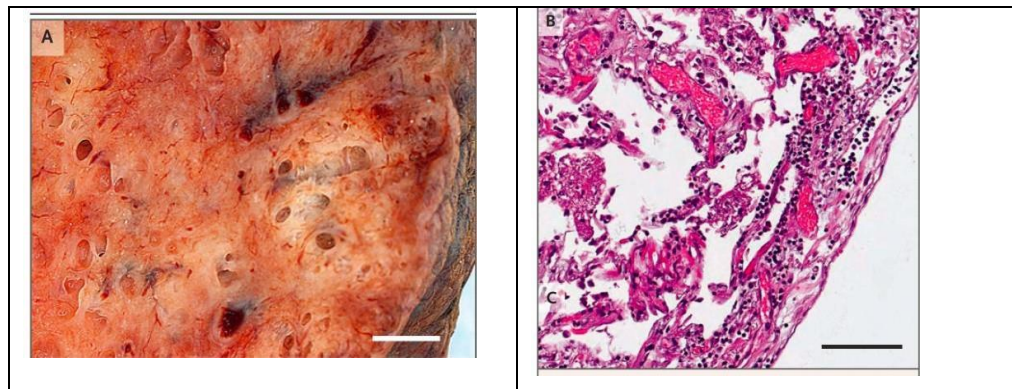
Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in COVID-19

Progressive respiratory failure is the primary cause of death in the coronavirus disease 2019 (Covid-19) pandemic. Despite widespread interest in the pathophysiology of the disease, relatively little is known about the associated morphologic and molecular changes in the peripheral lung of patients who die from Covid-19.

Ackermann et al. examined 7 lungs obtained during autopsy from patients who died from Covid-19 and compared them with 7 lungs obtained during autopsy from patients who died from acute respiratory distress syndrome (ARDS) secondary to influenza A(H1N1) infection and 10 age-matched, uninfected control lungs. The lungs were studied with the use of seven-color immunohistochemical analysis, micro-computed tomographic imaging, scanning electron microscopy, corrosion casting, and direct multiplexed measurement of gene expression.

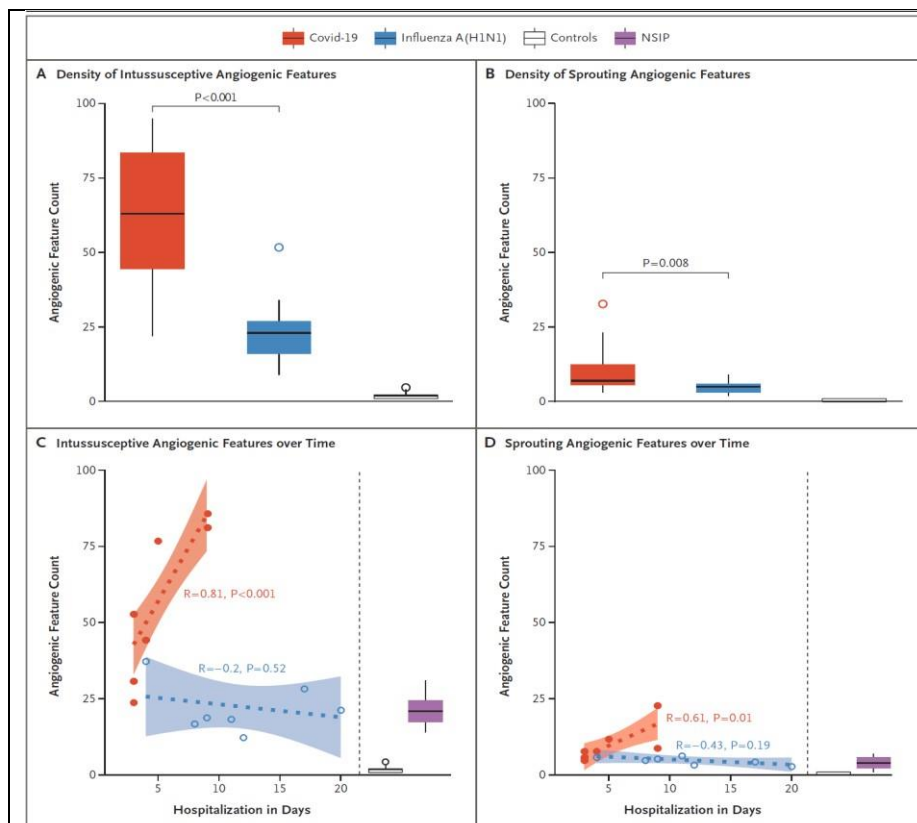
Vascular angiogenesis distinguished the pulmonary pathobiology of Covid-19 from that of equally severe influenza virus infection

In patients who died from Covid-19-associated or influenza-associated respiratory failure, the histologic pattern in the peripheral lung was diffuse alveolar damage with perivascular T-cell infiltration. The lungs from patients with Covid-19 also showed distinctive vascular features, consisting of severe endothelial injury associated with the presence of intracellular virus and disrupted cell membranes. Histologic analysis of pulmonary vessels in patients with Covid-19 showed widespread thrombosis with microangiopathy. Alveolar capillary microthrombi were 9 times as prevalent in patients with Covid-19 as in patients with influenza ($P<0.001$). In lungs from patients with Covid-19, the amount of new vessel growth — predominantly through a mechanism of intussusceptive angiogenesis — was 2.7 times as high as that in the lungs from patients with influenza ($P<0.001$).



Lymphocytic Inflammation in a Lung from a Patient Who Died from Covid-19.

The gross appearance of a lung from a patient who died from coronavirus disease 2019 (Covid-19) is shown in Panel A (the scale bar corresponds to 1 cm). The histopathological examination, shown in Panel B, revealed interstitial and perivascular predominantly lymphocytic pneumonia with multifocal endothelialitis (hematoxylin–eosin staining; the scale bar corresponds to 200 μ m).



Numeric Density of Features of Intussusceptive and Sprouting Angiogenesis in Lungs from Patients Who Died from Covid-19 or Influenza A(H1N1).

In this small series, vascular angiogenesis distinguished the pulmonary pathobiology of Covid-19 from that of equally severe influenza virus infection. The universality and clinical implications of our observations require further research to define

Source: Ackermann, M et al. N Engl J Med 2020;383:120-8. DOI: 10.1056/NEJMoa2015432

A Randomized Trial of a Multifactorial Strategy to Prevent Serious Fall Injuries: STRIDE Trial

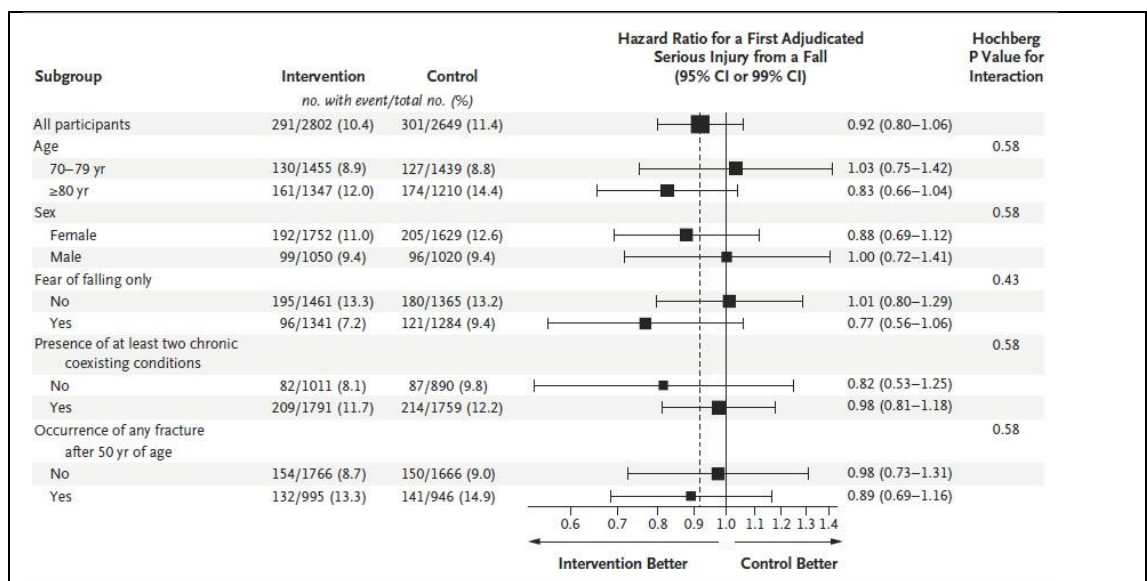
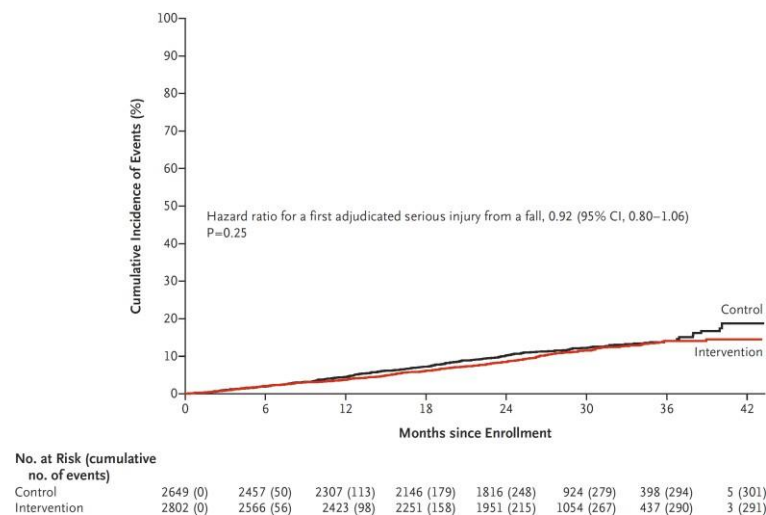
Among older Americans, falls are the leading cause of injury-related deaths. Approximately one in four older adults falls each year, and 20 to 30% of those who fall have moderate-to-severe injuries, resulting in approximately 30,000 deaths, 3 million emergency department visits, and 800,000 hospitalizations annually. Injuries from falls are major contributors to complications and death in older adults. Despite evidence from efficacy trials that many falls can be prevented, rates of falls resulting in injury have not declined.

A multifactorial intervention, administered by nurses, did not result in a significantly lower rate of a first adjudicated serious fall injury than enhanced usual care.

This STRIDE trial (Strategies to Reduce Injuries and Develop Confidence in Elders) was a pragmatic, cluster-randomized trial to evaluate the effectiveness of a multifactorial intervention that included risk assessment and individualized plans, administered by specially trained nurses, to prevent fall injuries. A total of 86 primary care practices across 10 health care systems were randomly assigned to the intervention or to enhanced usual care (the control) (43 practices each). The participants were community-dwelling adults, 70 years of age or older, who were at increased risk for fall injuries. The primary outcome, assessed in a time-to-event analysis, was the first serious fall injury, adjudicated with the use of participant report, electronic health records, and claims data. We hypothesized that the event rate would be lower by 20% in the intervention group than in the control group.

The demographic and baseline characteristics of the participants were similar in the intervention group (2802 participants) and the control group (2649 participants); the mean age was 80 years, and 62.0% of the participants were women. The rate of a first adjudicated serious fall injury did not differ significantly between the groups, as assessed in a time-to-first-event analysis (events per 100 person-years of follow-up, 4.9 in the intervention group and 5.3 in the control group; hazard ratio, 0.92; 95% confidence interval [CI], 0.80 to 1.06; P=0.25). The

rate of a first participant-reported fall injury was 25.6 events per 100 person-years of follow-up in the intervention group and 28.6 events per 100 person-years of follow-up in the control group (hazard ratio, 0.90; 95% CI, 0.83 to 0.99; $P=0.004$). The rates of hospitalization or death were similar in the two groups.



Prespecified Subgroup Analysis of the Primary Outcome.

The effect of the intervention on the first adjudicated serious fall injury was evaluated in five prespecified subgroups with the use of tests of interaction. Adjustment for multiple comparisons was made with the use of the Hochberg procedure to preserve an overall twosided type 1 error rate at 0.05. The point estimates of the hazard ratio and the associated confidence intervals (95% for the overall analysis and 99% for each subgroup) are shown. Participants in the “Fear of falling only” subgroup had a negative response to all the fall-related screening questions except the question about whether they had a fear of falling. The dashed vertical line represents the hazard ratio for the overall intervention effect. The size of each black square is proportional to the total number of participants in the subgroup

In this pragmatic, randomized trial conducted in primary care practices, an individually tailored intervention, administered by specially trained nurses, that

addressed multiple risk factors for falls did not result in a significantly lower rate of a first adjudicated serious fall injury than enhanced usual care among older adults who were at increased risk for fall injuries. The rate of all serious fall injuries, irrespective of when they occurred during the trial, also did not differ significantly between the two groups. The nurse-administered multifactorial intervention in a primary care setting did not result in a significantly lower rate of a first adjudicated serious fall injury than enhanced usual care among older adults at increased risk for fall injuries.

Source: Bhasin S et al. N Engl J Med 2020; 383:129-140 DOI: 10.1056/NEJMoa2002183

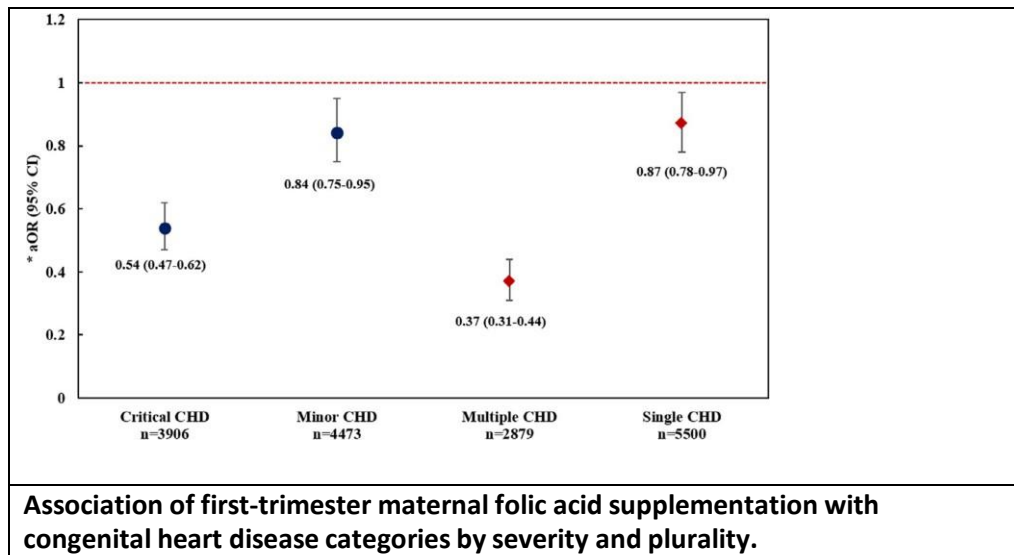
First-Trimester Maternal Folic Acid Supplementation and Congenital Heart Diseases: A Large Case-Control Study

Maternal folic acid supplementation (FAS) reduces the risk of neural tube defects in offspring. However, its effect on congenital heart disease (CHDs), especially on the severe ones remains uncertain. This study aimed to assess the individual and joint effect of first-trimester maternal FAS and multivitamin use on CHDs in offspring.

First-trimester maternal FAS, but not multivitamin use, was substantially associated with lower risk of CHDs

This is a case-control study including 8379 confirmed CHD cases and 6918 controls from 40 healthcare centers of 21 cities in Guangdong Province, China. Adjusted odds ratios (aORs) of FAS and multivitamin use between CHD cases (overall and specific CHD phenotypes) and controls were calculated by controlling for parental confounders. The multiplicative interaction effect of FAS and multivitamin use on CHDs was estimated. A significantly protective association was detected between first-trimester maternal FAS and CHDs among offspring (aOR, 0.69; 95% CI, 0.62–0.76), but not for multivitamin use alone (aOR, 1.42; 95% CI, 0.73–2.78). There was no interaction between FAS and multivitamin use on CHDs ($P=0.292$). Most CHD phenotypes benefited from FAS (aORs ranged from 0.03–0.85), especially the most severe categories (ie, multiple critical CHDs [aOR,

0.16; 95% CI, 0.12–0.22]) and phenotypes (ie, single ventricle [aOR, 0.03; 95% CI, 0.004–0.21]).



First-trimester maternal folic acid supplementation (FAS), even when initiated after conception, is associated with a lower risk of congenital heart diseases (CHDs) among offspring, and first-trimester multivitamin use alone does not protect against CHDs. Most CHD phenotypes benefit from first-trimester maternal FAS; the most severe categories, such as multiple critical CHDs and critical phenotypes like single ventricle, benefit most from FAS. Approximately 60 000 live births with CHDs could be saved annually by universal implementation of first trimester FAS. First-trimester maternal FAS, but not multivitamin use, was substantially associated with lower risk of CHDs, and the association was strongest for the most severe CHD phenotypes. Women planning to get pregnant should be advised to initiate FAS as early as possible to ensure coverage of critical fetal heart development periods and to decrease the risk of CHDs. Mothers who missed preconceptional FAS should also supplement folic acid rather than use only multivitamins during the first trimester of pregnancy to decrease the risk of CHDs.

Source: Qu Y et al. J Am Heart Assoc. 2020;9:e015652. DOI: 10.1161/JAHA.119.015652

