Supplementary Appendix

ENDPOINT DEFINITIONS

Gastric cancer

Gastric cancer was defined by receiving any of the following diagnosis code from ICD-9-CM:

| ICD-9-CM Code | Diagnosis Description |
|---------------|---|
| 151 | Malignant Neoplasm of Stomach |
| 151 (0) | Malignant neoplasm of stomach |
| 151 (1) | Cancer of stomach |
| 151.0 | Malignant Neoplasm of Cardia |
| 151.1 | Malignant Neoplasm of Pylorus |
| 151.2 | Malignant Neoplasm of Pyloric Antrum |
| 151.3 | Malignant Neoplasm of Fundus of Stomach |
| 151.4 | Malignant Neoplasm of Body of Stomach |
| 151.5 | Malignant Neoplasm of Lesser Curvature of Stomach, Unspecified |
| 151.6 | Malignant Neoplasm of Greater Curvature of Stomach, Unspecified |
| 151.8 | Malignant Neoplasm of Other Specified Sites of Stomach |
| 151.9 | Malignant Neoplasm of Small Intestine, Including Duodenum |

Death from gastric cancer

The cause of death was determined by the principal condition that resulted in the death, not the immediate mode of death. Managing physicians would utilize all available information provided, along with clinical expertise, in their adjudication of the cause of death.

BASELINE VARIABLES DEFINITIONS

Estimated glomerular filtration rate

Estimated glomerular filtration rate (eGFR) is calculated based on MDRD equation, expressed as:

186 x (Creatinine/88.4) - 1.154 x (Age) - 0.203 x (0.742 if female) x (1.210 if black)

where Creatinine is expressed in µmol/L.

Anemia

Anemia is defined as hemoglobin <13g/dL for men and hemoglobin <12g/dL for women.

PCI urgency

- Elective: Patient cardiac status has been stable in the days or weeks before the operation. The procedure can be deferred without increased risk of compromised cardiac outcome.
- Urgent: Procedure required during the same hospitalization to minimize chances of clinical deterioration or adverse outcome. Clinical conditions include (but are not limited to) acute or worsening chest pain, acute or worsening HF, acute MI, critical coronary stenosis, IABP support, UA with intravenous nitroglycerin, and rest angina.
- Emergency: Procedure required because of ongoing, refractory (difficult, complicated, and/or unmanageable), unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except PCI.

Supplementary Tables

Table S1. Baseline characteristics of patients of the entire cohort before propensity score matching.

| Characteristics | All patients | PPI users | PPI non-users | Missing data |
|---------------------------------------|---------------|--------------|---------------|--------------|
| | N = 25298 | N = 7708 | N = 14314 | |
| Female gender | 5606 (22.2%) | 1646 (21.4%) | 3083 (21.5%) | 0 |
| Age, mean (SD) | 63.5 (11.3) | 64.1 (11.7) | 62.9 (11.1) | 1 (0.03%) |
| Chinese | 23845 (94.3%) | 7230 (93.8%) | 13533 (94.5%) | 0 |
| Tobacco use | 11291 (47.3%) | 3426 (47.0%) | 6512 (48.2%) | 1424 (5.6%) |
| Diabetes mellitus | 8411 (33.2%) | 2245 (29.1%) | 4994 (34.9%) | 0 |
| Hypertension | 15296 (60.5%) | 4364 (56.6%) | 8759 (61.2%) | 0 |
| Dyslipidemia | 15140 (59.8%) | 4400 (57.1%) | 8735 (61.0%) | 0 |
| Cerebrovascular disease | 1982 (7.8%) | 561 (7.3%) | 1079 (7.5%) | 0 |
| Chronic obstructive pulmonary disease | 503 (2.0%) | 137 (1.8%) | 278 (1.9%) | 0 |
| Previous myocardial infarction | 2318 (9.2%) | 365 (4.7%) | 1487 (10.4%) | 0 |
| Previous CABG | 330 (1.3%) | 52 (0.7%) | 216 (1.5%) | 0 |
| Congestive heart failure | 1476 (5.8%) | 354 (4.6%) | 840 (5.9%) | 0 |
| Atrial fibrillation or flutter | 931 (3.7%) | 262 (3.4%) | 497 (3.5%) | 0 |
| Cirrhosis | 31 (0.1%) | 11 (0.1%) | 19 (0.1%) | 0 |
| Baseline eGFR <50ml/min/m2 | 2090 (8.3%) | 681 (8.8%) | 988 (6.9%) | 6 (0.02%) |
| Baseline anemia | 6554 (25.9%) | 2293 (29.8%) | 3200 (22.4%) | 7 (0.03%) |
| GERD | 162 (0.6%) | 60 (0.8%) | 61 (0.4%) | 0 |
| Peptic ulcer disease | 671 (2.7%) | 279 (3.6%) | 253 (1.8%) | 0 |
| Helicobacter pylori eradication | 673 (2.7%) | 245 (3.2%) | 239 (1.7%) | 0 |
| Acute myocardial infarction | 15232 (60.4%) | 5784 (75.1%) | 7600 (53.3%) | 67 (0.3%) |
| Urgent or emergency PCI | 10817 (42.8%) | 5185 (67.3%) | 4458 (31.1%) | 0 |
| Year of PCI | | | | 0 |
| 2004 - 2008 | 6235 (24.6%) | 391 (5.1%) | 5053 (35.3%) | |
| 2009 - 2012 | 7826 (30.9%) | 1114 (14.5%) | 5533 (38.7%) | |
| 2013 - 2016 | 5964 (23.6%) | 2657 (34.5%) | 2561 (17.9%) | |
| 2016 - 2017 | 5273 (20.8%) | 3546 (46.0%) | 1167 (8.2%) | |

Table S2. Medications on hospital discharge and post-procedure characteristics of the entire cohort before propensity score matching.

| Characteristics | All patients* | PPI users | PPI non-users |
|--|----------------|------------------|---------------|
| | N = 25298 | N = 7708 | N = 14314 |
| Duration of PPI after PCI, median (IQR) - days | 0 (0, 511) | 1309 (719, 1884) | 0 (0, 0) |
| On PPI >30 days after cessation of P2Y12 inhibitor | 6664 (26.8%) | 6578 (85.6%) | 0 (0.0%) |
| Aspirin on discharge | 24626 (97.3%) | 7563 (98.1%) | 13889 (97.0%) |
| P2Y12 inhibitors on discharge | 24909 (98.5%) | 7689 (99.8%) | 14009 (97.9%) |
| Potent P2Y12 inhibitors on discharge | 3193 (12.6%) | 2135 (27.7%) | 761 (5.3%) |
| Duration of P2Y12 inhibitor after PCI (IQR) - days | 365 (180, 400) | 366 (365, 425) | 365 (91, 386) |
| Anti-coagulation on discharge | 681 (2.7%) | 324 (4.2%) | 238 (1.7%) |
| Metformin on discharge | 5648 (22.3%) | 1719 (22.3%) | 3201 (22.4%) |
| Statin on discharge | 22611 (89.4%) | 7460 (96.8%) | 12240 (85.5%) |
| Angiotensin blockade on discharge | 16973 (67.1%) | 5669 (73.5%) | 9121 (63.7%) |
| Beta-blocker on discharge | 18843 (74.5%) | 5717 (74.2%) | 10713 (74.8%) |
| Drop in hemoglobin >2g/dL after PCI | 4453 (17.6%) | 1739 (22.6%) | 2038 (14.2%) |
| Gastrointestinal bleeding during follow up | 1557 (6.2%) | 410 (5.3%) | 929 (6.5%) |
| Upper endoscopy during follow up | 4298 (17.0%) | 1220 (15.8%) | 2434 (17.0%) |

^{*}Included patients who were neither PPI users nor PPI non-users if the PPI duration was >14

days but <180 consecutive days, refer to definition in the Method session for details.

Table S3. Hazard ratios for proton pump inhibitor users in the sensitivity analyses.

| Outcomes | Hazard Ratio | 95% Confidence Interval | | P value |
|----------------------------------|--------------|----------------------------|-------|---------|
| | | | | |
| Restricted to patients with ≥1 | | | | |
| upper endoscopy done after PCI | | | | |
| Gastric cancer | 3.09 | 1.20 | 7.94 | 0.019 |
| Death from gastric cancer | 2.73 | 0.70 | 10.64 | 0.148 |
| | | | | |
| All complete cases by cox | | | | |
| regression | | | | |
| Gastric cancer | 2.38 | 1.20 | 4.76 | 0.014 |
| Death from gastric cancer | 3.54 | 1.29 | 9.74 | 0.014 |
| | | | | |
| Falsification analysis | | | | |
| Lung cancer | 1.00 | 0.70 | 1.43 | 0.98 |
| | | | | |
| All cases by multiple imputation | | | | |
| Gastric cancer | 1.98 | 1.07 | 3.66 | 0.030 |
| Death from gastric cancer | 2.69 | 1.11 | 6.52 | 0.029 |

Table S3. Hazard ratios for all co-variates in the Cox regression model in the sensitivity analyses.

| Characteristics | Hazard ratio | 95% confidence interval | | P-value |
|---------------------------------------|--------------|-------------------------|-------|---------|
| | | | | |
| PPI use | 2.38 | 1.20 | 4.76 | 0.014 |
| Female gender | 0.35 | 0.16 | 0.80 | 0.012 |
| Age, mean (SD) | 1.07 | 1.04 | 1.10 | <0.001 |
| Chinese | 2.58 | 0.36 | 18.79 | 0.35 |
| Tobacco use | 1.10 | 0.63 | 1.91 | 0.75 |
| Diabetes mellitus | 0.86 | 0.40 | 1.85 | 0.70 |
| Hypertension | 0.89 | 0.51 | 1.57 | 0.70 |
| Dyslipidemia | 0.67 | 0.39 | 1.16 | 0.16 |
| Cerebrovascular disease | 0.19 | 0.03 | 1.39 | 0.10 |
| Chronic obstructive pulmonary disease | 1.18 | 0.28 | 5.01 | 0.82 |
| Previous myocardial infarction | 0.60 | 0.21 | 1.72 | 0.34 |
| Previous CABG | 1.60 | 0.21 | 12.3 | 0.65 |
| Congestive heart failure | 0.88 | 0.26 | 2.94 | 0.84 |
| Atrial fibrillation or flutter | 0.95 | 0.22 | 4.19 | 0.95 |
| Cirrhosis | N/A | N/A | N/A | N/A |
| Baseline eGFR <50ml/min/m2 | 1.52 | 0.62 | 3.73 | 0.36 |
| Baseline anemia | 0.87 | 0.47 | 1.60 | 0.65 |
| GERD | 2.62 | 0.36 | 19.41 | 0.34 |
| Peptic ulcer disease | 0.40 | 0.05 | 3.02 | 0.37 |
| Helicobacter pylori eradication | 2.47 | 0.74 | 8.21 | 0.14 |
| Acute myocardial infarction | 0.81 | 0.44 | 1.51 | 0.52 |
| Urgent or emergency PCI | 0.80 | 0.40 | 1.62 | 0.54 |
| Year of PCI | | | | |
| 2004 - 2008 | Reference | | | |
| 2009 - 2012 | 0.68 | 0.36 | 1.30 | 0.24 |
| 2013 - 2016 | 0.40 | 0.15 | 1.06 | 0.064 |
| 2016 - 2017 | 0.59 | 0.16 | 2.13 | 0.42 |
| Metformin on discharge | 0.87 | 0.34 | 2.19 | 0.76 |
| Aspirin on discharge | 0.60 | 0.18 | 1.96 | 0.40 |
| P2Y12 inhibitors on discharge | N/A | N/A | N/A | N/A |
| Anti-coagulation on discharge | 0.84 | 0.11 | 6.72 | 0.87 |
| Statin on discharge | 0.81 | 0.41 | 1.60 | 0.54 |
| Drop of hemoglobin >2g/dL after PCI | 0.35 | 0.14 | 0.90 | 0.028 |