GEMs of the Week

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Week of March 27 - 31, 2023

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LEEP Under Local Anesthesia: Is It Better?

Syringe or Mask? Loop Electrosurgical Excision Procedure Under Local or General Anesthesia: A Randomized Trial

Rezniczek GA, Hecken JM, Rehman S, Dogan A, Tempfer CB, Hilal Z. Syringe or mask? Loop electrosurgical excision procedure under local or general anesthesia: a randomized trial. *Am J Obstet Gynecol*. 2020;223(6):888.e1-888.e9. doi:10.1016/j.ajog.2020.06.041

KEY TAKEAWAY: Loop electrosurgical excision procedure (LEEP) under local anesthesia is well tolerated and offers patient-reported and procedure-related benefits over general anesthesia.

STUDY DESIGN: Prospective randomized single-site trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: LEEP is a common gynecological procedure, however, there is no high-level evidence that compares the use of local anesthesia (LA) vs general anesthesia (GA). This study aims to clarify these differences regarding cost effectiveness, quality of care, and patient satisfaction.

PATIENTS: Women requiring treatment with a LEEP procedure

INTERVENTION: LEEP procedure under local anesthesia

CONTROL: LEEP procedure under general anesthesia

PRIMARY OUTCOME: Patient satisfaction, pain, perception of bleeding severity and duration, if they would repeat the procedure with the same anesthetic Secondary Outcome: resection margin status, number of fragments, number of additional resections needed, procedure duration, time to complete hemostasis, interoperative and post-operative complications

METHODS (BRIEF DESCRIPTION):

- Inclusion criteria included women with an indication for LEEP, including biopsy with LSIL, biopsy with HSIL, or abnormal pap with inconclusive colposcopy results. They were randomized into either "LEEP-LA" to receive local anesthetic with LEEP, or "LEEP-GA" to receive a general anesthetic. Randomization occurred via a computer-generated list.
- Participants were similar in age (31 to 46 years), BMI (20 to 26), and cytology.
- The same three surgeons performed both LEEP-LA and LEEP-GA.
- In the LEEP-LA protocol, bupivacaine was used for local anesthesia.
- In the LEEP-GA protocol, fentanyl and propofol were used for anesthesia.
- Primary outcomes included the day of surgery and 14 days post-op patient satisfaction assessed using a Likert Scale, and post-procedure questionnaire. The Likert Scale assessed current pain level, pain during the procedure, level of anxiety, subjective report 14 days post-op of bleeding severity, duration, pain level, and pain duration on a 0 to 10 scale.
- Secondary endpoints included resection margin status (R1, involved margin; R0, free margin), resected cone mass (measured in grams before formalin embedding), intraoperative blood loss (pre and post-operative change in hemoglobin), procedure time (start of excision to hemostasis), cone fragmentation (additional resections), intraoperative and postoperative complications until 14 days post-op (bleeding, infection, UTI), and surgeon satisfaction using the Likert scale.
- Statistical analyses performed using the Mann-Whitney U test for continuous data failing the Shapiro-Wilk normality test OR using the Chi-square test or Fisher's exact test to compare frequencies.

INTERVENTION (# IN THE GROUP): 103

COMPARISON (# IN THE GROUP): 96

FOLLOW-UP PERIOD: 14 days post-op

RESULTS:

Primary Outcome –

- Patient satisfaction and pain level immediately post-procedure did not differ between LA or GA groups.
- There was no difference between the groups in patient satisfaction, pain level or duration, anesthesia preference, or perception of bleeding severity at 14 days post-op.
- LA reduced the patient-reported duration of post operative bleeding days compared to GA (7.5 vs 13, respectively; *P*=.026).

Secondary Outcome –

- There was no difference in patient satisfaction at 14 days, resection margin status, cone fragmentation,

procedure duration, time to complete hemostasis, intraoperative and postoperative complications.

- Cone values were less in the LA group compared to the GA group (1.1 vs 1.6 cm^3, respectively).
- LA resulted in less interoperative blood loss compared to GA (Hgb change 0.2 vs 0.5 g/dL, respectively).

LIMITATIONS:

- Selection bias: the study recruited only women referred to the specialized colposcopy clinic. Thus, measured outcomes of procedures by study participants may differ from women in population-based screening programs.
- Differences in practice: GA procedures utilizing fentanyl, propofol, and isoflurane may not represent the GA medications in other countries or institutions, thus limiting external validity.

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Finerenone: An Agent of Benefit in CKD with T2DM

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

Bakris GL, Agarwal R, Anker SD, et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. *N Engl J Med*. 2020;383(23):2219-2229. doi:10.1056/NEJMoa2025845

KEY TAKEAWAY: Treatment with finerenone in type 2 diabetes (T2DM) and chronic kidney disease (CKD) lowers the risk of CKD progression and cardiovascular events compared to placebo.

STUDY DESIGN: Phase three, randomized, double-blind, placebo-controlled, multicenter clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Finerenone, a nonsteroidal, selective mineralocorticoid receptor antagonist, reduces albuminuria in short-term trials involving patients with CKD and T2DM. However, its long-term effects on kidney and cardiovascular outcomes are unknown.

PATIENTS: Patients with CKD and T2DM

INTERVENTION: Finerenone + renin-angiotensin system blockade

CONTROL: Placebo + renin-angiotensin system blockade

PRIMARY OUTCOME: CKD progression

Secondary Outcome: Cardiovascular events, adverse events

METHODS (BRIEF DESCRIPTION):

- Patients from 48 countries including the United States with CKD and T2DM were randomly assigned in a 1:1 ratio to receive finerenone or placebo.
- Eligible patients had a urinary albumin-to-creatinine ratio of 30:300, an eGFR of 25–60 mL/min, and diabetic retinopathy, or urinary albumin-to-creatinine ratio of 300:5000 or an eGFR of 25–75 mL/min.
- Patients with an eGFR of 25–60 mL/min received an initial dose of 10 mg once daily, and those with an eGFR of ≥60 mL/min received an initial dose of 20 mg once daily.
- An increase in the dose from 10 to 20 mg was encouraged after one month, provided the serum potassium level was ≤4.8 mmol/L and the eGFR was stable; a decrease in the dose from 20 to 10 mg was allowed any time after the initiation of finerenone or placebo.
- Patients in the placebo group underwent sham adjustment of the dose.
- Finerenone or placebo was held if potassium concentrations exceeded 5.5 mmol/L and restarted when potassium levels fell to ≤5.0 mmol/L.
- Outcomes were assessed in time-to-event analyses.
- CKD progression included kidney failure, a sustained decrease of at least 40% in eGFR from baseline, or death from renal causes.
- Cardiovascular events included death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.

INTERVENTION (# IN THE GROUP): 2,833

COMPARISON (# IN THE GROUP): 2,841

FOLLOW-UP PERIOD: Median 2.6 years

RESULTS:

Primary Outcome –

- Finerenone reduced CKD progression more than placebo (hazard ratio [HR] 0.82; 95% CI, 0.73–0.93).

Secondary Outcome –

- Finerenone reduced cardiovascular events more than placebo (HR 0.86; 95% CI, 0.75–0.99).
- Overall, the frequency of adverse events (acute kidney injury, blood pressure, and hyperkalemia) were similar in the two groups.
  - Hyperkalemia-related hospitalizations were higher in the finerenone group than in the placebo group (1.4% vs 0.3%, respectively).
  - Discontinuation of the trial regimen was higher in the finerenone group than in the placebo group (2.3% vs 0.9%, respectively).

LIMITATIONS:

- Patients included in the study had advanced CKD, limiting conclusions regarding early CKD.
- Patients with nonalbuminuric CKD or CKD not due to diabetes were not included in the study, which limits generalizations for CKD.
- Only 4.7% of the population identified as Black.

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How Far Should We Lower Serum Urate in Patients with Erosive Gout?

Intensive Serum Urate Lowering with Oral Urate-lowering Therapy for Erosive Gout: A Randomized Double-Blind Controlled Trial

Dalbeth N, Doyle AJ, Billington K, et al. Intensive Serum Urate Lowering With Oral Urate-Lowering Therapy for Erosive Gout: A Randomized Double-Blind Controlled Trial. *Arthritis Rheumatol*. 2022; 74(6):1059-1069. doi:10.1002/art.42055

KEY TAKEAWAY: Intensive urate-lowering therapy did not improve bone erosion scores compared to standard urate-lowering therapy.

STUDY DESIGN: Randomized double-blind control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Bony erosions caused by gout can result in significant disability. If intensive uric acid lowering treatments could improve erosions and therefore disability that would be desirable.

PATIENTS: Adults with erosive gout on treatment

INTERVENTION: Intensive urate target

CONTROL: Standard urate target

PRIMARY OUTCOME: CT bone erosion

Secondary Outcome: Gout flares, tophus count, pain

METHODS (BRIEF DESCRIPTION):

- 104 participants over 18 years old diagnosed with gout and with at least one bone erosion on plain radiography, currently receiving oral urate-lowering treatment, and serum urate >0.30 mmol/L or 5.0 mg/dL were included.
- Participants were randomly assigned to either the intensive target group (<0.2 mmol/L or 3.4 mg/dL) or the standard target group (<0.30 mmol/L or 5.0 mg/dL).
- Urate lowering therapy per titration protocol:
  - Allopurinol was increased monthly by 50 to 100 mg daily (eGFR dependent and maximum dose of 900 mg/day).
  - If serum urate target was not reached, then probenecid 500 mg twice daily was added up to a max of 1 g twice daily after one month.
  - If not at target with allopurinol/probenecid combination, then these were replaced with febuxostat starting at 80 mg daily up to a max of 120 mg/day.
  - If the target was not reached with febuxostat, then benzobromarone 100 mg/day was prescribed in addition with allopurinol.
- Bone erosions were scored with CT scans on a scale of 1–10 in increments of 10% based on the proportion of bone involved.
  - A score of 1 would correspond to 1–10% bone involvement and a score of 10 would indicate 90–100% bone involvement.
- Pain was measured through a visual analog scale.

INTERVENTION (# IN THE GROUP): 52

COMPARISON (# IN THE GROUP): 52

FOLLOW-UP PERIOD: Two years

RESULTS:

Primary Outcome –

- After two years, there was no significant difference in CT erosion between intensive and standard target groups.

Secondary Outcome –

- After two years, there were no significant differences in gout flares tophus count, or pain between intensive and standard target groups.

LIMITATIONS:

- The study may not be relevant to patients without erosive disease or to health care systems without access to urate-lowering medications used in this study.

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Intranasal Corticosteroid Effects on COVID-19 Olfactory Dysfunction

Intranasal Corticosteroid Treatment on Recovery of Long-Term Olfactory Dysfunction Due to COVID-19

Hosseinpoor M, Kabiri M, Rajati Haghi M, et al. Intranasal Corticosteroid Treatment on Recovery of Long-Term Olfactory Dysfunction Due to COVID-19 [published online ahead of print, 2022 Aug 25]. *Laryngoscope.* 2022;10.1002/lary.30353. doi:10.1002/lary.30353

KEY TAKEAWAY: Intranasal corticosteroids do not significantly improve olfactory recovery in non-hospitalized COVID-19 patients.

STUDY DESIGN: Randomized, double-blind, controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size and short follow-up)

BRIEF BACKGROUND INFORMATION: As one of the first symptoms of COVID-19 infection, anosmia may hinder quality of life. Corticosteroids have been noted to block COVID-19 replication and inflammation. Second-generation intranasal corticosteroids have fewer systemic side effects than their oral and first-generation counterparts, with 30% nasal glucocorticoid receptor binding. However, controversy remains in the efficacy of topical nasal corticosteroids for the improvement of olfactory dysfunction.

PATIENTS: Non-hospitalized adults with persistent anosmia/microsmia secondary to COVID-19

INTERVENTION: Mometasone furoate intranasal spray

CONTROL: Sodium chloride intranasal spray (placebo)

PRIMARY OUTCOME: Improvement of olfactory dysfunction due to COVID-19

METHODS (BRIEF DESCRIPTION):

- Adults with definitive COVID-19 infection and persistent anosmia/microsmia following 30–90 days after diagnosis were included.
  - Non-hospitalized patients were referred to Mashhad University of Medical Sciences between April and July 2020.
  - Demographics:
    - Placebo: Mean age 35 years old, 60% female, olfactory dysfunction duration 57±15 days
    - Intervention: Mean age 32 years old in the intervention group, 69% female, olfactory dysfunction 58±17 days
- Patients were randomized to one of the following:
  - 0.05% wt/vol mometasone furoate intranasal spray in each nostril twice daily for four weeks
  - 0.65% wt/vol sodium chloride intranasal spray in each nostril twice daily for four weeks
- Smell function was evaluated at zero, two, and four weeks following treatment using the Iran Smell Identification Test (Iran-SIT) and the Visual Analog Scale (VAS) smell test.
  - Iran-SIT: The patient identifies smells based on odor releasing scratch stickers in relation to four option choices.
  - VAS: A numerical olfactory dysfunction rating scale ranging 0 to 10, with 10 being the best.

INTERVENTION (# IN THE GROUP): 35

COMPARISON (# IN THE GROUP): 35

FOLLOW-UP PERIOD: Four weeks

RESULTS:

Primary Outcome –

- Intranasal corticosteroid use did not improve olfactory dysfunction in non-hospitalized COVID-19 patients after two or four weeks.
- Olfactory dysfunction improved from baseline to two and four weeks in both the placebo and intervention groups independently based on the Iran-SIT scale (P<.001).
  - Placebo: 4 at baseline vs 19 at four weeks
  - Intervention: 4 at baseline vs 10 at four weeks

LIMITATIONS:

- There is a limited understanding of the patho-mechanism for inflammation in chronic sinusitis.
- The use of systemic steroids may have produced a better effect; however, the study did not evaluate given concerns for reduced immunity.
- There was a small sample size and a short follow-up period.
- The study was localized to one demographic location and hospital system.

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PRAPARE Social Risk Screening Tool and Associations with Chronic Disease Outcomes

Development of PRAPARE Social Determinants of Health Clusters and Correlation with Diabetes and Hypertension Outcomes

Wan W, Li V, Chin MH, et al. Development of PRAPARE Social Determinants of Health Clusters and Correlation with Diabetes and Hypertension Outcomes. *J Am Board Fam Med*. 2022;35(4):668-679. doi:10.3122/jabfm.2022.04.200462

KEY TAKEAWAY: The Protocol for Responding to and Assessing Patient Assets, Risks, and Experiences (PRAPARE) screening tool currently identifies that high-risk social background, social insecurities, and insurance/employment may correlate with uncontrolled diabetes and uncontrolled hypertension.

STUDY DESIGN: Cross-sectional study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to non-blinded cross-sectional study design)

BRIEF BACKGROUND INFORMATION: Social Determinants of Health (SDoH), such as social and economic factors, unemployment, and lack of quality housing, have a large impact on disparities in healthcare. However, there is limited research on how multiple SDOH factors affect an individual's chronic health. Primary care physicians often take care of patients with higher socioeconomic disadvantages and using social risk screening tools like PRAPARE may help improve patient care.

PATIENTS: Adult patients at the Siouxland Community Health Center in Iowa

INTERVENTION: Exposure/history of SDoH

CONTROL: No exposure/history of SDoH

PRIMARY OUTCOME: Uncontrolled diabetes and uncontrolled hypertension

METHODS (BRIEF DESCRIPTION):

- The PRAPARE survey was developed after reviewing literature and environmental scans which was implemented into a pilot study to assess the validity and reliability of approximately 3,000 patients. Then the survey was created to include the SDoH clusters.
- The study simplifies 22 PRAPARE SDoH into three clusters (Social Background, Social Insecurities, and Insurance/Employment) and three standalone clusters for Federal Poverty Level, Social Integration, and Housing Status.
- There was a greater percentage of females, non-Hispanic/Latino, White, English-speaking population in all categories.
- PRAPARE survey administered by clinical staff who arranged for resources for patients (18–75 years old) if SDOH barriers were noted.
- Immediate assistance was given if positive screening for homelessness, partner violence, neighborhood safety, food insecurity, or transportation issues.
- Standardization was achieved using binary coding and ordinal coding.
- SDOH cluster scores and total risk scores were obtained using exploratory and confirmatory factor analyses. A high score = higher risk while a low score = lower risk.
- The associations between the cluster scores and the clinical outcomes were determined by logistic regression.
    - 6.08% had diabetes only
    - 20.3% had hypertension only
    - 12.5% had diabetes and hypertension
    - 61.1% had neither diabetes nor hypertension
- Uncontrolled diabetes was defined as HbA1c greater than or equal to 9%.
- Uncontrolled hypertension was defined as SBP greater than or equal to 140 mmHg and/or DBP greater than or equal to 90 mmHg.

INTERVENTION (# IN THE GROUP): 11,773

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Not applicable

RESULTS:

Primary Outcome –

- Uncontrolled diabetes mellitus was significantly associated with higher PRAPARE scores in the following areas:
    - Social background (OR 1.1; 95% CI, 1.02–1.2)
    - Social insecurities (OR 1.2; 95% CI, 1.1–1.3)
    - Insurance/employment (OR 1.2; 95% CI, 1.1–1.5)
- Uncontrolled hypertension was significantly associated with social insecurities (OR 1.2; 95% CI, 1.1–1.3).

LIMITATIONS:

- There was limited generalizability given that the study was conducted at one FQHC.
- Missing data was due to incomplete answers to PRAPARE survey questions.
- Not all confounding variables were accounted for in this study.
- Other factors such as racism and trust in healthcare were not considered in this study.
- This study underestimated the SDoH needs for patients who may have received additional services from FQHC.

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Decreasing the Risk of Interval Post Colonoscopy Colorectal Cancer after FIT-Based Screening

Decreasing the Risk of Interval Post Colonoscopy Colorectal Cancer after FIT-Based Screening

Wisse PHA, Erler NS, de Boer SY, et al. Adenoma Detection Rate and Risk for Interval Post Colonoscopy Colorectal Cancer in Fecal Immunochemical Test-Based Screening: A Population-Based Cohort Study. *Ann Intern Med*. 2022;175(10):1366-1373. doi:10.7326/M22-0301

KEY TAKEAWAY: Higher endoscopist adenoma detection rates result in a decreased risk of interval post-colonoscopy colorectal cancer after FIT-positive colonoscopies.

STUDY DESIGN: Population-based cohort

LEVEL OF EVIDENCE: STEP 4 (downgraded due to disease-oriented outcomes)

BRIEF BACKGROUND INFORMATION: Adenoma detection rate (ADR) is a quality measure that reflects an endoscopist's ability to detect colorectal adenomas during colonoscopies. With the increased use of fecal immunochemical test (FIT)-based colon cancer screening, few studies have examined the relationship between ADR and the risk of post-colonoscopy colorectal cancer (PCCRC) after a positive FIT result.

PATIENTS: Patients with a positive FIT result

INTERVENTION: Interval colonoscopies

CONTROL: None

PRIMARY OUTCOME: Incidence of interval PCCR

Secondary Outcome: Association between ADRs and interval PCCRC, incidence of PCCRC for different ADRs

METHODS (BRIEF DESCRIPTION):

- Data was obtained from individuals through a Dutch national colorectal cancer (CRC) screening program.
- Patients were 55–75 years old and had a colonoscopy done after a positive FIT result between 2014–2016.
- Interval colonoscopy follow-up was based on an adenoma score that incorporated the number, size, location, and histologic villosity of adenomas found on the initial and subsequent colonoscopies. Patient data were followed from the time of their first colonoscopy to the diagnosis of PCCRC, their surveillance colonoscopy, or the end of the study (January 1st, 2020), whichever came first.
- Quality measures for individual endoscopists, including the ADR, were obtained. Colonoscopies in which CRC was detected at the initial colonoscopy were excluded. 103,900 colonoscopies performed by 311 endoscopists met the study criteria.
- ADR was defined as the number of colonoscopies with at least 1 adenoma detection divided by the total number of colonoscopies done. PCCRC was defined as an interval if it occurred before the next recommended surveillance colonoscopy. An ADR of at least 25% is the recommended standard for endoscopists.
- The incidence of interval PCCRC was assessed using a multivariable Cox proportional hazards model that included patient-specific demographics, diagnosis at initial colonoscopy, recommended surveillance, endoscopist ADR, and the type of endoscopy setting. Penalized smoothing splines were used to determine the association between ADRs and interval PCCRCs and the incidence of PCCRCs for varying ADRs.

INTERVENTION (# IN THE GROUP): 103,900

COMPARISON (# IN THE GROUP): None

FOLLOW-UP PERIOD: Six years

RESULTS:

Primary Outcome –

- The incidence of interval PCCRC after a positive FIT result steadily increased after five years.
  - 0% at 1 year (95% CI, 0.00-0.02)
  - 0.1% at 2 years (95% CI, 0.04-0.07)
  - 0.1% at 3 years (95% CI, 0.11-0.15)
  - 0.2% at 4 years (95% CI, 0.18-0.24)
  - 0.3% at 5 years (95% CI, 0.23-0.31)
  - 0.3% at 6 years (95% CI, 0.23-0.41)

Secondary Outcome –

- ADR is inversely associated with interval PCCRC rate (HR 0.95 per 1% ADR increase; 95% CI, 0.92–0.97).
- The incidence of interval PCCRC after five years decreases with higher ADRs.
  - Endoscopists with 70% ADR had an interval PCCRC incidence of 2 per 1000 patients.
  - Endoscopists with 65% ADR had an interval PCCRC incidence of 2.5 per 1000 patients.

- Endoscopists with 60% ADR had an interval PCCRC incidence of 3.5 per 1000 patients.
- Endoscopists with 55% ADR had an interval PCCRC incidence of 4.5 per 1000 patients.

LIMITATIONS:

- There were no patient-oriented outcomes, only disease-oriented outcomes.
- Because the study concluded after six years, patients in whom a 10-year colonoscopy surveillance was recommended could still develop an interval PCCRC.
- During the study the starting age of FIT-based CRC screening was lowered to include more individuals which may result in lower rates of adenomas.
- The cutoff for a positive FIT result may vary amongst different manufacturers.

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