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VIEWPOINTS
2023 GUIDELINE FOR ATRIAL FIBRILLATION MANAGEMENT

VIEWPOINTS COMPILED BY BHARAT BAJANTRI, MD.
ADOPTED FROM PULMCC AND CITED ARTICLES.

Regularly regular superseded Irregularly irregular!

Here are the revised key recommendations:

1. Early Rhythm Control Preferred: Opt for early rhythm control over a rate-control strategy, utilizing methods such as antiarrhythmic drugs or ablation.
2. Strong Recommendation for Ablation First: Prioritize catheter ablation over antiarrhythmic drugs as the initial treatment approach (Class I recommendation with high quality evidence from RCTs).
3. Catheter Ablation for Heart Failure Patients: Upgrade catheter ablation to a Class I (high quality evidence from RCTs) indication for patients with heart failure and reduced ejection fraction.
4. Broader Recommendation for Left Atrial Appendage Occlusion Devices: Expand the recommendation for left atrial appendage occlusion devices, elevating it to a Class 2A recommendation (Moderate quality evidence from metanalysis and non-randomized studies only) for those with contraindications to anticoagulation and a Class 2B (Limited data) recommendation for those preferring to avoid anticoagulation.
5. Holistic Approach to Anticoagulation in Device-Detected AF: Consider a comprehensive approach to anticoagulation in patients with device-detected atrial fibrillation. For AF episodes lasting ≥24 hours, treat them as clinical AF, while decisions regarding anticoagulation for episodes lasting <24 hours should consider the total density of AF and the CHA2DS2-VASc score.
6. Progressive Nature of AF: Recognize atrial fibrillation as a progressive disease, categorized into stages along a continuum: Stage I denotes AF risk due to predisposing factors, Stage II signifies pre-AF with structural or electrical abnormalities, Stage III represents paroxysmal AF transitioning to Stage IV, which is permanent AF.
7. Emphasis on Risk-Factor Modification and Prevention: Prioritize risk-factor modification and prevention measures more prominently than in previous guidelines.

Conclusion

We were due for a comprehensive AF update given the increasing data we have about AF, not only regarding ablation but also early rhythm-control strategies and modification of risk factors. This guideline has made a paradigm shift from our traditional learning that rate control is as good as rhythm control.

VIEWPOINTS

ANTICOAGULATION FOR TRANSIENT SUBCLINICAL ATRIAL FIBRILLATION?

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Benefits outweigh the risks... Does not really mean Benefits outweigh the risks!

The uncertainty regarding whether the benefits of anticoagulation outweigh the risks in patients with transient, incidentally discovered atrial fibrillation (AF) prompted researchers to investigate. They enrolled 4000 patients, with an average age of 77, who had CHA2DS2-VASc scores ≥3 and at least one episode of subclinical AF lasting between 6 minutes and 24 hours, as detected by implanted pacemakers, defibrillators, or cardiac monitors. These patients were randomly assigned to receive either apixaban or aspirin.
The study observed the following outcomes: Over an average follow-up period of 3.5 years, apixaban demonstrated a significantly lower incidence of stroke or systemic embolism compared to aspirin (0.78 vs. 1.24 per 100 patient-years).

It's noteworthy that approximately 40% of these strokes led to at least moderate disability. On the other hand, the incidence of major bleeding events was notably higher with apixaban compared to aspirin (1.71 vs. 0.94 per 100 patient-years), resulting in an excess of one major bleed per 130 apixaban recipients per year. Most of the excess bleeding incidents were nonfatal gastrointestinal bleeds. Mortality rates were similar between the two groups, approximately 18%.

Systematic review including the two randomized controlled trials NOAH-AFNET 6 (edoxaban vs. aspirin or placebo; 2536 patients with follow up period of 1.8 years) and ARTESiA (apixaban vs. aspirin; 4012 patients with follow up period of 3.5 years), actual rate of stroke in the control arm was lower than anticipated, around 1% per year. Anticoagulation did demonstrate a significant reduction in the risks of ischemic stroke (relative risk, 0.68) and a composite endpoint - cardiovascular death, all-cause stroke, peripheral arterial embolism, myocardial infarction, or pulmonary embolism (relative risk, 0.85).

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However, it did not reduce the risks of cardiovascular death or all-cause mortality. Notably, oral anticoagulation was associated with a significant increase in the risk of major bleeding (relative risk, 1.62). The estimated reduction in absolute risk for ischemic stroke with anticoagulation ranged from 3 to 6 events per 1000 patient-years, while the increase in absolute risk for major bleeding was estimated at 7 events per 1000 patient-years.

Conclusion
In these patients with subclinical AF, the incidence of stroke was observed to be much lower compared to rates typically seen in symptomatic AF cases, which is reassuring. Apixaban did demonstrate efficacy in preventing a small number of strokes; however, this benefit came with a higher number of bleeding events compared to strokes prevented. It's worth noting that the disability associated with strokes seemed to be less severe when occurring in patients receiving anticoagulation.

Despite these findings, there remains a sense of hesitation, if not outright ambivalence, regarding the use of anticoagulation in such patients, especially when adhering to the principle of "Above all, do no harm." The absolute risk of stroke in these individuals is low, while the use of anticoagulants introduces a significant increase in the risk of major bleeding.

This dilemma underscores the need for careful consideration and individualized decision-making when weighing the potential benefits against the risks of anticoagulation therapy in patients with subclinical AF. It may be reasonable to extrapolate these results and apply it to even some critically ill patients with new onset short-term atrial fibrillation by maintaining a higher threshold to start anticoagulation among critically ill patients.

ORIGINAL STUDY SUMMARIES:

Initiation of Continuous Renal Replacement Therapy Versus Intermittent Hemodialysis in Critically Ill Patients with Severe Acute Kidney Injury: A Secondary Analysis of STARRT-AKI Trial

Background and Aim of Study:
The STandard versus Accelerated Renal Replacement Therapy in Acute Kidney Injury (STARRT-AKI) trial was conducted to help determine the optimal renal-replacement therapy (RRT) modality for critically ill patients with acute kidney injury (AKI). This secondary analysis compared the patient treatment outcomes of continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD).

Methods: Inclusion/Exclusion:
Trial randomized critically ill patients with severe AKI to 2 strategies (CCT and IHD) for RRT initiation, accelerated or standard. Patients included in trial had received at least one session of RRT, either CRRT or IHD. Patients whose initial RRT modality was sustained low efficiency dialysis (SLED) were excluded due to infrequent treatment.
Patients were allocated to either accelerated-strategy (treatment start within 12 hours) or standard strategy, where RRT was held unless indications developed or AKI persisted for more than 72 hours. Since RRT modalities are sometimes delivered in an integrated fashion, the proportion of days on RRT in the ICU (occurring during the first 14 days from randomization) were also evaluated as a continuous variable and categorized into increments. Patients were evaluated for 90 days.

Results:
The primary outcome evaluated the all-cause mortality or RRT dependence 90 days after patient randomization. From the original 3019 trial patients, the remaining 2196 participants: 1590 received CRRT and 606 received IHD. (Missing data, SLED use, and death were exclusion factored).
The association between initial RRT modality and the composite of death or RRT dependence at 90-days was evaluated across 10 pre-specified subgroups, (RRT strategy, Age, Sex, Chronic kidney disease, Sepsis, Mechanical ventilation, Vasoactive support, Baseline SOFA score, SOFA score at RRT initiation, and Cumulative fluid balance at RRT initiation). There were no statistically significant interactions.
The composite primary outcome of death or RRT dependence at 90-days:

- Patients who initially started CRRT 823 (51.8%)
- Patients who initially started IHD 329 (54.3%)

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After addressing propensity scores via the overlap weights of initial receipt, patients who received CRRT, compared to IHD, were associated with a lower risk of the composite of death or RRT dependence at 90-days.
Secondary outcomes were measured over the 90 day period that were of note:

- Patients who started CRRT (compared with those who commenced IHD) had a lower risk of RRT dependence at 90-days.
- There were no statistically significant differences in ICU and hospital length of stay between randomized patients. However, patients who initially received CRRT had more ICU-free days at 28-days and hospital-free days at 90-days compared the IHD treated patients.

Clinical interpretation:
While the optimal modality for RRT delivery remains controversial, the STARRT-AKI trial observed, through a retrospective analysis, CRRT was associated with a lower risk of the composite of all-cause mortality or RRT dependence 90 days for critically ill patients with acute kidney injury. This new observation should serve as a springboard for future randomized trials that can thoroughly assess the impact of RRT modality on clinical outcomes and healthcare costs.

ORIGINAL STUDY SUMMARIES:

Blood Eosinophil-guided Oral Prednisolone for COPD Exacerbations in Primary Care in the UK (STARR2): A Non-Inferiority, Multicentre, Double-Blind, Placebo Controlled, Randomised Controlled Trial

Introduction and Aim of Study:

Blood eosinophil biomarker-directed therapy is increasingly advocated in precision medicine by major medical societies. Prior to the widespread adoption of inhaled glucocorticoids for the eosinophilic phenotype of COPD, historical data revealed that systemic glucocorticoid treatment for COPD exacerbations posed a significant risk of harm. This risk was quantified with a number needed to treat (NNT) of ten to prevent one treatment failure and a number needed to harm (NNH) of five. Nearly half of treated patients experienced treatment failure or adverse events.

Two randomized controlled trials (Badadhel 2012, Sivapalan 2019) demonstrated that tailoring systemic glucocorticoid therapy based on eosinophil counts could safely reduce their usage in patients with low eosinophil counts during exacerbations, without impacting treatment failure rates. The STARR2 study, a multicenter, double-blind, placebo-controlled randomized trial conducted in the UK, specifically investigated the utility of point-of-care blood eosinophil count testing to guide prednisolone use in COPD exacerbations.

Methods/Design:

The STARR2 study took place in the United Kingdom across 14 primary care practices, involving 308 participants from November 6, 2017, to April 30, 2020. Eligible participants had to either have been free from recent exacerbations for a minimum of six weeks or be experiencing the onset of an exacerbation. They were randomly assigned to receive either prednisolone or a placebo daily for 14 days, adhering to national guidelines. Moreover, all participants were provided with doxycycline from their local pharmacy, administered at a dosage of 200 mg daily for one week.

Outcomes/Results

Study participants were randomly assigned to one of two groups: those receiving blood eosinophil-directed treatment (BET) with prednisolone or placebo, and those receiving standard care treatment (ST). The primary outcome assessed was treatment failure within 30 days post-exacerbation, defined as exacerbations requiring further treatment, hospitalization, or resulting in death, with a secondary assessment at 90 days.

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In the BET group, there was a significant 40% reduction in treatment failures compared to those receiving standard treatment. Participants in the treatment arm were administered prednisolone for 14 days, deviating from the current recommendation of 5 days as per COPD GOLD guidelines. Within the subset with low (<2%) blood eosinophil counts, participants treated with placebo and antibiotics experienced fewer treatment failures compared to those receiving prednisolone, with a calculated number needed to harm of 6.

Conclusion:

This trial found that using eosinophil counts to guide therapy was non-inferior to standard care, achieving similar outcomes in lung function, symptom recovery, and quality of life with a lower cumulative dose of oral prednisolone. Notably, despite certain methodological limitations and termination of study secondary to COVID-19 pandemic patients, with high eosinophil counts who received prednisolone showed the greatest improvements in lung function and COPD- specific quality of life. It's important to note that individuals with moderate to severe COPD and low eosinophil counts who are undergoing treatment with inhaled glucocorticoids face a heightened risk of pneumonia compared to those with high eosinophil counts. However, whether systemic steroids yield a similar effect remains uncertain.

Clinical interpretation:

The cumulative evidence from the available studies suggests that COPD exacerbation treatment should be guided by blood eosinophil counts to identify patients who would benefit from systemic glucocorticoids. This approach can minimize the exposure to and toxicity of glucocorticoids, improving patient outcomes. The findings also caution against the prevalent use of self-initiated prednisolone rescue packs by patients, suggesting that a more systematic and precise biomarker-directed assessment during exacerbations is needed to optimize therapy and reduce potential harm.

ORIGINAL STUDY SUMMARY & PERSPECTIVE

Providing Cleaning Recommendations for Positive Airway Pressure Devices

Afterall, CPAP does not really need to be so clean!

Written by Bharat Bajantri, MD
in collaboration with
Srinivasan Devanathan, MD and
Manuel Martinez, MD

The burden of maintenance and cleaning of Positive Airway Pressure (PAP) equipment has been ignored. Instructions for the care of PAP equipment are complex and can overwhelm patients and their families, potentially limiting PAP uptake.

The aggressive cleaning of PAP devices is commonly advocated to mitigate the risk of respiratory infections, although the evidence supporting this is tenuous.

Studies have shown the following:

- While bacterial and yeast colonies can grow on PAP masks, they mainly consist of normal skin flora and do not necessarily lead to respiratory infections.
- Swabs from PAP devices and air blowing out typically reveal nonpathogenic microbes, with no substantial difference between used and new devices.
- No difference in nasal swab results between patients using versus not using PAP.
- Humidifier chamber of PAP machines, often suspected as a source of infection, may harbor gram-negative bacteria, but colonization has not led to increased infection risk. Legionella colonization, while rare, has been reported in humidifier chambers, but prospective studies have failed to confirm its prevalence. Overall, serious infections related to PAP equipment appear to be infrequent given the substantial number of devices in use globally.

ORIGINAL STUDY SUMMARY & PERSPECTIVE

Providing Cleaning Recommendations for Positive Airway Pressure Devices

- Studies assessing the frequency of respiratory tract infections among obstructive sleep apnea (OSA) patients treated with PAP therapy versus those untreated or nonadherent to PAP have found no significant differences. In fact, some studies suggest that increased PAP usage might even reduce the risk of viral respiratory infections. However, there may be a slightly higher incidence of rhinitis symptoms among PAP users, though this has not been conclusively linked to infectious causes.

Despite limited scientific evidence, the belief that infections may result from inadequate cleaning of PAP equipment has been widely propagated by durable medical equipment (DME) providers and medical practices. Trusted institutions like Harvard, Cornell, and the Mayo Clinic have emphasized the importance of rigorous cleaning routines, even though the evidence supporting these recommendations is lacking. Additionally, the American Thoracic Society has advocated for adhering to manufacturer-recommended cleaning instructions in patient education materials.

Even the U.S. Food and Drug Administration (FDA) states on a patient-facing website that “[a]ll types of CPAP machines need to be cleaned regularly so that these germs and contaminants do not grow inside your equipment and make you sick”. (Patel, 2024)

Many clinicians tend to underestimate the burdens associated with recommending frequent cleaning of PAP devices, while overestimating the risks of not cleaning them adequately. Manufacturer-recommended cleaning instructions entail disassembling the mask daily, emptying and drying the humidifier chamber, and weekly cleaning of various components. However, adhering to these instructions imposes a considerable time burden on patients, often during rushed mornings.

ORIGINAL STUDY SUMMARY & PERSPECTIVE

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Studies show that a considerable portion of PAP users struggle with cleaning their equipment, leading to poor adherence rates. Patients perceive the risk of infection from wearing a "dirty" mask as a barrier to PAP compliance, which can lead them to forgo treatment altogether. Third-party PAP cleaning systems, marketed to alleviate these concerns, often use ozone gas or ultraviolet light, despite lacking evidence of efficacy and safety. Reports of adverse effects from these cleaners have increased, raising concerns about both financial and medical harm.

Aggressive cleaning recommendations from PAP manufacturers and Durable Medical Equipment (DME) providers are primarily driven by legal liability concerns and profit motives. Manufacturers aim to mitigate potential lawsuits by emphasizing infection risks and promoting frequent equipment replacement, thereby increasing sales. Since most patients cannot feasibly adhere to these cleaning frequencies, they are more likely to opt for costly equipment replacements.

To counteract these conflicts of interest, physicians and professional organizations must take charge in defining evidence-based cleaning practices. This involves direct communication with patients, revising educational materials, and disseminating accurate information through various channels. Collaboration with patient organizations ensures information accessibility and relevance. Professional organizations should also engage with manufacturers and DME providers to establish clear standards and advocate for regulatory oversight of PAP accessories. Sustained efforts and focused advocacy are necessary to challenge existing beliefs and bring about meaningful improvements in patient care.

Dr. Devanathan recommends periodic, but NOT DAILY, cleaning due to the burden, and to refrain from using certain non-original manufactured cleaning products that utilize ozone, especially in individuals with comorbid lung issues. Dr Martinez also says that it is unclear if such devices could harm or prematurely shorten the functional life of positive pressure devices. The only reason, in his opinion, to consider the use of such cleaning devices, would be in patients who had such severe arthritis that they could not physically handle the tasks of cleaning the CPAP components.

SNAPSHOTS

How many steps a day can really be healthy? Not 10,000.

A systematic review and meta-analysis investigated the relationship between daily step count and cardiovascular health outcomes. The study included data from 111,309 individuals across 12 studies. Compared to those taking 2000 or fewer steps per day, statistically significant risk reductions were observed for all-cause mortality at 2517 steps/day (adjusted hazard ratio, 0.92) and for incident cardiovascular disease (CVD) at 2735 steps/day (aHR, 0.89). The relationship between step count and risk reduction was nonlinear, with additional steps associated with further risk reductions up to thresholds of 8763 steps for all-cause mortality (aHR, 0.40) and 7126 steps for reduced CVD risk (aHR, 0.49). Transitioning from a low to an intermediate or high cadence was also linked to significant decreases in all-cause mortality risk, with a 33% decrease for intermediate cadence and a 38% decrease for high cadence.

This study discovered that taking fewer than 3000 steps per day was linked to significant reductions in mortality and incident cardiovascular disease (CVD). The greatest benefits were observed at approximately 8700 steps/day for mortality and 7100 steps/day for incident CVD. These findings indicate that health improvements from walking occur at much lower step counts than the commonly cited threshold of 10,000 steps/day. This reinforces the advice to patients: "just keep moving." While encouraging higher daily step counts is beneficial, patients should not be discouraged if they cannot reach a specific threshold.

Sedona, AZ. Photo by Colleague Dr. Manuel Martinez

SNAPSHOTS

WEANSAFE says it's safe to wean: BE BRAVE!

A weaning from mechanical ventilation (MV) is a challenging phase in recovering from respiratory failure, imposing a substantial burden on healthcare resources. Pham and colleagues conducted the "WEAN SAFE" study across 481 ICUs in 50 countries to investigate current practices and outcomes of weaning from MV in patients requiring invasive ventilation for at least 2 days. Only 65.0% of the 5869 enrolled patients were successfully weaned at day 90. The median time to meet ventilator weaning eligibility criteria was 1 day, but a delay of 5 or more days (among 22.4% of the patient population) was associated with subsequent ventilator weaning failure. A sensitivity analysis revealed sedation at the time of weaning readiness and delaying weaning attempts were strongly linked to failure. The study highlights significant heterogeneity in weaning management across centers and underscores the importance of addressing clinician-modifiable factors, such as sedation and time to the first weaning attempt, to prevent weaning failure and improve patient prognosis.

We should probably be cognizant about evaluating and potentially start weaning attempts 24-48 hours (about 2 days) of mechanical ventilation if not sooner.

Somethings we do wrong, but cannot do it right either! Can we try harder?

There is a notable gap in medical knowledge regarding the accurate measurement of pH in pleural fluid. The only validated and recommended method for measuring pleural fluid pH is by using a blood gas analyzer or GEM iSTAT. Any other method employed for measuring pleural fluid pH is deemed inaccurate. Moreover, it is crucial to measure the pH of pleural fluid immediately after drainage to obtain the most precise result.
Regrettably, in most hospitals, the GEM and i-STAT instruments are not validated or FDA-approved for analyzing body fluids. Consequently, any fluid sample analyzed using these instruments is considered off-label, rendering it a complex test and potentially impacting the warranty status of the machine. Having said that delaying source control for conditions like empyema has shown to increase mortality, thus justifying the need to either validate GEM and i-STAT instruments or have more readily available point of care testing for pleural fluid pH.

SNAPSHOTS

Pleural fluid collection for cultures and microbiology has demonstrated significantly higher yield when directly collected in blood culture bottles, as evidenced by multiple past studies and more recent validations. Research indicates that pleural fluid collected in blood culture bottles outperforms standard culture bottles in terms of yield. Despite this evidence, it remains a lesser-known practice, with pleural fluid often being collected in presumed sterile plastic containers or glass tubes before being sent to the laboratory. In fact, samples are often rejected by microbiology labs if fluid samples are only collected only in blood cultures bottles without additional samples in sterile containers or tubes.

Delays in processing these samples are common due to the multitude of tests typically performed in laboratories. This combination of factors contributes to a notable decrease in yield for identifying microorganisms, estimated to be around 40-50%. Streamlined efforts to update pleural fluid specimen collection protocols are necessary in today's world where personalized medicine and antibiotic stewardship is taking more precedence.

GRATITUDES

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Dr. Manuel Martinez at the iconic IN-N-OUT Burger

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