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Acid Suppression to Prevent Gastrointestinal Bleeding in Patients with Ventricular Assist Devices

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ABSTRACT

Background: The high incidence of gastrointestinal bleeding (GIB) in patients with ventricular assist devices (VAD) is well known, but there is limited evidence to support the use of proton pump inhibitors (PPIs) or histamine receptor antagonists (H2RA) for preventing GIB in patients with VAD.

Materials and methods: The surgical ICU and VAD databases within a large regional academic cardiac mechanical support and transplant center were queried for patients who underwent VAD implantation between 2010 and 2014. An observational cohort study was conducted to identify which acid suppressing drug regimen was associated with the fewest number of GIB events within 30 d after VAD implantation: PPI, H2RA, or neither. Secondary outcomes included timing, etiology, and location of GIB. Multivariable logistic regression was used to compare treatment cohorts to GIB. Odds ratios, 95% confidence intervals, and *P*-values were reported from the model.

Results: One hundred thirty-eight patients were included for final analysis, 19 of which had a GIB within 30 days of VAD implantation. Both H2RA and PPI use were associated with reduced GIB compared with the cohort with no acid suppressive therapy. In the multivariate analysis, the PPI cohort showed a statistically significant reduction in GIB (Odds ratio 0.18 [95% confidence interval 0.04-0.79] $P = 0.026$).

Conclusions: Using PPI postoperatively in patients with new VAD was associated with a reduced incidence of GIB. Given that GIB is a known complication after VAD placement, clinicians should consider the use of acid suppressive therapy for primary prevention.

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Introduction

Providing mechanical circulatory support using ventricular assist devices (VAD) in patients with significant cardiac dysfunction has grown exponentially over the past decade. While VAD can be a life-saving option, they are associated with significant morbidity, including gastrointestinal bleeding (GIB).[1]

In 1994, Cook *et al.* published a sentinel paper investigating risk factors for clinically significant GIB in critically ill patients and reported that significant GIB occurred in only 1.5%.[2] However, in patients who required mechanical ventilation for greater than 48 h or had a coagulopathy, GIB incidence more than doubled to 3.7%. Patients with clinically important GIB had a significantly higher mortality rate (48.5%) compared with those who did not bleed (9.1%).[2] Evidence-based guidelines were published, clarifying the risk factors for GIB and the role for stress ulcer prophylaxis (SUP) using acid suppressing drugs such as proton pump inhibitors (PPIs) or histamine receptor antagonists (H2RA), but these guidelines have not been updated since 1999.[3-5] They do not address VAD as a risk factor. Despite the established problem of GIB in patients with VAD, there is no evidence or guideline recommendation to support the prophylactic use of acid suppression to prevent GIB.[3,6]

There are many etiologies for GIB in patients with VAD. These include angiodysplasias, arteriovenous malformations, acquired von Willebrand syndrome, impaired platelet function, shear stress phenomena, and lowered pulse pressure leading to relative hypoperfusion.[6-19] Although the need for therapeutic anticoagulation also complicates bleeding risk after VAD, an association between GIB risk and level of anticoagulation has not been established.[18,20,21] The variety of GIB etiologies in VAD complicates the identification and utilization of targeted preventions and treatments, and may cast doubt on the utility of acid suppression for GIB prevention. Therefore, our primary objective was to study the relationship between acid suppression regimens (PPI, H2RA, or neither) and GIB after VAD implantation. Descriptive secondary objectives included timing, etiology, and location of GIB.

Materials and methods

Our institution is an academic medical center within a 660-bed health care system that houses a regional comprehensive cardiac mechanical circulatory support and transplant program. The cardiovascular intensive care unit has 20 ICU beds and provides care for both critically ill medical and surgical cardiac patients. Mechanical circulatory support patient populations include those requiring temporary and/or permanent VAD implantation, as well as extracorporeal membrane oxygenation.

Patients for inclusion were retrospectively identified via admission diagnosis or procedure code for VAD placement between May 2010 and May 2014. Patients who had surgical placement of a VAD (biventricular, right, or left) and survived at least to the end of the 30-d postoperative study period were considered for inclusion. Patients with an existing VAD admitted for an acute GIB were not included. Exclusion criteria included age less than 18 y, any solid organ transplant, use of direct oral anticoagulants before VAD implantation, a temporary VAD duration of less than 7 d, or steady state use of both a PPI and H2RA during the study period. This study was approved by the University of Utah Institutional Review Board with a waiver for individual consent.

Using institutional databases (VAD team comprehensive database, cardiovascular intensive care unit database) and the electronic medical record, documentation of major GIB within 30 d after VAD implantation was captured for all new VAD within the study timeframe, regardless of inpatient or outpatient status. The definition used for major GIB was based on the INTERMACS definition of major bleeding as a suspected or overt bleed requiring transfusion and/or treatment,[1] modified to include only bleeding from the gastrointestinal tract. Treatment for all GIB in the study was performed at the study institution where implantation occurred, and all GIB were evaluated with a documented endoscopic exam.

Meaningful covariates were identified and collected using institutional databases. Data concerning bleeding risk factors established based on previous literature were collected, including age, sex, preoperative use of antiplatelets or steroids, preoperative hematocrit, renal dysfunction, history of GIB, nutrition status, anticoagulation, and respiratory failure.[7-16] Treatment exposure was defined as starting either a PPI or H2RA on or before postoperative day #4 and having this therapy continued for at least four doses to reach steady state.

Statistical methods

Patient characteristics (demographics, severity, preoperative, and postoperative but pre-treatment exposure variables) were summarized, analyzed, and stratified by treatment group and by the GIB outcome. Continuous variables were summarized as mean and standard deviation or median and interquartile range (IQR) depending on distribution skew. Categorical variables were summarized as count (%), using column percentages for the treatment groups and for GIB outcome. An analysis of variance (ANOVA) or Kruskal–Wallis test was used to compare continuous variables across treatment groups. A *t*-test or exact Wilcoxon rank sum test was used to compare continuous variables with the GIB outcome. A chi-squared or Fisher's exact test was used to compare categorical variables across treatment groups and the GIB outcome.

Logistic regression was used to assess the effect of acid suppressive treatment on GIB while controlling for select clinical covariates. A univariate analysis of baseline variables with GIB was used to inform which clinical covariates to include in the multivariate analysis along with clinical importance. Our multivariable logistic regression model was limited in the number of supportable predictors due to few GIB events. However, we relaxed the 10 events per predictor