News and Views

Sit-to-Stand: A Measure of Post-ICU Functional Recovery

Around 36% of critically ill patients are unable to perform sit-to-stand independently at 3 months after discharge from a medical ICU (MICU), as per a study from Taiwan published in December 2024 issue of the journal *Critical Care Medicine*[1].

This prospective cohort study examined the prevalence of the inability to perform sit-to-stand independently in survivors of critical illnesses, 3 months after discharge from MICU in a tertiary medical center, where they had been admitted from December 2018 to August 2020. The association between inability to sit-to-stand independently and post-ICU mortality at 6- and 12-months was also examined. The mean age of the study participants was 66.4 years and the median length of ICU stay was 6 days.

The study was conducted across 6 MICUs in a tertiary care hospital, with no interventions and included MICU survivors who could perform this task before their hospitalization. The inability to perform a sit-to-stand (yes/no) was assessed at four points after discharge: upon ICU discharge, and at 1-, 2-, and 3-months post-discharge. Mortality rates were evaluated at 6- and 12-months following MICU discharge.

Out of the 194 study participants, 128 (66%) were unable to perform a sit-to-stand independently at discharge from the MICU. Of these, 63 were totally dependent and 65 had assisted sit-to-stand function. Recovery was observed, with the sit-to-stand inability rates decreasing to 50% at 1 month, 38% at 2 months, and 36% at 3 months post-discharge, plateauing at 2 months.

Inability to sit-to-stand at 3 months was significantly associated with sixfold increased risk of mortality at 6 months with adjusted hazard ratio (aHR) of 6.01. The mortality was 21% at 12 months with a 4.2-fold increased risk of mortality (aHR 4.2). This heightened risk was independent of age, Sequential Organ Failure Assessment score, and ICU-acquired weakness. Improvement in sit-to-stand ability, even from "totally unable" to "able with assistance", was associated with a reduced mortality risk.

The inability to perform a sit-to-stand in MICU survivors even 3 months after ICU discharge, emphasizes the rehabilitation challenges they face. Also, those who could not perform a sit-to-stand at all had the highest mortality hazard, followed by those who required assistance suggesting its significance as a prognostic factor. In contrast, survivors who could sit-to-stand independently demonstrated the lowest risk of mortality. Since recovery appeared to plateau around 2 months after discharge, it is important to reassess sit-to-stand ability in MICU survivors at this point to initiate timely intervention for those in need.

Reference

1. Siao SF, et al. Inability to sit-to-stand in medical ICUs survivors: when and why we should care. Crit Care Med. 2024;52(12):1828-36.

Cardiovascular and Mortality Benefits of SGLT2 Inhibitors

Sodium-glucose cotransporter 2 (SGLT2) inhibitors significantly reduce the incidence of major adverse cardiovascular events (MACE), cardiovascular death, and hospitalization for heart failure in patients with varying levels of risk for kidney disease[1]. Greater benefits were observed in those at high-risk.

Bernardo F Spiazzi from the Federal University of Rio Grande do Sul, Porto Alegre in Brazil and colleagues conducted this systematic review and meta-analysis of large, randomized, placebo-controlled trials of SGLT2 inhibitors, up to August 8, 2023, with a minimum study duration of 1 year. Fourteen trials, covering 97,412 participants with a median follow-up of 2.5 years were included for the final analysis. The study aimed to evaluate the impact of SGLT2 inhibitors on cardiovascular outcomes and mortality across different KDIGO and urinary albumin-to-creatinine ratio (UACR) risk groups. The overall risk of bias was low.

SGLT2 inhibitors were found to significantly reduce MACE (hazard ratio [HR] 0.89), cardiovascular death or hospitalization for heart failure (HR 0.78), all-cause mortality (HR 0.89) and hospitalization for heart failure (HR 0.71). The benefits of SGLT2 inhibitors on MACE were particularly pronounced in KDIGO very high-risk group (HR 0.72) and those with UACR >300 mg/g (HR 0.76).

This study demonstrates that SGLT2 inhibitors are associated with marked reductions in cardiovascular outcomes and mortality. Their impact on MACE

varied significantly across KDIGO groups. While their use was associated with significant improvements in cardiovascular outcomes, patients in the high-risk groups for kidney disease benefited the most.

Reference

1. Spiazzi BF, et al. SGLT2 inhibitors, cardiovascular outcomes, and mortality across the spectrum of kidney disease: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2024;218:111933.

Long-Standing Hypertension and Risk of Incident Stroke

The risk of incident stroke increases as the number of years living with hypertension increases, regardless of use of antihypertensive medications, according to findings from the REGARDS (REasons for Geographic And Racial Differences in Stroke) cohort study published in the journal *Stroke*[1]. The longer the duration of hypertension, the more classes of antihypertensive medications patients needed to take.

In this study, 27,310 participants in the US from the REGARDS cohort study, enrolled between 2003 and 2007, who were stroke-free at baseline were followed for a median of 12.4 years to assess incident stroke events. Participants were divided into four groups according to the duration of diagnosed hypertension: normotensive (0 years), ≤5 years, 6 to 20 years, and ≥21 years. The study evaluated baseline systolic blood pressure (BP), the number of antihypertensive medication classes used, and the risk of stroke across these groups, while adjusting for demographics, cerebrovascular risk factors, systolic BP, and use of antihypertensives where applicable.

Out of 30,239 study participants, 27,310 were included in the analysis; their average age was 65 years and 45% of them were male. Over a median follow-up of 12.4 years, 1,763 incident stroke events occurred.

Participants who had hypertension for a duration of 21 years or more were taking 2.28 classes of antihypertensive medications on average compared to 1.68 classes of antihypertensive medications for those who had had hypertension for 5 years or less. Those who had hypertension for 6 to 20 years were taking 2.04 classes of antihypertensive drugs. The adjusted mean systolic BP increased with longer durations of recognized hypertension: 123.9 mmHg for 0 years, 129.7 mmHg for ≤5 years, 131.7 mmHg for 6 to 20 years, and 132.6 mmHg for 21+ years.

Participants with hypertension for up to 5 years had a 31% higher likelihood of having a stroke compared to those without hypertension with HR of 1.31. Those with hypertension for 6 to 20 years faced a 50% increased risk (HR 1.50), while participants with more than 20 years of hypertension were 67% more likely to experience a stroke than participants with normal blood pressure (HR 1.67).

Stroke can be a disabling condition with adverse impact on quality of life. These findings show that prolonged hypertension is the key factor contributing to the enhanced stroke risk. Hence, these findings further highlight the urgency of identifying and addressing high BP early, before hypertension sets in. The American Heart Association (AHA) recommends following a healthy diet, avoiding or limiting alcohol consumption, maintaining a healthy body weight, managing stress, staying physically active, quitting smoking, and taking medications when necessary.

Reference

1. Howard G, et al. Association of duration of recognized hypertension and stroke risk: The REGARDS study. Stroke. 2025;56(1):105-12.

Optimal Time Interval from Myomectomy for Better Pregnancy Outcomes

A time interval from myomectomy to pregnancy (TIMP) of 6 to 11 months is associated with lower risks of gestational hypertensive disorders and neonatal death compared to both shorter (<6 months) and longer (≥12 months) intervals, particularly for women aged 35 years and older. These findings were published in the *International Journal of Gynaecology & Obstetrics*[1].

A retrospective population-based cohort study was conducted between 2008 and 2017, utilizing data from the National Health Insurance Research Database and the Taiwan Maternal and Child Health Database. The study included a total of 2,024,379 births from 1,391,856 pregnancies. Eligible cases were found through diagnostic and procedure codes, resulting in the identification of 4,006 first singleton births among 4,006 women following their first laparotomic myomectomy. The risks of pregnancy and obstetric outcomes were assessed based on the time interval from myomectomy to pregnancy, categorized as <6 months, 6 to 11 months, and ≥12 months. Subgroup analyses were conducted by further stratifying the cohort according to maternal age at birth (18-34 years vs. ≥35 years).

This study attempted to decipher the associations between the TIMP and pregnancy outcomes such as uterine rupture, preterm delivery, or miscarriage. It also sought to examine whether younger or older maternal age influences how TIMP impacts outcomes.

The study observed that a shorter TIMP of <6 months was associated with significantly higher risks of gestational hypertensive disorders and neonatal deaths. The risk of gestational hypertensive disorders was nearly doubled with adjusted odds ratio (aOR) of 1.97. The risk of neonatal deaths increased 4.5 times with aOR of 4.59. Showing a similar trend, a TIMP of ≥12 months was linked to an increased risk of gestational hypertensive disorders (aOR 1.72) and neonatal death (aOR 3.27) compared to a TIMP of 6 to 11 months.

Subgroup analysis revealed that women aged 35 years and older continued to face higher risks of gestational hypertensive disorders when the TIMP was <6 months (aOR 2.26) or ≥12 months (aOR 2.04). These women also had a higher risk of neonatal death when the TIMP was <6 months (aOR 4.05). Conversely, women aged 18 to 34 years did not show these associations.

The study concluded that a TIMP of 6 to 11 months appears optimal, particularly for women over 35 years, to reduce adverse pregnancy outcomes like hypertensive disorders and neonatal death.

Reference

1. Chen WH, et al. Associations between the time interval from myomectomy to subsequent pregnancy and the obstetric outcomes: a population-based cohort study. Int J Gynaecol Obstet. 2024;167(2):631-40.

Impact of BP Variability on Cognitive Health

Older adults, with fluctuating BP have a higher likelihood of having lower cognitive skills, as per a study published online on December 11, 2024 in *Neurology*[1].

This prospective observational cohort study enrolled 4,770 individuals, mean age 71.3 years, who participated in the Chicago Health and Aging Project, a population-based study conducted from 1993 to 2012. Nearly 63% of the participants were women; two-thirds were Black. BP was measured every 3 years during 18 years of follow-up. Systolic and diastolic BP variability was calculated as the sum of the absolute differences between successive BP measurements, divided by the number of assessments minus one. Standardized cognitive tests were used to evaluate cognitive function. In view of the age-related fluctuations in BP, this study specifically investigated the association between visit-to-visit variability and cognition in older adults.

The researchers found that the mean systolic BP variability was 17.7 mmHg among Black individuals and 16.0 mmHg among White participants. Higher systolic and diastolic BP variability were associated with lower cognitive scores at the end of the study. Compared to those in the first tertile (with lowest BP variability), participants in the third tertile (with highest BP variability) had cognitive scores that were 0.074 standardized units lower, equivalent to an additional 1.8 years of cognitive aging. This association differed by race and was only significant in older Blacks.

Black participants in the third tertile of systolic BP variability had cognitive scores that were 0.115 standardized units lower than those in the first tertile, corresponding to 2.8 years of additional cognitive aging. Similar trends were observed for diastolic BP variability.

Hypertension is an established risk factor for cognitive impairment. This study demonstrates the association of elevated BP variability with lower cognitive scores. This association was particularly robust among older Black adults. These findings highlight the importance of routine BP monitoring, given the high prevalence of cardiovascular risk factors, including hypertension, to identify and address the potential negative impact of BP variability on cognitive function in older adults.

Reference

1. Dhana A, et al. Blood pressure variability and cognition in Black and White older adults over 18 years of follow-up: a population-based cohort study. Neurology. 2025;104(1):e210151.

Impact of Multimorbidity on COPD Outcomes

Patients with chronic obstructive pulmonary disease (COPD) are more likely to have comorbid conditions such as gastroesophageal reflux disease (GERD), diabetes, or osteoporosis/osteopenia. These comorbidities increase the risk of COPD exacerbations and are associated with a higher likelihood of emergency department visits and hospitalizations compared to patients without these conditions.

The objective of this retrospective, noninterventional study was to explore how the presence of three coexisting conditions in patients with COPD affects the frequency of COPD exacerbations and the utilization of COPD-related health care resources (HCRU) over a 5-year follow-up period. A total of 1,58,106 adults with COPD were age-matched with 1,58,106 adults without COPD. Real-world data from a large health care database was utilized for the analysis.

The prevalence of GERD, diabetes, and osteoporosis/osteopenia was evaluated and compared between age-matched COPD and non-COPD cohorts. COPD exacerbations and related HCRU, including hospitalizations and emergency department visits, were

compared between age-matched COPD patients with and without specific comorbidities of GERD, diabetes, and osteoporosis/osteopenia. Additional weight-matching was conducted to refine comparisons for COPD patients with and without diabetes, as well as those with and without osteoporosis/osteopenia.

This results showed that the prevalence of comorbidities was higher in participants with COPD. Nearly 45% of COPD patients had GERD (vs. 27.8% in non-COPD) and ~41% had diabetes (vs. 31.1% in non-COPD). Although less prevalent, nevertheless ~19% of COPD patients had osteoporosis/osteopenia (vs. 14.1% in non-COPD).

COPD patients with either GERD, diabetes, or osteoporosis/osteopenia had significantly higher risks of severe, moderate, and any exacerbations compared to those without these conditions. The odds ratio (OR) of severe exacerbations was OR = 1.81 in COPD patients with GERD, 1.11 in COPD patients with diabetes, and 1.37 in COPD patients with osteoporosis/osteopenia. The OR of moderate exacerbations was OR = 1.69 in COPD patients with GERD, 1.10 in COPD patients with diabetes, and 1.32 in COPD patients with osteoporosis/osteopenia. The OR of any exacerbations was OR = 1.84 in COPD patients with GERD, 1.09 in COPD patients with diabetes, and 1.38 in COPD patients with osteoporosis/osteopenia.

COPD patients with comorbidities showed significantly higher odds of health care use, including emergency department (ED) and hospital visits. In COPD patients with GERD, diabetes, and osteoporosis/osteopenia, the ORs for ED visits were 1.98, 1.09, and 1.34, respectively. The ORs for hospital visits were 2.22, 1.26, and 1.36, respectively for COPD patients with GERD, diabetes, and osteoporosis/osteopenia.

This study provides evidence that GERD, diabetes, and osteoporosis are common comorbidities in patients with COPD highlighting the importance of understanding the systemic effects of COPD. Additionally, these and other extrapulmonary comorbidities significantly impact the risk of exacerbations and increase emergency department visits and hospitalizations, thereby complicating management. Hence, there is a need for integrated management strategies aimed at both COPD and comorbidities to reduce the frequency of COPD exacerbations including health care burden.

Reference

1. Krishnan JK, et al. Multimorbidities in COPD are associated with increased exacerbations and health care resource utilization in real-world patients from a U.S. database. Chronic Obstr Pulm Dis. 2024;11(5):472-81.

Perinatal Outcomes of Early and Late Gestational Diabetes

Early gestational diabetes mellitus (GDM) is associated with an increased incidence of adverse perinatal outcomes despite treatment beginning at 24 to 28 weeks of gestation, according to a secondary analysis of the Treatment of Booking Gestational diabetes Mellitus (TOBOGM) trial published online December 1, 2024 in the journal *Diabetes Care*[1].

This randomized controlled treatment trial evaluated early GDM (<20 weeks' gestation) among women with risk factors, using the WHO 2013 criteria. Women receiving early treatment for GDM were not included in the study. GDM was treated only if it persisted at 24 to 28 weeks of gestation. The primary outcome was a composite measure, including preterm birth (<37 weeks of gestation), birth weight ≥4,500 g, birth trauma, neonatal respiratory distress, phototherapy, stillbirth, or neonatal death, and shoulder dystocia. The aim was to compare perinatal outcomes among three distinct groups of participants: 254 women with early GDM (diagnosed before 20 weeks of gestation but untreated until 24-28 weeks of gestation, if GDM persisted) and 467 women with late GDM (diagnosed only at 24-28 weeks' gestation). A total of 2,339 women with normoglycemia at 24 to 28 weeks of gestation acted as the control group).

Women with early and late gestational diabetes experienced shorter pregnancy durations compared to the control group. Participants with late GDM had the lowest BMI. The incidence of the composite outcome was higher in the group with early GDM with OR of 1.59. But this was not observed in the late GDM group (OR 1.19). Both GDM groups had higher rates of labor induction compared to controls. The early GDM group had higher birth centiles, increased rates of preterm birth, and a higher incidence of neonatal jaundice. Additionally, this group had the greatest need for insulin and/or metformin treatment.

These findings highlight the need for early screening and treatment initiation to mitigate the impact of prolonged exposure to severe maternal hyperglycemia from early pregnancy and reduce perinatal complications.

Reference

1. Simmons D, et al; TOBOGM Research Group. Perinatal outcomes in early and late gestational diabetes mellitus after treatment from 24-28 weeks' gestation: a TOBOGM secondary analysis. Diabetes Care. 2024;47(12):2093-101.

Characterizing Glucose Variability in Normoglycemic Individuals Using CGM

Individuals with normoglycemia, without elevated blood glucose or glycated hemoglobin (HbA1c) spent on average, nearly 3 hours daily with glucose levels >140 mg/dL with many experiencing continuous glucose monitoring (CGM) glucose levels >180 mg/dL for more than 15 minutes daily, according to study findings published in the *Journal of Clinical Endocrinology and Metabolism*[1].

Researchers analyzed data from the Framingham Heart Study, a long-term prospective cohort study. This analysis focused on the grandchildren of the original participants of the Framingham Heart Study, specifically those who were recruited in 2002 as part of the Third-Generation cohort (n = 4,095), New Offspring Spouses cohort (n = 103), and Omni 2 cohort (n = 410). The objective of the study was to determine the physiological range of CGM time-in-range values across varying glycemic levels, including individuals without diabetes, to provide a valuable reference for clinicians. The main outcome measures were CGM metrics including mean glucose and time spent in glucose ranges.

A total of 1,175 participants, who attended follow-up visits between 2022 and 2023, wore a Dexcom G6 Pro CGM sensor, placed on the upper arm or abdomen, for at least 7 days. Glucose trends were assessed based on glycemic status.

A "tight range" was defined as glucose levels between 70 and 140 mg/dL. Prediabetes was identified using HbA1c levels of 5.7% to 6.4% or venous fasting glucose levels between 100 and 125 mg/dL. Diabetes was defined as HbA1c ≥6.5%, venous fasting glucose of ≥126 mg/dL, self-reported or taking glucose-lowering medications at the time of their study visit.

Out of the 1,175 study participants, 560 were normoglycemic, 463 had prediabetes, and 152 had diabetes. Those with normoglycemia were younger (mean age 58.8 years), while participants with prediabetes and diabetes groups were older.

Analysis of data revealed that normoglycemic participants spent 87.0% time in the 70-140 mg/dL (tight CGM range) and 1.2% time (>15 min/day) in the above 180 mg/dL range. They spent 12.1% time (~3 hr/day) with CGM glucose >140 mg/dL. As expected, participants with prediabetes and diabetes spent significantly less time within the target range. Those with prediabetes spent, on average, 77.1% of their time within the glucose range of 70-140 mg/dL, while those with diabetes spent 46.2% of their time in this range.

Participants with prediabetes spent nearly 20% of their time in the 140-180 mg/dL range and over 3% of their time (>45 min/day) with CGM glucose levels exceeding 180 mg/dL. In contrast, those with diabetes spent the majority of their time (>57%) with glucose levels above 140 mg/dL.

The mean CGM glucose levels showed a similar range, being only 8.6 mg/dL higher in individuals with prediabetes compared to those with normoglycemia (123.1 mg/dL vs. 114.5 mg/dL).

However, a larger difference was observed in CGM time spent in the tight range (70-140 mg/dL) between nonobese individuals younger than 60 years (89.0%) and nonobese individuals ≥60 years (85.8%). Obesity at any age was also linked to reduced time in the tight range, with older obese adults spending the least time in this range on average (83.7%) compared to other normoglycemic individuals.

These findings enhance the understanding of the "physiological time spent in specific ranges of CGM glucose" in individuals without diabetes. These results provide an important reference for clinicians as CGM sensors become increasingly accessible to individuals without a known history of diabetes, conclude the authors.

Reference

1. Spartano NL, et al. Defining continuous glucose monitor time in range in a large community-based cohort without diabetes. J Clin Endocrinol Metab. 2024 Sep 11:dgae626.