

General

Early Versus Later Anticoagulation for Stroke with Atrial Fibrillation

Atrial fibrillation is a major cause of ischemic stroke necessitating anticoagulation to prevent future cerebrovascular events. The optimal timing for starting anticoagulation is, however, unclear. Researchers in this study compared early (within 48 hours for minor stroke, and 6 or 7 days for major stroke) to later anticoagulation (day 2 or 3 for minor stroke, and day 12 or 14 for major stroke) using direct oral anticoagulants in 2013 persons with atrial fibrillation that had had an ischemic stroke. The primary outcome was a composite of recurrent ischemic stroke, among other complications, within 30 days. The study found that the primary outcome occurred more in the later anticoagulation arm (4.1%) than in the early anticoagulation arm (2.9%). The researchers recommended that early treatment initiation can be supported if indicated or if desired without a significant increase in adverse events.

Reference

Fischer U, et al. (2023). Early versus Later Anticoagulation for Stroke with Atrial Fibrillation. *N Engl J Med.* 2023 Jun 29;388(26):2411-2421. doi: 10.1056/NEJMoa2303048

Second-Line Switch to Dolutegravir for Treatment of HIV Infection

Second-line antiretroviral therapy that includes a ritonavir-boosted protease inhibitor (PI) presents challenges, including pill burden, drug toxicities, cost, and drug interactions. It's unclear if switching to dolutegravir in those who attain viral suppression is feasible. Researchers in this non-inferiority study included 795 patients without genotype information who had viral suppression while receiving treatment containing a ritonavir-boosted PI to either switch to dolutegravir or continue the current regimen. The primary outcome was an HIV viral load of at least 50 copies per milliliter at week 48. The study found no difference between groups in regard to the primary outcome, or adverse events. The researchers found that dolutegravir treatment was non-inferior to a ritonavir-boosted PI-based regimen in viral-suppressed patients on second-line treatment.

Reference

Ombajo, L. A., et al. (2023). Second-Line Switch to Dolutegravir for Treatment of HIV Infection. *The New England Journal of Medicine*, 388(25), 2349–2359. <https://doi.org/10.1056/NEJMoa2210005>

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Sexually transmitted infections (STIs) among men who have sex with men (MSM) are a huge burden and measures to avert them are needed. Researchers in this study included over 501 MSM and transgender women either on pre-exposure prophylaxis (PrEP) or living with HIV with a history of an STI in the past year, randomized to either receive 200mg of doxycycline within 72 hours or standard of care after sex without a condom. The primary outcome was the incidence of an STI per

follow-up quarter. In both PrEP and those living with HIV, the outcome was much lower in the doxycycline group compared to controls i.e. 10.7% versus 31.9% and 11.8% versus 30.5% respectively. These findings support doxycycline use in this patient population.

Reference

Luetkemeyer, A. F., et al. (2023). Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *The New England Journal of Medicine*, 388(14), 1296–1306. <https://doi.org/10.1056/NEJMoa2211934>

BCG Vaccine to Protect Against Covid-19 in Health Care Workers

The bacille Calmette–Guérin (BCG) vaccine has immunomodulatory effects and has been hypothesized to protect against Covid-19. In this international double-blind study, 3988 healthcare workers were randomized to receive BCG- Denmark vaccine or saline placebo and followed up for 12 months. The primary endpoint was symptomatic or severe Covid-19 assessed at 6 months. The study found no difference in risk for symptomatic (14.7% versus 12.3%) or severe Covid-19 (7.6% versus 6.5%) in the BCG vaccine and placebo arms respectively. No safety concerns were reported. The researchers hence concluded that the BCG-Denmark vaccine doesn't lower the risk of Covid-19 among health workers compared to a placebo.

Reference

Pittet, L. F., et al (2023). Randomized Trial of BCG Vaccine to Protect against Covid-19 in Health Care Workers. *The New England Journal of Medicine*, 388(17), 1582–1596. <https://doi.org/10.1056/NEJMoa2212616>

Daily Aspirin is Associated with a reduced Risk of Hepatocellular Carcinoma in Patients with non-alcoholic fatty liver Disease

Non-alcoholic fatty liver disease (NAFLD) is increasing globally and is associated with hepatocellular carcinoma (HCC). Preliminary laboratory and animal data show that aspirin may reduce the risk of HCC though this isn't evidenced. Researchers used a Taiwan national insurance database to compare 33,484 patients that received a daily dose of aspirin for 90 days or more (treated group), with 55,543 patients who had not received antiplatelet therapy (untreated group) and cumulative incidence was analyzed. The study found that the 10-year cumulative incidence of HCC in the treated group was significantly lower than that in the untreated group (0.25% versus 0.67%), a finding that was consistent even in the high-risk patients. The researchers thus concluded that daily aspirin therapy reduces HCC risk in NAFLD patients.

Reference

Lee, T.-Y., et al. (2023). Daily aspirin associated with a reduced risk of hepatocellular carcinoma in patients with non-alcoholic fatty liver disease: a population-based cohort study. *EclinicalMedicine*, 61, 102065. <https://doi.org/10.1016/j.eclinm.2023.102065>.

Effectiveness of spironolactone for women with acne vulgaris

Spironolactone has been suggested as an alternative to antibiotics in the treatment of acne vulgaris. Researchers in this study compared these two treatments. A total of 342 adult women were randomized to either receive placebo or spironolactone, initially at 50mg up to 6 weeks, increased to 100mg up to week 24. The primary outcome was the Acne-Specific Quality of Life (Acne-QoL) symptom subscale score at week 12. The study found that the Acne-QoL was better in the spironolactone group compared to the placebo at 12 weeks, with an even better score at 24 weeks i.e. 21.2 (5.9) versus 17.4 (5.8) respectively with no serious adverse events reported. The researchers hence concluded that spironolactone is an alternative to oral antibiotics for women with acne.

Reference

Santer M, Lawrence M, Renz S, Emlinton Z, Stuart B, Sach T H, et al. Effectiveness of spironolactone for women with acne vulgaris (SAFA) in England and Wales: pragmatic, multicentre, phase 3, double-blind, randomized controlled trial *BMJ* 2023; 381:e074349 doi:10.1136/bmj-2022-074349

Hydrocortisone in Severe Community-Acquired Pneumonia

The use of corticosteroids in severe infections has been controversial. Researchers in this study evaluated the role of glucocorticoids on mortality among patients with severe community-acquired pneumonia. The study conducted in France recruited 800 adults admitted to the intensive care unit (ICU) for community-acquired pneumonia, and randomized patients to receive hydrocortisone or placebo along with standard therapy. The primary endpoint was mortality at 28 days. The study found mortality benefits with hydrocortisone, with fewer patients (6.2%) dying by 28 days compared to 11.9% in the placebo arm. Also, fewer patients (18.0%) in the hydrocortisone arm required endotracheal intubation compared to 29.5% in the placebo group. The researchers concluded that hydrocortisone could have mortality benefits in patients with severe pneumonia.

Reference

Dequin, P.-F., et al. (2023). Hydrocortisone in Severe Community-Acquired Pneumonia. *The New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2215145>

MCH

Left Ventricular Hypertrophy in African Children Infected with HIV/AIDS

HIV/AIDS has been reported to exhibit cardiac complications, which may be clinically subtle but later adversely affect this patient population. Researchers in Nigeria conducted a case-control study among African children with HIV/AIDS to determine the prevalence and risk factors of echocardiography-confirmed left ventricular hypertrophy (LVH). A total of 168 participants were enrolled with 84 as cases. The prevalence of LVH was high, 67.7%, with the mean left ventricular mass

index (g/m²) significantly higher in the cases than in controls i.e. 90.37± 35.50 versus 89.37 ± 14.25. LVH was associated with low body mass index for age and lower CD4 count. The researchers concluded that LVH was high, justifying the need for baseline and periodic echocardiography in the management of children with HIV/AIDS.

Reference

Arodiwe, I. O., Eke, C. B., & Arodiwe, E. B. (2023). Left ventricular hypertrophy in African children infected with HIV/AIDS: a case-control study. *PAMJ*. 2023; 45:110, 45(110). <https://doi.org/10.11604/PAMJ.2023.45.110.37095>

Maternal Anemia and the Risk of Postpartum Hemorrhage.

The prevalence of anemia among reproductive-age women is high, with the burden greatest in low and middle-income countries. The association between anemia and postpartum hemorrhage (PPH), a major cause of maternal mortality and morbidity, is not well established. Researchers in this prospective multi-centric cohort study examined the association between hemoglobin and PPH. Of the 10620 women enrolled in the study, the mean estimated blood loss was 301 mL for 83.2% of women with moderate anemia and 340 mL for 16.8% of women with severe anemia. The risk of clinical PPH was higher (11.2%) in women with severe anemia compared to those with moderate anemia (6.2%), with higher odds of death. The researchers thus re-emphasized the need for prevention and treatment of anemia in women of reproductive age.

Reference

Mansukhani, R., et al. (2023). Maternal anemia and the risk of postpartum hemorrhage: a cohort analysis of data from the WOMAN-2 trial. *The Lancet Global Health*, 0(0). [https://doi.org/10.1016/S2214-109X\(23\)00245-0](https://doi.org/10.1016/S2214-109X(23)00245-0)

Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer

Breast cancer recurrence amongst young women who interrupt breast cancer endocrine therapy to attempt pregnancy isn't well established. Researchers in this study included a total of 515 patients, 42 years of age or younger; had had stage I, II, or III disease; had received adjuvant endocrine therapy for 18 to 30 months; and desired pregnancy. The primary outcome was the number of breast cancer events during follow-up. A total of 368 (74.0%) had at least one pregnancy. The incidence of breast cancer events was 8.9% in the treatment-interruption group and 9.2% in the control cohort. The researchers thus concluded that in select breast cancer patients, discontinuing therapy to attempt pregnancy did not increase the short-term risk of breast cancer events

Reference

Partridge AH, et al (2023): Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer. *N Engl J Med*. 2023 May 4;388(18):1645-1656. doi: 10.1056/NEJMoa2212856

Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage

Postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality, hence its prompt identification and treatment is likely beneficial. Researchers in this international cluster-randomized trial compared a multi-component intervention (blood-collection drape and bundle of first-response treatments) to the usual care in patients having vaginal delivery. The primary endpoint was a composite of severe PPH, laparotomy for bleeding, or maternal death from bleeding. The outcome occurred less in the intervention arm (1.6%) compared to 4.3% in the usual-care arm, and PPH was detected more in the intervention arm (93.1%) compared to 51.1% in the usual-care group. The researchers concluded that early PPH detection and the use of bundled treatment lead to a lower risk of postpartum complications than usual care.

Reference

Gallos, I., et al. (2023). Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage. *The New England Journal of Medicine*. <https://doi.org/10.1056/NEJMOA2303966>

Tranexamic Acid to Prevent Obstetrical Hemorrhage After Cesarean Delivery

The use of tranexamic acid at the time of Cesarean delivery as prophylaxis to reduce blood loss has been evidenced. Its effect on the need for blood transfusions is however unclear. This study enrolled 11,000 participants at 31 US hospitals and randomized them to either receive tranexamic acid or a placebo. The primary outcome was a composite of transfusion or maternal death at 7 days whichever came first. The study found no significant difference in the incidence of the primary outcome in the tranexamic acid or placebo groups i.e. 3.6% versus 4.3% respectively. Adverse events were similar in both groups. The researchers hence concluded that tranexamic acid during Cesarean delivery does not lead to a significantly lower risk of maternal death or blood transfusions than a placebo.

Reference

Pacheco, L. D., et al. (2023). Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery. *The New England Journal of Medicine*, 388(15), 1365–1375. <https://doi.org/10.1056/NEJMOA2207419>

Long-term outcomes of hysterectomy with bilateral salpingo-oophorectomy.

Hysterectomy is usually performed together with or without bilateral salpingo-oophorectomy (BSO), but the long-term outcomes of which have not been well evaluated or compared. In this systematic review and meta-analysis, researchers compared the long-term outcomes of hysterectomy with BSO to hysterectomy without BSO. They found that hysterectomy with BSO was associated with decreased risk of breast cancer (Hazard ratio 0.78), but increased risk of colorectal cancer (hazard ratio 1.27), thyroid cancer, renal cancer, cardiovascular diseases (CVD), and CVD risk factors.

Comparison of all-cause mortality rate between the two groups was rather inconclusive. The researchers concluded that hysterectomy with BSO was associated with multiple long-term adverse outcomes and that the benefits of the addition of BSO to hysterectomy should be weighed against its risks.

Reference

Hendin, N., et al (2023). Higher incidence of preeclampsia among participants undergoing in-vitro fertilization after fewer sperm exposures. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, 0(0).

Timing of antenatal corticosteroids and survival without neurological disabilities in children born before 35 weeks of gestation.

The efficacy of antenatal corticosteroids declines after 7 days of treatment, but the effects of longer treatment-to-birth time have not been evaluated. Researchers analyzed data from a population-based cohort in France. Participants in the primary study had been children born preterm with a complete corticosteroid course. Exposure was defined as the interval between first doses of antenatal corticosteroid course to delivery, and was categorized into two: day 3 to day 7 and after day 7. The primary outcome was survival without moderate/severe neurological disability at 5½ years of age. Of the 2427 children alive at 5½ years, the researchers found less survival without disability in the after-day 7 arm (85%), compared to the day 3 to 7 interval arm (87%) emphasizing a need to optimize timing for benefit.

Reference

Guerini, C., et al. (2023). Timing of antenatal corticosteroids and survival without neurological disabilities at 5½ years in children born before 35 weeks of gestation. *American Journal of Obstetrics & Gynecology*, 0(0). <https://doi.org/10.1016/j.ajog.2023.06.047>

Postpartum Home Blood Pressure Monitoring

Home-based blood pressure measurement (HBPM) has been increasingly recommended as a better alternative to office-based measurements. Its effectiveness in postpartum individuals has however not been well assessed. Researchers through this systematic review that included 12 studies sought to answer this question. According to the study, HBPM was significantly associated with an increased likelihood of at least one blood pressure measurement being ascertained (relative risk 2.11), and a significant reduction in unplanned hypertension-related hospital admissions (adjusted relative risk 0.12). It was, however, not associated with the rate of blood pressure treatment initiation (adjusted relative risk 1.03). The authors concluded that HBPM likely aids early recognition of hypertension in postpartum individuals but whether it reduces maternal mortality or morbidity remains unclear.

Reference

Dale W. Steele, et al (2023): Postpartum Home Blood Pressure Monitoring: A Systematic Review. *Obstetrics & Gynecology* ():10.1097/AOG.0000000000005270, June 13, 2023.

General Surgery

Point-of-care ultrasound versus radiography in children with suspected distal forearm fractures

The role of point-of-care ultrasound (POCUS) as an initial imaging tool for forearm fractures in children and adolescents is unclear. Researchers in the study compared POCUS to radiography, in patients aged 5 to 15 years with isolated distal forearm injuries, without visible deformity. The outcome measure was the physical function of the affected arm at 4 weeks. A total of 270 participants were enrolled. The study found that the performance score of the limb at 4 weeks in the POCUS group was non-inferior to the radiography group 36.4 and 36.3 points (confidence interval -1.3 to 1.4) respectively. No clinically relevant fractures were missed and no difference in adverse events between groups. The findings support POCUS as an alternative initial diagnostic method in distal forearm injuries.

Reference

Snelling, P. J., et al. (2023). Ultrasonography or Radiography for Suspected Pediatric Distal Forearm Fractures. *The New England Journal of Medicine*, 388(22), 2049–2057. <https://doi.org/10.1056/NEJMOA2213883>

Dexamethasone versus Surgery for Chronic Subdural Hematoma

Patients with chronic subdural hematomas are traditionally managed with dexamethasone or surgery, but the role of glucocorticoids without surgery is unevidenced. Researchers in this open-label study enrolled 252 patients and randomized them to either a tapering course of dexamethasone or burr-hole drainage, the outcome measurement being functional outcome at 3 months using a modified Rankin scale (mRs). The trial was terminated early for safety. The odds ratio for a better mRs score at 3 months with dexamethasone compared with surgery was 0.55, failing to show non-inferiority. Complications, as well as additional surgery were more in the dexamethasone arm compared to the surgery arm. The researchers concluded that in patients with chronic subdural hematoma, dexamethasone was inferior to surgery.

Reference

Miah, I. P., et al. (2023). Dexamethasone versus Surgery for Chronic Subdural Hematoma. *The New England Journal of Medicine*, 388(24), 2230–2240. <https://doi.org/10.1056/NEJMOA2216767>

Craniotomy or craniectomy for acute subdural hematoma

Acute subdural hematoma (SDH) is managed by surgical evacuation with either craniotomy (bone flap is replaced) or craniectomy (bone flap is not replaced). It is unclear which of the two approaches is better. Four hundred fifty (450) patients with acute SDH undergoing surgical evacuation were enrolled, and equally randomized to either approach. The primary end-point was the Extended Glasgow Outcome Scale (GOSE) score at 12 months. No significant difference in outcome was found between groups; death at 12 months occurred in 30.2% of the patients in the craniotomy group and 32.2% of

those in the craniectomy group. Additional surgery at 2 weeks was twice more in the craniotomy group than in the craniectomy group. The results support the use of either technique

Reference

P. J., Adams, H., et al. (2023). Decompressive Craniectomy versus Craniotomy for Acute Subdural Hematoma. *The New England Journal of Medicine*, 388(24). <https://doi.org/10.1056/NEJMOA2214172>

Balanced crystalloid solution versus saline in deceased donor kidney transplantation

Kidney transplant recipients receive regular perioperative intravenous fluids to maintain volume and optimize graft function. Saline (0.9% sodium chloride) is commonly used but has been associated with hyperchloremia, metabolic acidosis, renal vasoconstriction, decreased glomerular filtration rate, and renal damage and as such might increase the risk of delayed graft function (DGF) defined as the need for dialysis 7 days after transplantation. A randomized study involving over 800 kidney transplant recipients found that a balanced low-chloride crystalloid solution reduced the incidence of DGF compared to saline (30% versus 40%; adjusted relative risk of 0.74, confidence interval of 0.66 to 0.84). The researchers thus recommended that a balanced crystalloid solution should be the standard-of-care intravenous fluid used in cadaveric donor kidney transplantation.

Reference

Collins, M. G., et al. (2023). Balanced crystalloid solution versus saline in deceased donor kidney transplantation (BEST-Fluids): a pragmatic, double-blind, randomized, controlled trial. *Lancet (London, England)*. [https://doi.org/10.1016/S0140-6736\(23\)00642-6](https://doi.org/10.1016/S0140-6736(23)00642-6)

Tranexamic acid for severe trauma-related hemorrhage

Administration of tranexamic acid (TXA) reduces early mortality in patients at risk of major trauma-related bleeding. Long-term outcomes have however not been evaluated. In this multi-centric placebo-controlled study involving more than 1,300 people, similar to previous studies, 6-month survival with favorable functional outcome as assessed by the Glasgow Outcome Scale-Extended (GOS-E) was similar in both groups, but 1-month mortality was higher in the TXA group (21.8 versus 17.3 percent). There was no difference in the number of serious adverse events between groups. This study provides support for the practice of administering TXA to at-risk patients (for instance profusely bleeding) within 3 hours after injury, although its long-term benefits were not proven.

Reference

PATCH-Trauma Investigators and the ANZICS Clinical Trials Group, Gruen, et al (2023). Prehospital Tranexamic Acid for Severe Trauma. *The New England Journal of Medicine*. <https://doi.org/10.1056/NEJMOA2215457>