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Patterns of Proton Pump Inhibitor Continuation After Hospital Discharge and Their Relationship with Documented Clinical Indications

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Abstract

Proton pump inhibitors (PPIs) are commonly initiated during hospitalization and are commonly continued even post-discharge in the absence of a well-defined review plan. In this study, we have looked at the pattern of continuation of PPIs and its association with documented indications. We conducted a retrospective observational cohort study on 412 adults who received PPI prescriptions upon discharge from a tertiary care teaching hospital, with follow-up regarding PPI prescription for 6 months. The indications were categorized into documented ongoing, documented time-limited, and undocumented based on discharge and admission notes and continuation evaluated at 1, 3, and 6 months. The data analysis was done using descriptive statistics, chi-square test, and logistic regression on SPSS version 26.0. The documented ongoing indication was found in 51.2% of the participants, documented time-limited in 20.1%, and undocumented in 28.6%. The overall rate of continuation was 77.2% at 3 months and 67.0% at 6 months. For those patients with no documented indication, 49.8% continued on PPIs after six months, accounting for 36.2% of six-month PPI use overall. In these patients, continuing PPIs was less common if there was a documented stop date or review plan in the discharge summary (21.9% vs 62.8%; $p < 0.001$), and lack of such a plan was the strongest independent predictor of continuation (adjusted OR 5.34; 95% CI 2.61–10.92). Continuing PPI therapy after discharge is commonly not associated with an indicated use and may be prevented by documenting duration/review at discharge.

Keywords: Proton Pump Inhibitors, Hospital Discharge, Medication Continuation, Clinical Indication, Deprescribing, Transitions of Care, Retrospective Cohort.

1 INTRODUCTION

1.1 Background

PPIs are the most frequently prescribed class of medications in hospitals and the community (Haroon et al., 2013; Leri et al., 2013). They are useful for conditions involving excessive acid secretion like erosive esophagitis, peptic ulcers, and upper GI bleeding; in addition, they are employed to shield the lining of the stomach in high-risk cases where individuals are on anti-thrombotic or anti-inflammatory agents that can cause bleeding. The good tolerance and availability of PPIs have been associated with an extended use of the drugs beyond these indications, especially among hospitalized patients where acid suppression is instituted early in acute illness.

1.2 Hospital Discharge as a Point of Medication Transition

The discharge of a patient from hospital represents a crucial time when medicines that have been introduced during the patient's stay will cease to be used, be extended with an aim, or be extended without any further evaluation of this decision. For example, use of PPI initiated for stress ulcer prophylaxis or for a short-time indication would be discontinued once the need for such treatment ends (Katz et al., 2013; Wilhelm et al., 2013). However, in reality, the medicine will be prescribed and included into the discharge letter without any mention of duration and will be automatically extended by other community prescribers. Thus, use of the drug can continue for many months or even years without a proper reason, putting patients to unnecessary risk of taking extra pills.

1.3 Research Problem and Rationale

While the problem of overprescribing PPIs is well known, the level of continuity due to an indication has not been adequately described in many cases. Studies that look at the amount of prescribing alone are unable to differentiate between necessary and automatic continuation of the prescription (Maggio et al., 2013). Associating the treatment plan after discharge with the indication found at discharge makes it possible to quantify the level of unnecessary continuation and to understand the documentation factors that affect this process.

1.4 Aim and Objectives

The purpose of this research was to analyze the trends of PPI continuation after hospitalization and the association with the presence of clinical indications. The specific purposes were:

- To categorize the clinical indications reported for PPI treatment at discharge from hospitals.
- To assess the rate of PPI treatment continuation 1 month, 3 months, and 6 months after discharge.
- To compare the rate of PPI continuation between categories of clinical indications.
- To evaluate the percentage of prolonged PPI treatment without any reported clinical indications.

- To analyze the patient and documentation-related factors influencing continuation without indications.

2 REVIEW OF LITERATURE

2.1 Appropriate Indications for Proton Pump Inhibitor Therapy

Currently, there are established indications for PPIs including Gastroesophageal Reflux Disease (GERD) with erosive esophagitis, peptic ulcer disease, eradication of Helicobacter pylori, upper gastrointestinal bleeding and its management, Barrett's esophagus, gastroprotection in patients at risk of upper gastrointestinal injury due to age, ulcers, antithrombotic therapy, steroids, and non-steroidal anti-inflammatory drugs (Corleto et al., 2014; Larsen et al., 2014). In cases where therapy is required for a certain condition for a short while, it will only last for a limited time and then will be re-assessed, while in others, the use of PPIs will last as long as the risks associated remain. Stress ulcer prophylaxis is done in critically ill patients and when their risks end, they should stop taking the PPIs (Pappas et al., 2016).

2.2 Continuation of Therapy Started in Hospital

Several observational studies from various healthcare systems have reported patients who have been initiated on an acid suppressant medication during their hospitalization but continue with the same prescription on discharge, in many cases without clear indication or intended duration. This practice is frequently followed by primary care physicians who are unaware of the reasons for starting the drug (Haastrup et al., 2014; Ladd et al., 2014). Incomplete or unclear documentation at the time of discharge is one of the factors that can contribute to this practice, since the details required to discontinue the medication are not available to the patient.

2.3 Consequences of Prolonged Use

PPI use for extended periods of time has been linked to a number of possible adverse effects, such as enteral infection, lack of micronutrients, decreased bone mineral density, and drug interactions; however, the level of evidence varies between these risks, and the causal relationship may not be proven for some of these. Even in cases when the harmful effect of PPIs is not entirely certain, their unnecessary extended use leads to increased burden and expense of medications, as well as difficulties in treating multimorbid patients.

2.4 Research Gap

In few investigations has patient follow-up been carried out after discharge with patients being classified based on the actual indication recorded in the hospital notes. Even fewer studies have focused on looking at whether recording a stopping date or a review schedule plays any part in continued use. This research tries to bridge this knowledge gap.

3 METHODOLOGY

3.1 Study Design and Setting

The retrospective observational cohort study was carried out in a tertiary care teaching hospital. Patients over 18 years who were discharged from medical, surgical, and critical care step-down units in a span of twelve months with a PPI included in the medication on discharge were selected through electronic discharge records, and follow-up of prescription was done for six months after discharge using outpatient and pharmacy records. The study protocol was cleared by the Institutional Ethics Committee, which waived the need for obtaining informed consent since this was an observational study based on the already available data in the database.

3.2 Study Population and Sample Size

All consecutive eligible discharges throughout the study period were selected. This went beyond the minimal number of 385 subjects needed to generate an estimate of 50% proportion with a 5% precision at the 95% confidence interval. A total of 468 discharges were recruited. Among them, 56 were disqualified due to death of the patient before the follow-up period ended (n=21), lack of traceability of records from outpatient and dispensing services (n=19), and incomplete documentation (n=16), resulting in 412 eligible patients. Patients who were released alive after being prescribed a PPI on the discharge prescription list, being 18 years old or more, were selected. On the other hand, patients who were transferred to other facilities, discharged to nursing home facilities where medication is supplied by the facility, or those with incomplete discharge information were not included.

3.3 Data Collection

Abstraction of data was conducted by two trained reviewers using a standardized form. Variables that were captured included the patient’s age, gender, service admitted, length of stay, number of discharge medications, the source of PPI treatment (initiation during the index hospitalization or continuation after the admission), the drug used, and the dose. Other variables included the content of the discharge summary regarding the indication, duration, and stop date or review of the drug.

3.4 Classification of Indications and Outcome Measures

The indication that was documented for each patient was derived from discharge summary, admission notes, and endoscopy, imaging, and medication files and categorized in three groups. Documented indication for ongoing use was documented if the condition which warranted ongoing treatment was documented, that is, reflux disease with esophagitis, peptic ulcer disease or recent upper gastrointestinal bleeding, gastroprotection of a patient at high risk or another well-known condition, including Barrett's esophagus. A documented time-limited indication was documented if the documented reason was expected to resolve, that is, stress ulcer prophylaxis in the period of acute illness or short period after endoscopic procedure. Documentation of no indication was documented if no reason for treatment could be found in the medical record. Inter-rater reliability between the two

reviewers was good (κ = 0.84). The primary end point was persistence with PPI therapy at 3 and 6 months, which was defined as use or at least one fill within 30 days before each measurement. Persistence at 1 month was also measured. Persistence without a documented indication for use was defined as persistence at 6 months in a patient with a time-limited indication or without a documented indication.3.5 Study Framework

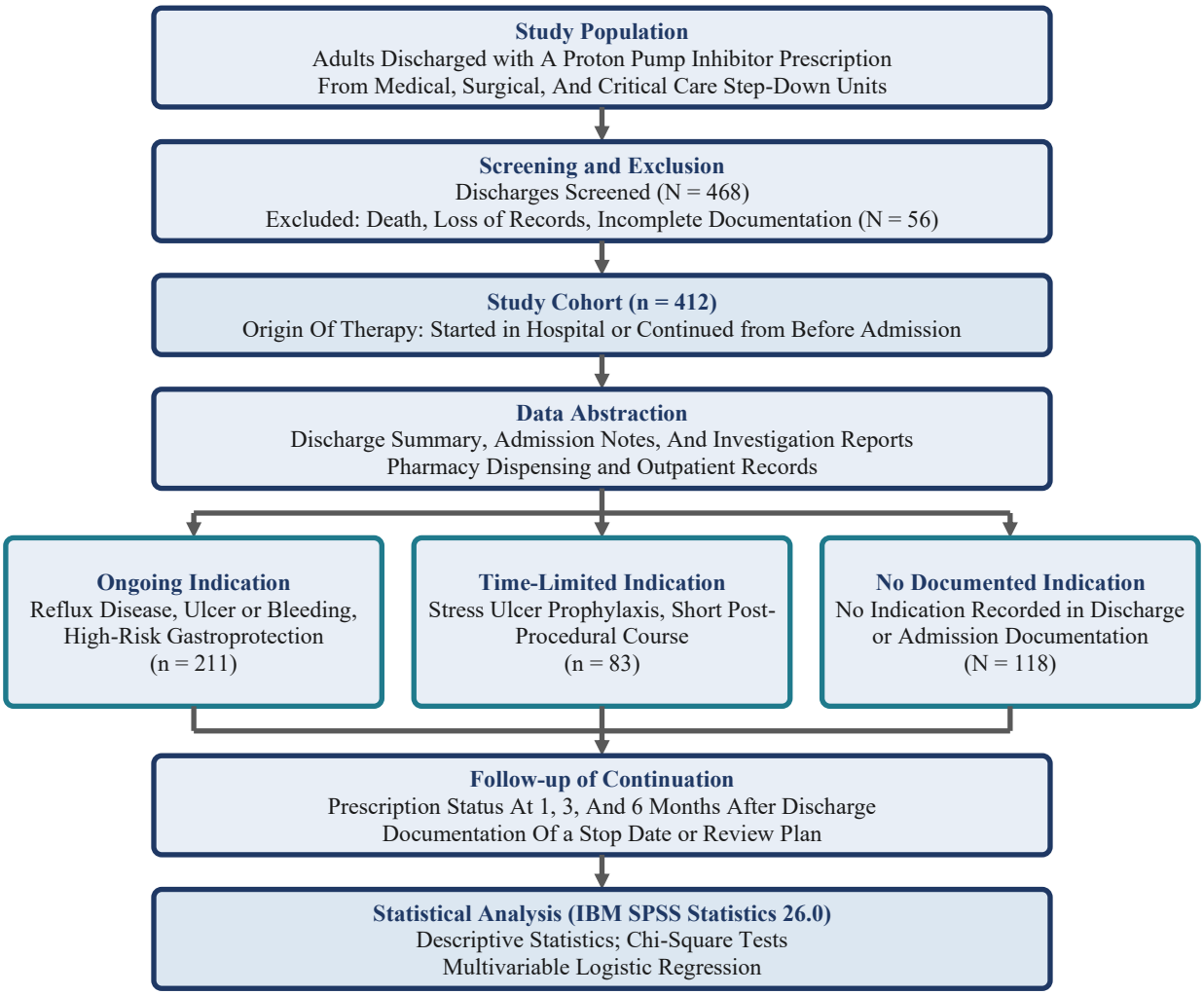


Figure 1: Methodological Architecture of The Study Showing Screening, Cohort Formation, Data Abstraction, Classification of Documented Indications, Follow-Up of Continuation, And Statistical Analysis

The research design is presented in figure 1. Patients who were discharged on a PPI were screened and the eligible sample selected. Data on clinical characteristics and PPI prescription were collected from medical charts and prescription records, and patients were categorized according to their indication for the PPI and monitored post-discharge.

3.6 Statistical Analysis

The analyses were done by using IBM SPSS Statistics 26.0. The continuous data were presented in mean ± standard deviation or median (interquartile range) while the categorical data were presented in frequencies (percentages). Comparison between continuation and indication categories was done by

chi-square test. Multivariable logistic regression was used to identify factors associated with continuation at six months amongst patients without an indication for their medications, such as age, gender, polypharmacy (taking five or more discharge medications), source of treatment, having a stop date or follow-up plan, and the odds ratio with 95% confidence interval was calculated. P<0.05 was considered statistically significant.

4 RESULTS

4.1 Characteristics of the Cohort

The cohort comprised 412 patients with a mean age of 61.3 ± 14.8 years; 224 (54.4%) were men and 188 (45.6%) were women. Patients were discharged from medical units in 214 cases (51.9%), surgical units in 118 (28.6%), and critical care step-down units in 80 (19.4%). The median length of stay was 6 days (interquartile range 4–10), and 231 patients (56.1%) were discharged on five or more medicines. The PPI had been started during the index admission in 247 patients (60.0%) and was a continuation of pre-admission therapy in 165 (40.0%).

4.2 Documented Clinical Indications

Table 1. Documented Indication at Discharge and Continuation of Proton Pump Inhibitor Therapy (N = 412)

Documented indication	n (%)	Continued at 3 months, n (%)	Continued at 6 months, n (%)
Documented ongoing indication	**211 (51.2)**	**187 (88.6)**	**176 (83.4)**
Reflux disease with esophagitis	74 (18.0)	66 (89.2)	64 (86.5)
Peptic ulcer disease or recent upper GI bleeding	58 (14.1)	49 (84.5)	46 (79.3)
Gastroprotection in high-risk patients	61 (14.8)	55 (90.2)	50 (82.0)
Other recognized indication	18 (4.4)	17 (94.4)	16 (88.9)
Documented time-limited indication	**83 (20.1)**	**59 (71.1)**	**45 (54.2)**
No documented indication	**118 (28.6)**	**72 (61.0)**	**55 (46.6)**
Total cohort	**412 (100)**	**318 (77.2)**	**276 (67.0)**

Ongoing indication documentation was noted for 211 subjects (51.2%), time-limited indication documentation for 83 subjects (20.1%), and no indication documentation for 118 subjects (28.6%)

(Table 1). Reflux disease with esophagitis was the most common among the patients having an ongoing indication (74 patients, 18.0% of the total), followed by gastroprotection in high-risk patients (61, 14.8%) and peptic ulcer disease or recent upper gastrointestinal bleed (58, 14.1%). Indication for stress ulcer prophylaxis constituted 52 out of 83 cases of the time-limited indication (62.7%). The pattern of indication varied depending on the source of therapy. For those who were administered PPI during the period of hospitalization, 98 (39.7%), 71 (28.7%), and 78 (31.6%) had ongoing, time-limited, and no indications, respectively. Those who continued pre-admission therapy had 113 (68.5%), 12 (7.3%), and 40 (24.2%) ongoing, time-limited, and no indications, respectively.

4.3 Patterns of Continuation After Discharge

Continuation rates were reduced steadily following discharge. As a whole, 77.2% of the subjects were on a PPI at 3 months and 67.0% at 6 months. This reduction was highly variant depending on the indication of therapy (Figure. 2). For those with a sustained indication of therapy, continuation rates were 96.2% at 1 month, 88.6% at 3 months, and 83.4% at 6 months. For patients with a limited indication for the medication, the rate of reduction was greater, with 71.1% at 3 months and 54.2% at 6 months, and those without indication had the largest reduction at 1 month, with 84.7%, with 46.6% at 6 months. There was a significant difference in six-month continuation between the three groups ($\chi^2 = 54.02$, $p < 0.001$), as well as at three months ($p < 0.001$). Six-month continuation was also lower for patients starting their therapy during hospitalization than patients receiving pre-admission therapy (59.9% vs 77.6%; $p < 0.001$).

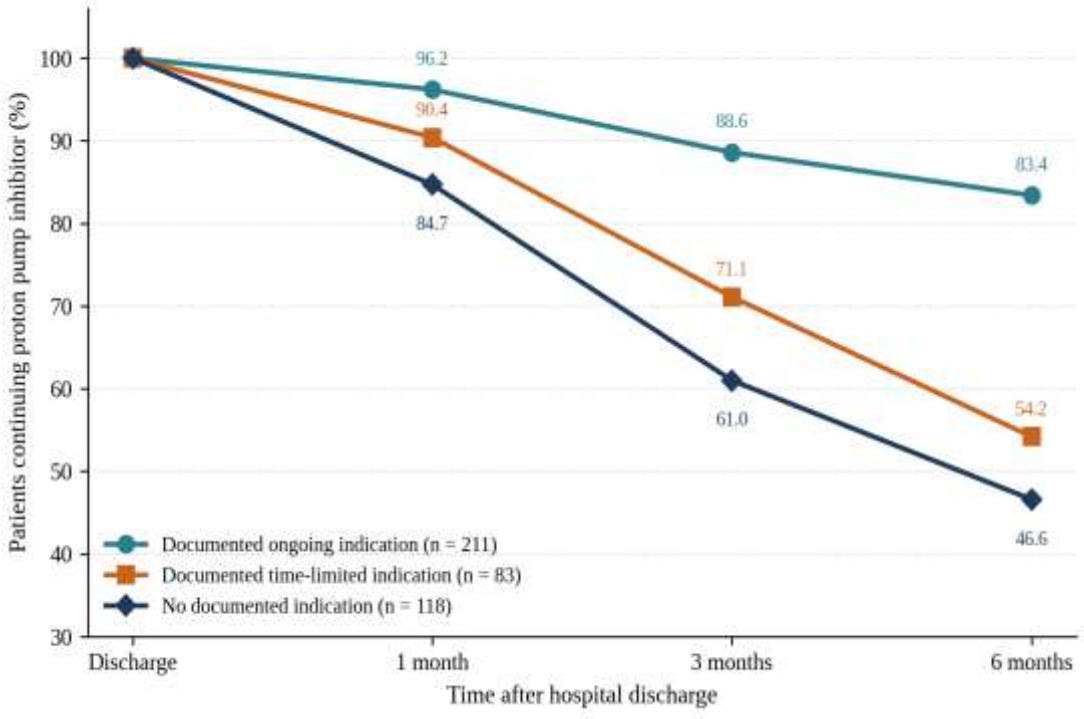


Figure 2: Proportion of Patients Continuing Proton Pump Inhibitor Therapy After Hospital Discharge, By Category of Documented Indication

4.4 Continuation Without a Documented Ongoing Indication

Among the 201 patients with a time-limited indication or no indication documented, 100 (49.8%) patients were still on PPI at six months. They constituted 36.2% of the total 276 patients who were on treatment at six months, which means that over one third of long-term use had no document-based indication at all. Among the 201 patients, there was a stop date or a plan for review documented in their discharge summary in 64 cases (31.8%). The continuation at six months was much less likely to occur in the presence of such documentation (14 of 64; 21.9%) compared to its absence (86 of 137; 62.8%) ($\chi^2 = 29.19$, $p < 0.001$).

In the multivariate analysis, lack of documented stop date or plan for review was the most significant correlate of continuation (aOR 5.34; 95% CI 2.61–10.92; $p < 0.001$). Being 65 years of age or older was also an independent predictor of continuation (aOR 1.92; 95% CI 1.04–3.55; $p = 0.037$), while polypharmacy had the same effect but without statistical significance (aOR 1.71; 95% CI 0.94–3.12; $p = 0.080$). Gender and origin of therapy were not significantly related to continuation in adjusted analysis.

5 DISCUSSION

5.1 Interpretation of Major Findings

In the current research, the continuation of PPI therapy post-discharge was found to be partially influenced by the presence of a documented clinical indication. Continuation at six months was quite high, accounting for 83.4% of patients with a documented indication, which is the usual trend for patients who continue their treatment. Nonetheless, almost half of those patients who had a time-limited indication or lack of documented indication were still on a PPI at six months after being discharged. This group made up almost one third of all long-term users of PPIs, implying that a substantial amount of long-term PPI use was due to a temporarily intended therapy or without indication.

The pattern of discontinuation varied by type of indication in a way that is clinically sensible. Patients whose indications were time-limited and in whom stress ulcers prophylaxis was common terminated the drug use more frequently compared to those whose indications were ongoing, implying that some of the therapies had been discontinued properly. However, over half of these patients were still under medication after six months, a scenario that is more than could be expected if the indication had been met properly. Patients who had no indication whatsoever terminated their use the fastest, mostly during the first month, but even here the rate of continuation was over half, implying that this was not complete termination either.

Most compelling of all was the result regarding documentation. The proportion of those without an indication who continued when the discharge letter included a stop date or follow-up plan was less than a quarter, in contrast to more than three fifths when there was no such plan documented. This relationship remained significant even after controlling for age, gender, polypharmacy, and source of

medication. This indicates that continuation is frequently the result of lack of information and not a decision to continue, in light of the fact that a community prescriber will not have any reason to stop a medication if he is not told otherwise.

5.2 Clinical Implications

These results suggest that discharge documentation provides a concrete intervention opportunity. Requiring that all PPIs included in a discharge list have indication stated along with a period of treatment and either stop or review date will turn implicit continuation into explicit indication. Review of medications listed in discharge prescription forms by pharmacists, prompting in electronic discharge form, and informing primary care physicians about the list are possible strategies to fill this gap. The special focus should be made on patients whose medication was initiated during hospitalization, older people, and polypharmacy patients where continuation without indication was more frequent. With the continued indication, the proper medication will be protected from unintended discontinuation.

5.3 Strengths and Limitations

The strengths of this study include the selection of consecutive discharges, independent classification of indications by two reviewers with excellent agreement between them, and the linking of hospital documentation with dispensing information for six months. The following limitations need to be recognized. The retrospective study is based on the documentation and an indication that was not documented would be considered an undocumented one, resulting in overestimation of unnecessary use. Dispensing information confirms that medication has been dispensed rather than consumed and over-the-counter purchase cannot be accounted for. The single center design with six months' follow-up reduces the possibility of generalization and evaluation of long-term medication use. The final limitation is that the effects of discontinuing therapy on the outcome were not assessed.

6 CONCLUSION

6.1 Summary of Key Findings

PPI continuation after discharge from hospital was frequent, with 77.2% and 67.0% of patients on treatment at three months and six months, respectively. The highest rate of continuation was found in patients with an ongoing indication, whereas it was much lower but considerable in the case of a time-limited indication and no indication. More than 50% of patients without an ongoing indication continued treatment for six months, and they comprised more than one-third of all continued therapy. A stop date or review plan at discharge was related to a substantially lower rate of continuation in these patients.

6.2 Clinical Recommendations and Future Research

Discharge protocols ought to be accompanied by an indicated rationale, planned period, and follow-up/termination date for each PPI prescription with pharmacist review and proper

communication to primary care physicians. Further research needs to employ prospective and multicenter studies and incorporate patient outcomes after the discontinuation of PPI prescriptions. It also needs to investigate whether discharge protocols or deprescribing strategies decrease unnecessary prolonged PPI therapy.

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