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Proton pump inhibitor use is not significantly associated with severe COVID-19 related outcomes after extensive covariate adjustment*

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OBJECTIVES/GOALS: Using the covariate-rich Veteran Health Administration data, estimate the association between Proton Pump Inhibitor (PPI) use and severe COVID-19, rigorously adjusting for confounding using propensity score (PS)-weighting. METHODS/STUDY POPULATION: We assembled a national retrospective cohort of United States veterans who tested positive for SARS-CoV-2, with information on 33 covariates including comorbidity diagnoses, lab values, and medications. Current outpatient PPI use was compared to non-use (two or more fills and pills on hand at admission vs no PPI prescription fill in prior year). The primary composite outcome was mechanical ventilation use or death within 60 days; the secondary composite outcome included ICU admission. PS-weighting mimicked a 1:1 matching cohort, allowing inclusion of all patients while achieving good covariate balance. The weighted cohort was analyzed using logistic regression. RESULTS/ANTICIPATED RESULTS: Our analytic cohort included 97,674 veterans with SARS-CoV-2 testing, of whom 14,958 (15.3%) tested positive (6,262 [41.9%] current PPI-users, 8,696 [58.1%] non-users). After weighting, all covariates were well-balanced with standardized mean differences less than a threshold of 0.1. Prior to PS-weighting (no covariate adjustment), we observed higher odds of the primary (9.3% vs 7.5%; OR 1.27, 95% CI 1.13-1.43) and secondary (25.8% vs 21.4%; OR 1.27, 95% CI 1.18-1.37) outcomes among PPI users vs non-users. After PS-weighting, PPI use vs non-use was not associated with the primary (8.2% vs 8.0%; OR 1.03, 95% CI 0.91-1.16) or secondary (23.4% vs 22.9%;OR 1.03, 95% CI 0.95-1.12) outcomes. DISCUSSION/SIGNIFICANCE: The associations between PPI use and severe COVID-19 outcomes that have been previously reported may be due to limitations in the covariates available for adjustment. With respect to COVID-19, our robust PS-weighted analysis provides patients and providers with further evidence for PPI safety.

Contemporary Research Challenges

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Engineering Synthetic Scaffolds to Achieve Periodontal Ligament Cell-Mediated Tissue Regeneration*

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OBJECTIVES/GOALS: Autologous periodontal ligament cells (PDLCs) are a promising tool for rebuilding tooth-supporting (periodontal) tissues but require scaffolds that enable delivery while maintaining PDLC bioactivity. The goal of this study was to design a synthetic hydrogel that fulfilled these criteria to support clinical translation of PDLC delivery. METHODS/STUDY POPULATION: Hydrogels were formed using poly(ethylene glycol) (PEG) polymers and synthetic peptides. PDLCs were isolated from human 3rd molars following informed consent and were cultured using established techniques. Integrin-binding peptides were utilized to promote specific PDLC behaviors, testing PDLCs from 3 human donors in a design of experiments (DOE) approach. Two promising hydrogel designs, identified in the DOE, were selected for validation testing using PDLCs from 3 additional donors. Finally, a small animal model for hydrogel-mediated PDLC delivery was used to determine if benchtop outcomes could predict in vivo tissue regeneration. RESULTS/ANTICIPATED RESULTS: Hydrogel scaffolds maintained high PDLC viability and controlled differentiation of each donor's PDLCs based on differential presentation of integrin-binding peptides RGD and GFOGER. Two hydrogel designs were selected that optimized either PDLC alkaline phosphatase (ALP) activity or matrix mineralization, outcomes typically associated with cementum and bone formation. ALP activity-optimized hydrogels displayed enhanced PDLC pyrophosphate regulation while mineralization-optimized hydrogels promoted PDLC osteogenic differentiation. When used to deliver PDLCs to periodontal defects, both ALP activity-optimized and mineralization-optimized hydrogels stimulated new cementum formation with inserting PDL fibers, while mineralization-optimized hydrogels promoted enhanced bone formation. DISCUSSION/SIGNIFICANCE: Numerous challenges remain for translating PDLC regenerative potential to clinical practice. This study demonstrates that a synthetic hydrogel scaffold could overcome certain barriers, including controlling PDLC bioactivity with a simplified fabrication and delivery scheme, and may be a promising scaffold for periodontal tissue regeneration.