Prophylactic use of proton pump inhibitors post-cardiac surgery

Abstract

Aims/Background Gastrointestinal bleeding significantly increases morbidity and mortality rates postoperatively in patients undergoing cardiac surgery. The prophylactic prescribing of proton pump inhibitors post-cardiac surgery is currently a class IIa recommendation of the European Association of Cardio-Thoracic Surgery.

Method A retrospective review of patients who underwent cardiac surgery between July and December 2019 in the authors' hospital was carried out, using discharge summaries. New treatment charts were introduced with a pre-printed proton pump inhibitor included in the 'regular medication' section of the treatment chart and two reaudits were performed using the same methodology.

Results Before the intervention, 47% were prescribed omeprazole postoperatively, compared to 74% ($P<0.001$) and 66% ($P=0.008$) in the first and second reaudits respectively. Gastrointestinal bleeding was more common pre-intervention (4% vs 1% respectively; $P=0.10$).

Conclusions This intervention resulted in a statistically significant improvement in the prescription of postoperative omeprazole and a decrease in gastrointestinal bleeds. However, other risk factors such as diabetes mellitus, arteriosclerosis and procedure urgency may have contributed to the absence of statistical significance in the latter.

Key words: Cardiac surgery; Duodenal ulcer; Gastrointestinal bleeding; Proton pump inhibitors

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Introduction

Gastrointestinal bleeding post-cardiac surgery is associated with a high mortality and a significantly lengthened hospital stay. In a study involving 150 000 patients, postoperative gastrointestinal bleeding was found in 0.39%, with a 30-day mortality rate of 19% (Rodriguez et al, 2010). As cardiac surgical techniques have evolved, the age of patient undergoing surgery has increased, yielding more comorbidities (Mangano et al, 1992). This makes prophylactic treatment for gastrointestinal bleeding post-cardiac surgery a potentially important intervention to reduce mortality.

The two most common causes of postoperative bleeding are stress-related mucosal breakdown causing gastritis and gastric erosions, and duodenal ulceration associated with peptic ulcer disease. Cardiac surgery can lead to splanchnic territory ischaemia and gastrointestinal mucosal defects as a result of perioperative hypotension, use of vasoconstrictive agents, low left ventricular ejection fraction and prolonged cardiopulmonary bypass time (van der Voort and Zandstra, 2000). Apart from this, patients undergoing cardiac surgery have the added risk of being fully heparinised to an activated clotting time of over 450 seconds and are given aspirin immediately postoperatively. These factors further increase the probability of gastrointestinal mucosal damage and postoperative gastrointestinal haemorrhage.

Seven risk factors were reported to be associated with an increased risk of upper gastrointestinal bleed after cardiac surgery (Krawiec et al, 2017). These are:

1. Age >70 years
2. Ejection fraction <35%
3. Congestive heart failure
4. Cerebrovascular disease

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5. Chronic kidney disease
6. Preoperative atrial fibrillation
7. Valve procedures.

Studies have shown that post-cardiac surgery patients treated with a proton pump inhibitor suffer a much lower rate of active gastrointestinal ulcers than patients treated with a histamine-2-antagonist or a mucosal protector (Hata et al, 2005; Shin and Abah, 2012). The prophylactic use of proton pump inhibitors in all post-cardiac surgery patients is a class IIa recommendation in the European Association of Cardio-Thoracic Surgery guidelines (Sousa-Uva et al, 2018).

This project evaluated the risk factors for gastrointestinal bleeding present in cardiac surgery patients at Mater Dei Hospital, ascertained whether these patients were given prophylactic proton pump inhibitors, and improved current practice, thus improving patient safety.

Methods

A retrospective review of patients who underwent elective or urgent cardiac surgery over a period of 6 months (July–December 2019) at Mater Dei Hospital was first carried out. The complete list of patients operated on during this period was derived from the cardiothoracic unit database. Data regarding patient demographics, comorbidities, postoperative complications and treatment given were collected from their discharge summaries. The risk factors present at time of surgery and the prescription of postoperative proton pump inhibitors were analysed.

In January 2020 new treatment charts with a proton pump inhibitor (omeprazole) printed on them in the 'regular medication' section were introduced in the cardiothoracic unit to replace the old treatment charts. Two reaudit cycles were then performed to assess the long-term sustainability of the change; from May–October 2020 (cohort one) and November 2020–April 2021(cohort two). The same information was collected and the same methodology was used.

All patients selected were operated on by three cardiothoracic surgeons who were not involved in the audit study and design. To eliminate any bias in prescribing, these surgeons were not informed about this audit. The results were then published with the surgeons' consent, in an anonymised manner.

A chi-square test of independence (2x2) was used to compare the differences in proton pump inhibitor prescribing before and after the intervention. It operated on the null hypothesis that proton pump inhibitor prescribing was not affected by pre-printed treatment charts. The α-value used was 0.01.

Results

In the first cycle, 124 cases were reviewed, of which six cases were excluded. In the post-intervention cycle, a total of 102 cases in cohort one and 81 cases in cohort two were analysed, with seven exclusions in each cohort. Cases were excluded because they did not have case summaries available. Pre-intervention, 55 of 118 patients (47%) were prescribed postoperative proton pump inhibitors compared to 70 out of 95 patients (74%) in post-intervention cohort one (χ^2=15.911, df=1, P<0.001), and 49 out of 74 patients (66%) in cohort two (χ^2=7.0417, df=1, P=0.008) (Figure 1). The average post-intervention prescribing rate of prophylactic proton pump inhibitors was 70%, an increase of 49%.

Risk factors identified in all patient cohorts are shown in Table 1.

A total of 83 patients from the first cycle had at least one risk factor for gastrointestinal bleed; of these, 33 (45%) were prescribed prophylaxis. The 35 patients with no risk factors had a 51% rate (18 patients) of prophylaxis prescribed (Figure 1).

In post-intervention cohort one, 52 (73%) out of the 71 patients who had at least one risk factor for gastrointestinal bleeding were prescribed proton pump inhibitor prophylaxis (χ^2=17.3448, df=1, P<0.001), while 75% (18) of the 24 patients with no risk factors were given postoperative proton pump inhibitors (χ^2=3.3256, df=1, P=0.07) (Figure 1). In the second post-intervention cohort, 33 of the 47 patients (70%) at risk of gastrointestinal

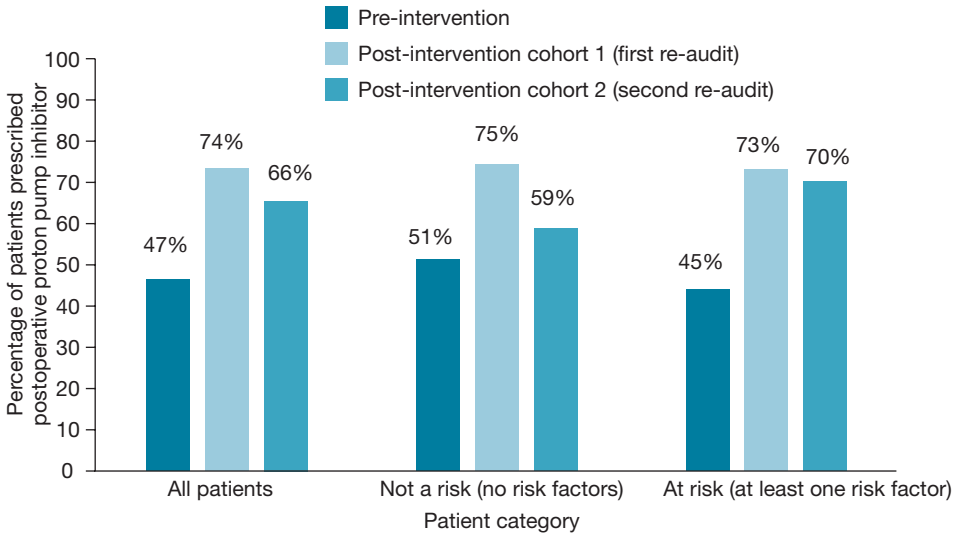

Figure 1. Percentage of patients prescribed a postoperative proton pump inhibitor, before and after the intervention.

Table 1. Risk factors documented in all patient cohorts

	Pre-intervention cohort	Post-intervention cohort one (first reaudit)	Post-intervention cohort two (second reaudit)
Age >70 years	44 (37%)	25 (26%)	28 (38%)
Chronic kidney disease	18 (15%)	8 (8%)	4 (5%)
Ejection fraction <35%	2 (2%)	0	1 (1%)
Congestive cardiac failure	2 (2%)	15 (16%)	12 (16%)
Atrial fibrillation	2 (2%)	5 (5%)	4 (5%)
Cerebrovascular disease	2 (2%)	3 (3%)	4 (5%)
Valve surgery	2 (2%)	42 (44%)	29 (39%)

bleeds were prescribed postoperative proton pump inhibitors (χ^2=11.1346, df=1, P<0.001), compared to 16 out of 27 patients (59%) who had no risk factors (χ^2=0.3774, df=1, P=0.54).

A further breakdown of prophylactic proton pump inhibitor prescription according to the number of risk factors found is illustrated in Figure 2.

With regards to documented gastrointestinal bleeding, between July and December 2019, five out of 118 patients (4%) had gastrointestinal bleeds, but over both post-intervention cohorts only two out of 169 patients (1%) suffered a post-cardiac surgery gastrointestinal bleed (χ^2 = 2.7233, df=1, P=0.10) (Figure 3).

Finally, the percentage of patients who were prescribed postoperative proton pump inhibitors per consultant was analysed in both post-intervention cohorts (Figure 4).

Discussion

The first cycle of this audit revealed that only 47% of patients were discharged on a proton pump inhibitor post cardiac surgery in the second half of 2019. Interestingly, patients with no risk factors had a higher rate of being prescribed proton pump inhibitors on discharge (51%) than patients who had risk factors for gastrointestinal bleeding (45%).

The first cycle of this audit found that 60% of patients who were at a moderate risk of gastrointestinal bleed were discharged on a proton pump inhibitor. While this is a better figure than the low-risk group (40%), there is still room for improvement.

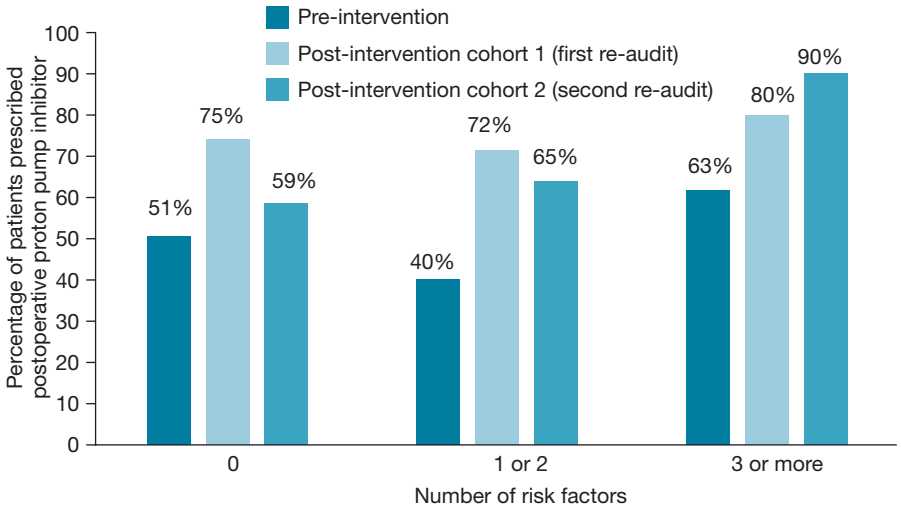

Figure 2. Percentage of patients prescribed a postoperative proton pump inhibitor per risk category, before and after the intervention.

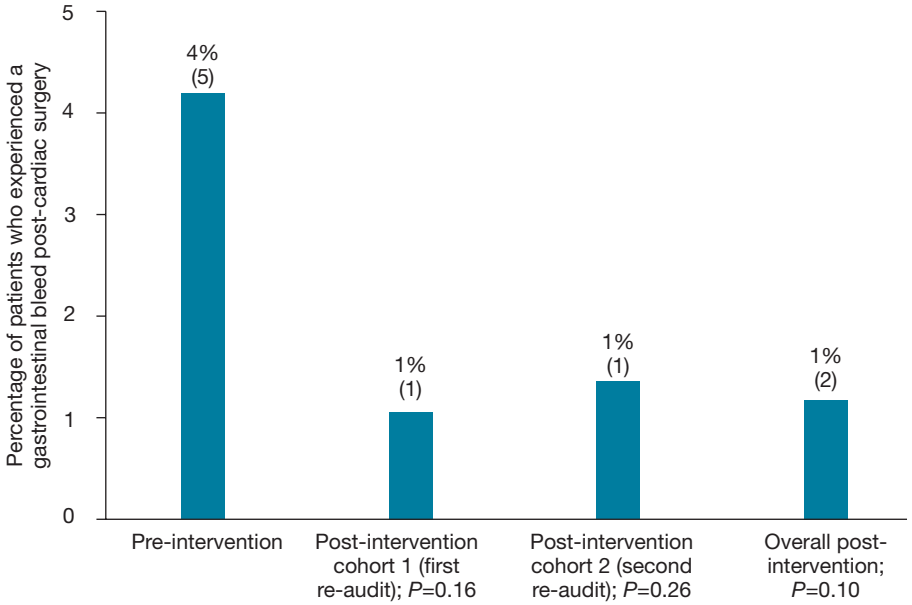

Figure 3. Comparison of the percentage of patients who experienced a gastrointestinal bleed post-cardiac surgery, pre-intervention and post-intervention. Total patient number pre-intervention=118, post-intervention: cohort 1 = 95, cohort 2 = 74 ([cohort 1] χ^2=1.9498, df=1, *P*=0.16; [cohort 2] χ^2=1.2512, df=1, *P*=0.26; [overall post-intervention] χ^2 = 2.7233, df=1, *P*=0.10).

A statistically significant improvement in prophylactic prescription of proton pump inhibitors was noted post-intervention, with an average 49% increase in prescribing of proton pump inhibitors. Compared to 47% before the intervention, 74% of patients in the first post-intervention cohort (*P*<0.001) were given prophylactic postoperative proton pump inhibitors. This statistically significant improvement was maintained in the second reaudit, with the prophylactic proton pump inhibitor prescribing rate found to be 66% (*P*=0.008). This demonstrates the long-lasting effect of the intervention implemented.

This improvement was also noted to be statistically significant in the low-risk group, with a prescription rate of 72% in the first post-intervention cohort (*P*<0.001) and 65% in the second post-intervention cohort (*P*=0.02), compared to the pre-intervention rate of 40%. In the moderate-to-high risk group, an improvement in proton pump inhibitor prescribing was also noted, but it was not found to be as statistically significant (Figure 2).

To account for all variables, the compliance with this intervention by different consultants in the department was assessed. Most patients under the care of consultants A (average 81%)

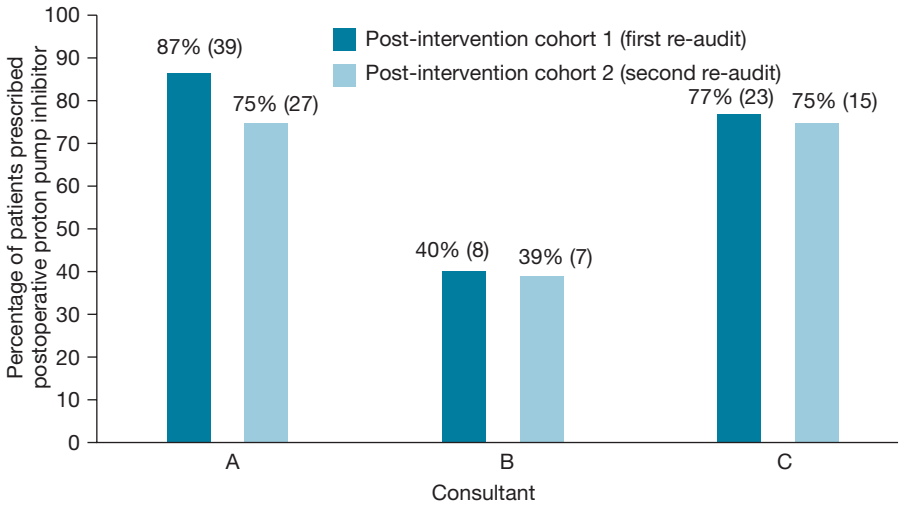

Figure 4. Percentage of patients prescribed postoperative proton pump inhibitor per consultant. Total patient number cohort 1: A=45, B=20, C=30; total patient number cohort 2: A=36, B=18, C=20 ([cohort 1] χ^2=15.7519, df=2, P<0.001; [cohort 2] χ^2=7.9403, df=2, P=0.02).

and C (average 76%) were given postoperative proton pump inhibitors, but less than half of patients under the care of consultant B (average 39%) were prescribed prophylactic proton pump inhibitors (Figure 4). This difference was found to be statistically significant in both post-intervention cohorts (cohort 1 post-intervention P<0.001; cohort 2 post-intervention P=0.02). This shows that while the intervention significantly improved the department's practice, compliance with protocols is still an issue that has to be addressed.

Between July and December 2019, 4% of patients had a gastrointestinal bleed as a complication. Of the 118 patients, three had gastrointestinal bleeds during their inpatient stay and a further two were readmitted within 30 days of discharge because of a gastrointestinal bleed. All five of these bleeds were the result of a duodenal ulcer (found on oesophagogastroduodenoscopy). The three patients who had a duodenal ulcer during their hospital stay were all discharged on a postoperative proton pump inhibitor, but those who presented after discharge with a gastrointestinal bleed had not been given postoperative proton pump inhibitors. While the mean length of hospital stay for all patients was 6.6 days, the mean length of hospital stay for these five patients with gastrointestinal complications was 21 days (range 6–43 days). The gastrointestinal complications in these patients contributed to a longer hospital stay, although some had other complications that contributed to their prolonged stay, such as sternal wound infections.

After the intervention only 1% suffered a postoperative gastrointestinal bleed, which is much less than the 4% observed in the first cycle. This shows that the intervention may have helped to decrease the rate of gastrointestinal bleeds in postoperative patients, and enhanced patient safety. However, the low numbers of gastrointestinal bleeds do not allow for significance (P=0.10).

One patient who suffered a postoperative gastrointestinal bleed in the second cycle had been discharged on a proton pump inhibitor. This indicates that while postoperative prophylaxis with proton pump inhibitors is beneficial and recommended, other risks have to be addressed as well. For example, this patient was taking a total of 18 different medications, including aspirin, clopidogrel and amitriptyline, which all increase the risk of gastrointestinal bleeding.

Other risk factors that increase gastrointestinal bleeding post-cardiac surgery include diabetes mellitus, postoperative low cardiac output, advanced arteriosclerosis, postoperative need for haemodialysis, prolonged cardiopulmonary bypass time, and procedure urgency (Yoshida et al, 2005; Rodriguez et al, 2007; Bhat et al, 2012). This varied list may render risk factor-based prediction of postoperative gastrointestinal bleeds inaccurate and inconsistent. This further supports the recommendation to start all post-cardiac surgical patients on proton pump inhibitors, irrespective of the number of risk factors present, while addressing any preventable or treatable risk factors. However, proton pump inhibitor use has been associated with an increased risk of both community- and hospital-acquired pneumonia (Eom et al, 2011). This raises concern in patients who are immunologically more susceptible

Key points

- The prophylactic use of proton pump inhibitors in all patients post-cardiac surgery is a class IIa recommendation in the European Association of Cardio-Thoracic Surgery guidelines.
- Gastrointestinal bleeding is a complication of cardiac surgery, which is unfortunately associated with high mortality and a prolonged length of hospital stay.
- A statistically significant improvement was noted in the prescription of postoperative proton pump inhibitors after the intervention.
- Post-intervention, only 1% suffered a postoperative gastrointestinal bleed compared to 4% pre-intervention, showing that the intervention possibly helped to decrease the rate of gastrointestinal bleeds in postoperative patients, and enhanced patient safety. However, the low number of gastrointestinal bleeds does not allow for significance.
- One patient who suffered a postoperative gastrointestinal bleed had been discharged on a proton pump inhibitor, indicating that while postoperative prophylaxis with proton pump inhibitors is beneficial and recommended, other risks have to be addressed, including comorbidities and medications.

in the immediate postoperative period, especially since proton pump inhibitor-associated pneumonia tends to occur in the first month after initiation of treatment (Lambert et al, 2015). However, other studies contradict this association, so more conclusive studies are required (Othman et al, 2016).

Study limitations

Since this is a retrospective audit and data were primarily collected from discharge letters, some information regarding the patients' hospital stay might be missing. In addition, patients were followed up only for 30 days (19% mortality rate) after discharge to see whether there was a readmission as a result of gastrointestinal bleeding.

Conclusions

A statistically significant and sustainable improvement in prophylactic proton pump inhibitor prescription was noted after the introduction of pre-printed treatment charts. Post-intervention, a decrease in the rate of gastrointestinal bleeding post-cardiac surgery was observed, but a larger cohort is required to assess for significance. Taking a proton pump inhibitor post-cardiac surgery is now a class IIa recommendation according to the European Association of Cardio-Thoracic Surgery, and should be considered in all patients post-cardiac surgery. However, any other preventable or treatable risk factors have to be addressed in conjunction with this. Compliance with guidelines and recommendations has to be addressed as well, possibly through journal clubs and staff education programmes. This audit has successfully demonstrated how patient care can be improved, with long-lasting effect, through simple interventions.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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