Abstract: Postoperative thromboembolism (TE) is a serious, but preventable, complication in surgical patients. Orthopedic surgery, neurosurgery, and vascular surgery are considered high risk for TE, and current guidelines recommend TE prophylaxis. However, insufficient data exist regarding TE risk in other general surgeries. This study identified the actual incidence and relative risk of postoperative TE in the real world, according to surgery type. Twenty-six surgeries between 1 December 2017 and 31 August 2019 were selected from the Health Insurance Review and Assessment Service database and analyzed for postoperative TE events. Among all patients, 2.17% had a TE event within 6 months of surgery and 0.75% had a TE event owing to anticoagulant treatment. The incidence of total TE events was the highest in total knee replacement (12.77%), hip replacement (11.46%), and spine surgery (5.98%). The incidence of TE with anticoagulant treatment was the highest in total knee replacement (7.40%), hip replacement (7.20%), and coronary artery bypass graft (CABG) surgery (3.81%). Hip replacement, total knee replacement, CABG surgery, spine surgery, and cardiac surgery except CABG surgery, showed relatively higher risks for total claimed venous TE. The relative risk of venous TE with anticoagulant treatment was the highest for hysterectomy, partial hepatectomy, hip replacement, cardiac surgery except CABG surgery, and total knee replacement. The relative risk of arterial TE was the highest for cardiac surgery, total knee replacement, and hip replacement. In the real world, the incidence of postoperative TE events from total knee replacement and those from hip replacement remain high, and some surgeries could have a relatively higher risk of TE than other surgeries. For patients undergoing these surgeries, studies to reduce the incidence of postoperative TE in clinical practice should be conducted.

Keywords: thromboembolism; incidence; surgical procedures

1. Introduction

Postoperative thromboembolism (TE) is a serious, but preventable, complication in patients undergoing surgery. Three factors affect the development of TE: vascular injury, impairment of blood flow, and hypercoagulability [1]. To reduce the incidence of postoperative TE, surgical patients may be advised early walking, use of sequential compression devices, and antiplatelet or anticoagulant treatment. This is more apparent in patients who are particularly at risk for TE, namely those with cancer, atrial fibrillation, atrial flutter, or history of TE, as well as those scheduled to undergo surgeries that are known to be high risk for TE [2–5].
Surgery, in itself, increases the risk of TE, but some surgeries are categorized as having a high risk of postoperative TE [6,7]. Historically, these surgeries include orthopedic surgery, neurosurgery, and vascular surgery, and current guidelines recommend mechanical and pharmacological prophylaxis for TE in patients undergoing such procedures [5,8,9]. In the case of other general surgeries, patients are assessed for postoperative TE risk, either clinically or with the help of more objective measures such as the Caprini risk assessment model or the Rogers score [10,11]. The benefit of adding pharmacological prophylaxis to counteract the risk of bleeding is then left to the discretion of the physician [9,11–15]. Although objective measures exist, the risk for TE is mainly judged based on patient characteristics, and there are limited data on the extent of postoperative TE risk according to the type of surgery. In particular, there are limited data on TE risk in the Asian population, wherein TE risk is generally thought to be lower than that in Western countries.

Using a nationally representative database, this study aimed to identify the real-world incidence and pattern of postoperative TE in patients who had undergone commonly practiced surgeries and assess the relative risk for TE according to the type of surgery.

2. Materials and Methods

2.1. Data Source

In the Republic of Korea, the National Health Insurance (NHI), a universal health coverage system, covers approximately 98% of the population. NHI pays medical costs based on claims data, which consists of diagnosis, treatment, procedures, and drug prescriptions [16,17]. The claims data are anonymized and made available for healthcare service research in the Health Insurance Review and Assessment Service (HIRA) database, which was used for this study. All procedures involving human participants in this study were performed in accordance with the ethical standards of the institutional and national research committees and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the institutional review board of the Korea University Anam Hospital (No. 2020AN0136). The requirement for informed consent was waived by the institutional review board of the Korea University Anam Hospital, owing to the use of anonymized patient data.

2.2. Patients

The 2019 Statistical Information Report for Major Surgical Statistics provided by the National Statistical Office was used to select surgeries commonly performed in the Republic of Korea (http://kostat.go.kr/, accessed on 1 April 2020). The report consisted of data on 33 surgeries, including 16 surgeries of international interest and 17 surgeries reflecting domestic conditions. Among them, 26 surgeries that either required general anesthesia or were considered commonly performed procedures were selected for the present study.

We extracted all data from the HIRA database of each patient who had undergone the selected surgeries between 1 December 2017 and 31 August 2019 and analyzed TE events of these patients from the date of surgery up to 6 months (Table S1).

2.3. Clinical Endpoints

The primary endpoints were the incidence of postoperative TE and its relative risk according to the type of surgery. ‘Postoperative TE events’ was defined as (1) patients with any venous and arterial TE events that were claimed within 6 months from the date of the surgery (total claimed TE); and (2) patients with venous and arterial TE events that were claimed within 6 months from the date of the surgery and treated with anticoagulant medications within 3 days of the date of TE diagnosis (TE with anticoagulant treatment).

‘The patients who underwent prophylactic anticoagulant treatment’ were defined as patients satisfying the following conditions, to distinguish them from those using the anticoagulant treatment for therapeutic purposes: (1) patients who were administered anticoagulant medications within 3 days of the date of the surgery, among those who had...
no TE events; or (2) patients who were administered anticoagulant medications from the day of surgery to 1 day before the diagnosis of TE events among those who had TE events.

The risk factors for TE included age, sex, history of cancer, atrial fibrillation or atrial flutter, history of TE, history of taking antiplatelet or anticoagulant drugs between 2 weeks and 3 months before surgery, antiplatelet or anticoagulant use on the day of surgery, and use of prophylactic anticoagulant treatment. The claims data for cancer, atrial fibrillation or atrial flutter, and TE diagnosis were limited to within 3 months from the date of surgery. Antiplatelet drugs included aspirin, clopidogrel, cilostazol, and ticagrelor, and anticoagulant drugs included apixaban, edoxaban, dabigatran, argatroban, enoxaparin, dalteparin, heparin, and warfarin.

2.4. Statistical Analysis

Continuous data are presented as means and standard deviations, and categorical data are presented as frequencies and percentages. The incidence of TE according to each surgery was calculated as the number of patients who met the definition for TE mentioned above. The adjusted odds ratios (ORs) for TE events were obtained using a multiple logistic regression model, with the following independent variables: age, sex, history of cancer, atrial fibrillation or atrial flutter, TE, antiplatelet or anticoagulant drug use between 2 weeks and 3 months before surgery and on the day of surgery, and use of prophylactic anticoagulant treatment. The multivariable analysis results are presented as adjusted ORs and their 95% confidence intervals (CIs). Transurethral prostatectomy was used as a reference category for the types of surgery. All statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Incidence of TE within 6 Months from the Date of Surgery

Data of a total of 2,799,293 patients who underwent the selected surgeries between 1 December 2017 and 31 August 2019 were analyzed. Among those patients, 60,683 (2.17%) had a TE event within 6 months from the date of surgery and 21,063 (0.75%) had a TE event following anticoagulant treatment (Table 1). With respect to TE in the anticoagulant treatment group, the median duration of anticoagulant therapy was 13 days (range: 1–442 days).

Table 1. Incidence of thromboembolism within 6 months from the date of each surgery.

| Surgery                                         | Total Patients, n | A: Total Claimed Thromboembolism, n (%) | B: Thromboembolism with Anticoagulant Treatment, n (%) | B/A (%) * |
|-------------------------------------------------|-------------------|----------------------------------------|---------------------------------------------------------|-----------|
| Total knee replacement                          | 108,111           | 13,811 (12.77)                         | 7995 (7.40)                                             | 57.89     |
| Hip replacement                                 | 43,415            | 4975 (11.46)                           | 3124 (7.20)                                             | 62.79     |
| Spine surgery                                   | 265,317           | 15,857 (5.98)                          | 3336 (1.26)                                             | 21.04     |
| Coronary artery bypass graft                    | 6591              | 343 (5.20)                             | 251 (3.81)                                              | 73.18     |
| Partial hepatectomy                             | 9322              | 429 (4.60)                             | 331 (3.55)                                              | 77.16     |
| Cardiac surgery (except coronary artery bypass graft) | 10,296          | 443 (4.30)                             | 386 (3.75)                                              | 87.13     |
| Gastrectomy                                     | 27,203            | 1114 (4.10)                            | 302 (1.11)                                              | 27.11     |
| Hysterectomy                                    | 20,831            | 714 (3.43)                             | 540 (2.59)                                              | 75.63     |
| Endoscopic spine surgery                        | 12,157            | 392 (3.22)                             | 23 (0.19)                                               | 5.87      |
| Brain tumor surgery                             | 11,516            | 302 (2.62)                             | 173 (1.50)                                              | 57.28     |
| Open prostatectomy                              | 3387              | 81 (2.39)                              | 23 (0.68)                                               | 28.40     |
| Cholecystectomy                                 | 129,081           | 2511 (1.95)                            | 828 (0.64)                                              | 32.97     |
Table 1. Cont.

| Surgery                                | Total Patients, n | Thromboembolism within 6 Months from the Date of Surgery |
|----------------------------------------|-------------------|----------------------------------------------------------|
|                                        | A: Total Claimed  | B: Thromboembolism with Anticoagulant Treatment, n (%)  |
|                                        | Thromboembolism, n (%) |                             | B/A (%) *  |
|----------------------------------------|-------------------|----------------------------------------------------------|
| Transurethral prostatectomy            | 18,547            | 342 (1.84)                                               | 85 (0.46) | 24.85 |
| Skull base surgery                     | 674               | 10 (1.48)                                                | 4 (0.59)  | 40.00 |
| Cataract surgery                       | 907,397           | 12,819 (1.41)                                            | 2489 (0.27) | 19.42 |
| Total mastectomy                       | 22,091            | 280 (1.27)                                               | 98 (0.44)  | 35.00 |
| Repair of inguinal hernia              | 56,698            | 671 (1.18)                                               | 153 (0.27) | 22.80 |
| Partial excision of mammary gland      | 63,033            | 586 (0.93)                                               | 130 (0.21) | 22.18 |
| Appendectomy                           | 137,344           | 1024 (0.75)                                              | 263 (0.19) | 25.68 |
| Thyroidectomy                          | 51,506            | 351 (0.68)                                               | 80 (0.16)  | 22.79 |
| Sinus surgery                          | 158,677           | 867 (0.55)                                               | 82 (0.05)  | 9.46  |
| Endoscopic sinus surgery               | 109,454           | 578 (0.53)                                               | 115 (0.11) | 19.90 |
| Operation for hemorrhoid               | 303,456           | 1401 (0.46)                                              | 158 (0.05) | 11.28 |
| Cesarean section                       | 255,600           | 864 (0.37)                                               | 84 (0.03)  | 12.28 |
| Cleft lip and/or palate surgery        | 1282              | 2 (0.16)                                                 | 1 (0.08)   | 50.00 |
| Tonsillectomy                          | 66,307            | 96 (0.14)                                                | 9 (0.01)   | 9.38  |
| Total                                  | 2,799,293         | 60,683 (2.17)                                            | 21,063 (0.75) | 34.71 |

Note: * B/A represents the ratio of thromboembolism events with anticoagulant treatment from the total claimed thromboembolism events.

The incidence of total claimed TE events was the highest for total knee replacement (13,811/108,111 patients, 12.77%), hip replacement (4975/43,415 patients, 11.46%), and spine surgery (15,857/265,317 patients, 5.98%). In the case of TE in the anticoagulant treatment, the incidence was the highest in total knee replacement (7995/108,111 patients, 7.40%), hip replacement (3124/43,415 patients, 7.20%), and coronary artery bypass graft surgery (251/6591 patients, 3.81%). Approximately 65% of TE events occurred within 1 month of surgery (Figure 1).

Figure 1. Distribution of TE events within 6 months from the date of surgery. The distribution of TE events within 6 months from the date of surgery is shown as the percentage from a total of 60,683 patients with TE (pink bar: total claimed TE, blue bar: TE with anticoagulant treatment).

3.2. Proportion of Patients Who Underwent Prophylactic Anticoagulant Treatment and Its Effect on the Incidence of TE Events

Among 2,799,293 patients enrolled in this study, 158,987 patients underwent prophylactic anticoagulant treatment (mean: 5.68%, range: 0.06–96.77% according to the type of surgery). The proportions of patients who underwent prophylactic anticoagulant treatment...
for each type of surgery were 52.62% in total knee replacement, 41.17% in hip replacement, 9.06% in spine surgery, 40.77% in partial hepatectomy, 26.18% in gastrectomy, and 18.96% in hysterectomy. The incidence of postoperative TE events from prophylactic anticoagulant treatment was approximately 90% lower than that with no treatment (Table 2).

3.3. Type of TE within 6 Months from the Date of Surgery

The types of total claimed TE and TE with anticoagulant treatment are summarized in Table 3. In the total claimed TE, 79.78% (48,412/60,683 patients) of patients were diagnosed with venous TE and 20.22% (12,271/60,683 patients) with arterial TE. In the cases where the location was identified, the lower extremities were the most common location for venous TE (18,690/48,410 patients, 38.61%). For arterial TE, the extremities in general were the most common location (1780/12,273 patients, 14.50%). In TE with anticoagulant treatment, 91.27% (19,224/60,683 patients) of patients were diagnosed with venous TE and 8.73% (1839/60,683 patients) with arterial TE. Myocardial infarction occurred in 0.023% of patients (14/60,683 patients), stroke in 0.089% (54/60,683 patients), and pulmonary embolism in 0.003% (2/60,683 patients). The types of total claimed TE and TE with anticoagulant treatment according to each surgery type are presented in Tables S2 and S3.
Table 2. Proportion of patients who underwent prophylactic anticoagulant treatment and its effect on the incidence of TE events.

| Surgery                                      | Total Patients, n | Patients Who Underwent Prophylactic Anticoagulant Treatment, n (%) | Total Claimed Thromboembolism, n (%) | Thromboembolism with Anticoagulant Treatment, n (%) | p Value |
|----------------------------------------------|-------------------|---------------------------------------------------------------------|--------------------------------------|------------------------------------------------------|--------|
|                                              |                   | With Prophylactic Anticoagulant Treatment                           | Without Prophylactic Anticoagulant Treatment | n (%)                                                | p Value |
| Total knee replacement                        | 108,111           | 56,887 (52.62)                                                     | 1717 (1.59)                          | 12,094 (11.19)                                       | <0.001 |
| Hip replacement                               | 43,415            | 17,876 (41.17)                                                     | 684 (1.58)                           | 4291 (9.88)                                          | <0.001 |
| Spine surgery                                 | 265,317           | 24,029 (9.06)                                                      | 1131 (0.43)                          | 14,726 (5.55)                                        | <0.001 |
| Coronary artery bypass graft                  | 6591              | 6378 (96.77)                                                       | 162 (2.46)                           | 181 (2.75)                                           | 0.305  |
| Partial hepatectomy                           | 9322              | 3801 (40.77)                                                       | 134 (1.44)                           | 295 (3.16)                                           | <0.001 |
| Cardiac surgery (except coronary artery bypass graft) | 10,296           | 9799 (95.17)                                                       | 216 (2.10)                           | 227 (2.20)                                           | 0.601  |
| Gastrectomy                                   | 27,203            | 7123 (26.18)                                                       | 164 (0.60)                           | 950 (3.49)                                           | <0.001 |
| Hysterectomy                                  | 20,831            | 3949 (18.96)                                                       | 178 (0.85)                           | 536 (2.57)                                           | <0.001 |
| Endoscopic spine surgery                      | 12,157            | 86 (0.71)                                                          | 3 (0.02)                             | 389 (3.20)                                           | <0.001 |
| Brain tumor surgery                           | 11,516            | 4888 (42.45)                                                       | 126 (1.09)                           | 176 (1.53)                                           | 0.004  |
| Open prostatectomy                            | 3387              | 1708 (50.43)                                                       | 44 (1.30)                            | 37 (1.09)                                            | 0.437  |
| Cholecystectomy                               | 129,081           | 10,164 (7.87)                                                      | 356 (0.28)                           | 2155 (1.67)                                          | <0.001 |
| Transurethral prostatectomy                    | 18,547            | 678 (3.66)                                                         | 41 (0.22)                            | 301 (1.62)                                           | <0.001 |
| Skull base surgery                            | 639               | 258 (38.28)                                                        | 6 (0.89)                             | 4 (0.59)                                             | 0.527  |
| Cataract surgery                              | 907,397           | 2432 (0.27)                                                        | 760 (0.08)                           | 12,059 (1.33)                                        | <0.001 |
| Total mastectomy                              | 22,091            | 2278 (10.31)                                                       | 66 (0.30)                            | 214 (0.97)                                           | <0.001 |
| Repair of inguinal hernia                     | 56,698            | 559 (0.99)                                                         | 54 (0.10)                            | 617 (1.09)                                           | <0.001 |
| Partial excision of mammary gland             | 63,053            | 1341 (2.13)                                                        | 68 (0.11)                            | 518 (0.82)                                           | <0.001 |
| Appendectomy                                  | 137,344           | 1291 (0.94)                                                        | 88 (0.06)                            | 936 (0.68)                                           | <0.001 |
| Thyroidectomy                                 | 51,506            | 1372 (2.66)                                                        | 40 (0.08)                            | 311 (0.60)                                           | <0.001 |
| Sinus surgery                                 | 158,677           | 275 (0.17)                                                         | 39 (0.02)                            | 828 (0.52)                                           | <0.001 |
| Endoscopic sinus surgery                      | 109,454           | 801 (0.73)                                                         | 32 (0.03)                            | 546 (0.50)                                           | <0.001 |
| Operation for hemorrhoid                      | 303,456           | 179 (0.06)                                                         | 34 (0.01)                            | 1367 (0.45)                                          | <0.001 |
| Cesarean section                              | 255,600           | 690 (0.27)                                                         | 16 (0.01)                            | 668 (0.26)                                           | <0.001 |
| Cleft lip and/or palate surgery               | 1282              | 5 (0.39)                                                           | -                                    | 2 (0.16)                                             | -      |
| Tonsillectomy                                 | 66,307            | 140 (0.21)                                                         | 7 (0.01)                             | 89 (0.13)                                            | <0.001 |
| Total                                         | 2,799,293         | 158,987 (5.68)                                                      | 6166 (0.22)                          | 4517 (1.95)                                          | <0.001 |

Total Thromboembolism: 158,987 (5.68%) Thromboembolism with Anticoagulant Treatment: 2993 (0.11%)
Table 3. Type of TE within 6 months from the date of each surgery.

| Type of TE | No. | Details | Total Claimed TE \( (n = 60,683) \) | TE with Anticoagulant Treatment \( (n = 21,603) \) |
|-----------|-----|---------|-------------------------------------|-----------------------------------------------|
|           |     |         | Number of Patients, \( n \) | Events (%) | Number of Patients, \( n \) | Events (%) |
| 1         | I26 | Pulmonary embolism | 2 | 0.003% | 2 | 0.009% |
| 2         | I80 | Phlebitis and thrombophlebitis | 5 | 0.008% | - | 0.000% |
| 3         | I80.0 | Phlebitis and thrombophlebitis of superficial vessels of lower extremities | 884 | 1.457% | 147 | 0.698% |
| 4         | I80.1 | Phlebitis and thrombophlebitis of femoral vein | 87 | 0.143% | 31 | 0.147% |
| 5         | I80.2 | Phlebitis and thrombophlebitis of other deep vessels of lower extremities | 13,931 | 22.957% | 7717 | 36.638% |
| 6         | I80.3 | Phlebitis and thrombophlebitis of lower extremities, unspecified | 3788 | 6.242% | 1299 | 6.167% |
| 7         | I80.8 | Phlebitis and thrombophlebitis of other sites | 2811 | 4.632% | 350 | 1.662% |
| 8         | I80.9 | Phlebitis and thrombophlebitis of unspecified site | 6977 | 11.497% | 1505 | 7.145% |
| 9         | I81 | Portal vein thrombosis | 389 | 0.641% | 174 | 0.826% |
| 10        | I82 | Other venous embolism and thrombosis | 8 | 0.013% | 1 | 0.005% |
| 11        | I82.0 | Budd–Chiari syndrome | 55 | 0.091% | 12 | 0.057% |
| 12        | I82.1 | Thrombophlebitis migrans | 11 | 0.018% | 2 | 0.009% |
| 13        | I82.2 | Embolism and thrombosis of vena cava | 63 | 0.104% | 38 | 0.180% |
| 14        | I82.3 | Embolism and thrombosis of renal vein | 84 | 0.138% | 22 | 0.104% |
| 15        | I82.8 | Embolism and thrombosis of other specified veins | 2867 | 4.725% | 1538 | 7.302% |
| 16        | I82.9 | Embolism and thrombosis of unspecified vein | 15,327 | 25.257% | 6067 | 28.804% |
| 17        | I63.6 | Cerebral infarction due to cerebral venous thrombosis, nonpyogenic | 66 | 0.109% | 16 | 0.076% |
| 18        | I67.6 | Nonpyogenic thrombosis of intracranial venous system | 50 | 0.082% | 12 | 0.057% |
| 19        | O22.2 | Superficial thrombophlebitis in pregnancy | 3 | 0.005% | - | 0.000% |
| 20        | O22.3 | Deep phlebothrombosis in pregnancy | 106 | 0.175% | 2 | 0.009% |
| 21        | O22.5 | Cerebral venous thrombosis in pregnancy | 3 | 0.005% | - | 0.000% |
| 22        | O87.1 | Deep phlebothrombosis in the puerperium | 126 | 0.208% | 11 | 0.052% |
| 23        | O87.3 | Cerebral venous thrombosis in the puerperium | 3 | 0.005% | 2 | 0.009% |
| 24        | G08 | Intracranial and intraspinal phlebitis and thrombophlebitis | 69 | 0.114% | 20 | 0.095% |
| 25        | G09 | Other diseases of spinal cord | 0 | 0.000% | 0 | 0.000% |
| 26        | K55.0 | Acute vascular disorders of intestine | 519 | 0.855% | 223 | 1.059% |
| 27        | K55.1 | Chronic vascular disorders of intestine | 178 | 0.293% | 33 | 0.157% |
|           | Total |        | 48,412 | 79.779% | 19,224 | 91.269% |
Table 3. Cont.

| Type of TE | No. | Details | Total Claimed TE (n = 60,683) | TE with Anticoagulant Treatment (n = 21,603) |
|------------|-----|---------|-------------------------------|---------------------------------------------|
|            |     |         | Number of Patients, n | Events (%) | Number of Patients, n | Events (%) |
| Arterial TE | 28  | I21, I22, I24 Myocardial infarction and other acute ischemic heart disease | 14 | 0.023% | 2 | 0.009% |
|            | 29  | I63 Cerebral infarction | 54 | 0.089% | 1 | 0.005% |
|            | 30  | I74.0 Embolism and thrombosis of abdominal aorta | 145 | 0.239% | 44 | 0.209% |
|            | 31  | I74.1 Embolism and thrombosis of other and unspecified parts of aorta | 159 | 0.262% | 51 | 0.242% |
|            | 32  | I74.2 Embolism and thrombosis of arteries of upper extremities | 163 | 0.269% | 61 | 0.290% |
|            | 33  | I74.3 Embolism and thrombosis of arteries of lower extremities | 3 | 0.005% | - | 0.000% |
|            | 34  | I74.4 Embolism and thrombosis of arteries of extremities, unspecified | 1614 | 2.660% | 402 | 1.909% |
|            | 35  | I74.5 Embolism and thrombosis of iliac artery | 203 | 0.335% | 74 | 0.351% |
|            | 36  | I74.8 Embolism and thrombosis of other arteries | 2757 | 4.543% | 484 | 2.298% |
|            | 37  | I74.9 Embolism and thrombosis of unspecified artery | 6686 | 11.018% | 478 | 2.269% |
|            | 38  | N28.0 Ischemia and infarction of kidney | 473 | 0.779% | 242 | 1.149% |
|            | Total | | 12,271 | 20.221% | 1839 | 8.731% |

Abbreviation: TE, thromboembolism.

3.4. Relative risk of TE According to Surgery Type

To analyze the relative risk of TE for each surgery, the adjusted ORs for TE events were calculated, after correcting for TE risk factors. In this study, 2.84% of patients (79,498/2,799,293 patients) had a history of cancer, 0.002% (48/2,799,293 patients) had atrial fibrillation or atrial flutter, 0.44% (12,420/2,799,293 patients) had a history of TE, 11.11% (310,994/2,799,293 patients) were taking antiplatelet or anticoagulant drugs between 2 weeks and 3 months prior to surgery, 7.03% (196,745/2,799,293 patients) were taking antiplatelet or anticoagulant drugs on the day of surgery, and 5.68% (158,987/2,799,293 patients) underwent prophylactic anticoagulant treatment. The baseline characteristics (whole cohort and each surgery group) and the ORs and 95% CI of each risk factor are presented in Tables S4 and S5. Transurethral prostatectomy was used as a reference surgery.

The relative risk of the total claimed venous TE for each surgery, after correcting for TE risk factors, revealed that the highest risk was associated with hip replacement (OR = 7.771, 95% CI: 6.749–8.946), total knee replacement (OR = 7.755, 95% CI: 6.747–8.913), and coronary artery bypass graft surgery (OR = 5.183, 95% CI: 4.234–6.344), followed by spine surgery (OR = 4.941, 95% CI: 4.308–5.667), cardiac surgery (except for coronary artery bypass graft surgery) (OR = 4.584, 95% CI: 3.769–5.575), partial hepatectomy (OR = 4.032, 95% CI: 3.384–4.804), gastrectomy (OR = 3.911, 95% CI: 3.363–4.549), and hysterectomy (OR = 3.751, 95% CI: 3.196–4.403) (Figure 2A). The relative risk of the total claimed arterial TE for each surgery after correcting for TE risk factors revealed that the highest risk was associated with cardiac surgery (except for coronary artery bypass graft surgery) (OR = 12.969, 95% CI: 9.422–17.851), total knee replacement (OR = 11.061, 95% CI: 8.669–14.111), and coronary artery bypass graft surgery (OR = 10.567, 95% CI: 7.610–14.673) (Figure 2B).
Figure 2. Odds ratios of total claimed thromboembolism events for each type of surgery after correcting for thromboembolism risk factors. Abbreviation: CABG, coronary artery bypass graft. (A) The total claimed venous thromboembolism events, (B) the total claimed arterial thromboembolism events.

The relative risk of venous TE with anticoagulant treatment for each surgery after correcting for TE risk factors revealed that the highest risk was associated with hysterectomy (OR = 9.355; 95% CI: 7.145–12.247), partial hepatectomy (OR = 6.015; 95% CI: 4.547–7.958), and hip replacement (OR = 5.915, 95% CI: 4.598–7.610), followed by cardiac surgery (except for coronary artery bypass graft surgery) (OR = 5.812, 95% CI: 4.348–7.768), total knee replacement (OR = 5.469, 95% CI: 4.257–7.026), coronary artery bypass graft surgery (OR = 5.214, 95% CI: 3.865–7.033), and brain tumor surgery (OR = 4.693, 95% CI: 3.482–6.325) (Figure 3A). The relative risk of arterial TE with anticoagulant treatment for each surgery after correcting for the TE risk factors revealed that the highest risk was associated with cardiac surgery (except for coronary artery bypass graft surgery) (OR = 14.958, 95% CI: 7.826–28.590),
cleft lip and/or palate surgery (OR = 13.000, 95% CI: 1.630–103.672), and coronary artery bypass graft surgery (OR = 7.511, 95% CI: 3.863–14.607) (Figure 3B).

4. Discussion

In this study of 2,799,293 patients who underwent selected surgeries from 1 December 2017 to 31 August 2019 in the Republic of Korea, 60,683 patients had claimed TE events (average: 2.17%, and range according to surgery type: 0.14–12.77%) and 21,063 had a TE event with anticoagulant treatment (average: 0.75%, and range according to surgery type: 0.01–7.40%). Approximately 65% of TE events occurred within 1 month of surgery, and the incidence of TE events differed according to the surgery type. Patients undergoing total knee replacement and hip replacement, i.e., 12.77% (13,811 of 108,111 patients) and

![Figure 3. Odds ratios of thromboembolism events with anticoagulant treatment for each type of surgery after correcting for thromboembolism risk factors. Abbreviation: CABG, coronary artery bypass graft. (A) venous thromboembolism events with anticoagulant treatment (B) arterial thromboembolism events with anticoagulant treatment.](image)
11.46% (4975 of 43,415 patients), respectively, had a higher incidence of total claimed TE. In addition, the relative risk of venous TE in these surgeries was also higher than that in other procedures. Several surgeries, including hysterectomy, partial hepatectomy, and gastrectomy, also showed a relatively higher risk of venous TE. The relative risk of arterial TE was the highest in cardiac surgery, total knee replacement, and hip replacement.

In Western countries, the incidence of postoperative TE events in patients undergoing total knee or hip replacement and spine surgery without TE prophylaxis ranges from 40% to 60% and 15% to 40%, respectively [18–20]. In Asian populations, the incidence of TE events reportedly ranges from 10% to 60% in total knee or hip replacement surgeries and approximately 30% in spine surgery, which is relatively lower than the rates in the Western population [21–23]. When pharmacological prophylaxis is added, postoperative TE events can be reduced by approximately 70–90% or more [24–26]. In this study, the incidence of total claimed TE in total knee replacement, hip replacement, and spine surgery was 12.77%, 11.46%, and 5.98%, respectively, which are higher incidence rates than those reported in previous studies [18–26]. Even considering the incidence of TE with anticoagulant treatment, total knee replacement and hip replacement were associated with a higher incidence of 7.4% and 7.2%, respectively. There are several possible explanations for these differences. First, previous studies focused on reporting the incidence of deep vein thrombosis of the lower extremities or pulmonary embolism. However, this study reported all TE events in the real world, including venous TE and arterial TE, using claims data. Second, adherence to postoperative TE prophylaxis, especially pharmacological prophylaxis, is usually lower in clinical practice than the guideline recommendations according to patients’ condition or the guidelines of each institution [27–29]. In fact, in this study, the rates of pharmacological prophylaxis were 52.62% and 41.17% in total knee replacement and hip replacement surgery, respectively, which are generally recommended for pharmacological prophylaxis. In addition, in the patient group that underwent pharmacological prophylaxis, it was confirmed that the incidence of postoperative TE events was reduced by approximately 90% compared with that in the no treatment group, as demonstrated in previous studies [24–26]. Taken together, in the real world, the incidence of postoperative TE may appear higher than that expected in previous studies because of low compliance with pharmacological prophylaxis.

Among all claimed TE events, TE events with anticoagulant treatment warrant the attention of physicians, excluding cases of superficial TE or subclinical TE events (Table 1). However, in the case of patients undergoing cardiac surgery, in which postoperative anticoagulant treatment is used in most patients, TE events with anticoagulant treatment may be overestimated. Conversely, in spine surgery, where the use of anticoagulant treatment is often difficult, because of the risk of bleeding, TE events with anticoagulant treatment in these patients may be underestimated. Therefore, this study presented both the total claimed TE, and TE with anticoagulant treatment, as the primary endpoints. However, the duration of anticoagulant treatment was shorter than that in the recommended guidelines for patients with postoperative TE events (median, 13 days; range, 1–442 days) [30,31]. This may be because of poor compliance with postoperative TE treatment guidelines, or patients using anticoagulant drugs for reasons other than postoperative TE treatment may have been included in the analysis. Thus, proper interpretation is necessary, to consider this aspect when applying the results of this study to clinical practice.

This study had the following differences compared to previous studies. First, as mentioned above, in most studies, TE events were counted by focusing on pulmonary embolism and deep vein thrombosis of the lower extremities [32,33]. Although pulmonary embolism and deep vein thrombosis of the extremities are clinically meaningful, in the real world, TE may occur in rare locations, such as intra-abdominally; and arterial TE, such as myocardial infarction and stroke, may also occur. In this study, we presented the situation of all TE events that can occur in the real world. Second, existing studies reported the risk of TE limited to one-area surgery or cancer-related surgeries [32–35]. Based on this information, it is impossible to sufficiently explain the relative risk for TE in each type of surgery in patients undergoing that surgery. Unlike other studies, this study aimed to
present the relative risk for TE according to the type of surgery in patients who underwent commonly performed surgeries in clinical practice. Third, this study also presented the incidence of arterial TE in the real world. Although the rate was lower than that of venous TE, fatal arterial TE, such as that resulting in postoperative myocardial infarction or stroke, can occur [36–39]. However, there are insufficient data on the incidence of arterial TE in surgical patients in the real world, and this study manifested this fact.

This study had several limitations. First, since the analysis used claims data, there were limitations in identifying all TE risk factors, such as information on individual and family medical history related to thrombophilia and detailed laboratory tests. Furthermore, it was not possible to correct for cases of mechanical heart valve surgery as a major TE risk factor, because we analyzed patients who underwent each selected surgery for the first time during the study period. However, the proportion of patients who had undergone mechanical heart valve surgery among all the patients was 0.002% (5921/2,799,293 patients); therefore, the effect of this was small. Second, because details such as the patient’s condition at the time of each surgery, purpose of the surgery, and situation at the time of the surgery were unknown, other factors in each surgery that were associated with an increased relative risk of TE could not be analyzed. Nevertheless, this study is considered to be meaningful because it presents the incidence and pattern of all postoperative venous or arterial TE of the commonly practiced surgeries in the real world and relative risk according to the type of surgery, using a nationally representative database.

In conclusion, in the real world, the incidence of postoperative venous TE in total knee replacement and hip replacement is still high, and some surgeries could have a relatively higher risk of venous TE than other surgeries. For patients undergoing these surgeries, studies to reduce the incidence of postoperative TE in clinical practice should be conducted.

**Supplementary Materials:** The following supporting information can be downloaded at: [https://www.mdpi.com/article/10.3390/jcm11061477/s1](https://www.mdpi.com/article/10.3390/jcm11061477/s1), Table S1: Classification codes for type of each surgery; Table S2: Type of total claimed thromboembolism for each surgery; Table S3: Type of thromboembolism with anticoagulation treatment for each surgery; Table S4: Baseline characteristics of the whole cohort and those of each surgery group; Table S5: Multivariate analysis of variables associated with postoperative thromboembolism events.

**Author Contributions:** B.S.K. and K.-W.K. designed the study. K.-W.K. and J.Y.L. analyzed the data and summarized the results. K.-W.K. wrote the manuscript. B.-H.L., M.J.J., E.S.Y., D.S.K., S.R.L., H.J.S., C.W.C., Y.P. and B.S.K. reviewed the data analysis. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was supported by a grant from Korea University (grant number: K2125711).

**Institutional Review Board Statement:** All procedures involving human participants were performed in accordance with the ethical standards of the institutional and national research committees and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the institutional review board of the Korea University Anam Hospital (No. 2020AN0136).

**Informed Consent Statement:** The requirement for informed consent was waived by the institutional review board of the Korea University Anam Hospital (No. 2020AN0136), owing to the use of anonymized patient data.

**Data Availability Statement:** Data are available from the corresponding author upon reasonable request.

**Conflicts of Interest:** The authors declare that they have no competing interest.

**References**

1. Jerjes-Sanchez, C. Venous and arterial thrombosis: A continuous spectrum of the same disease? *Eur. Heart J.* 2004, 26, 3–4. [CrossRef] [PubMed]
2. Kreutzer, L.; Minami, C.; Yang, A. Preventing venous thromboembolism after surgery. *JAMA* 2016, 315, 2136. [CrossRef] [PubMed]
3. D’Astous, J.; Liederman, Z.; Douketis, J.D. Venous thromboembolism prophylaxis in high-risk orthopedic and cancer surgery. *Postgrad. Med.* 2021, 133, 20–26. [CrossRef] [PubMed]
4. Spyropoulos, A.C.; Douketis, J.D. How I treat anticoagulated patients undergoing an elective procedure or surgery. *Blood* 2012, 120, 2954–2962. [CrossRef] [PubMed]

5. Anderson, D.R.; Morgan, G.P.; Bennett, C.; Dental, F.; Francis, C.W.; Garcia, D.A.; Kahn, S.R.; Rahman, M.; Rajasekhar, A.; Rogers, F.B.; et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: Prevention of venous thromboembolism in surgical hospitalized patients. *Blood Adv.* 2019, 3, 3898–3944. [CrossRef]

6. Kyri, P.A.; Eichinger, S. Deep vein thrombosis. *Lancet* 2005, 365, 1163–1174. [CrossRef]

7. van Veen, J.J.; Makris, M. Peri-operative anti-thrombotic therapy. *Anaesthesia* 2015, 70, 58-e23. [CrossRef]

8. Falck-Ytter, Y.; Francis, C.W.; Johanson, N.A.; Curley, C.; Dahl, O.E.; Schulman, S.; Ortel, T.L.; Pauker, S.G.; Colwell, C.W., Jr. Prevention of VTE in orthopedic surgery patients: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *CHEST* 2012, 141, e278S–e325S. [CrossRef]

9. Gee, E. The National VTE Exemplar Centres Network response to implementation of updated NICE guidance: Venous thromboembolism in over 16s: Reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (NG89). Br. J. Haematol. 2019, 186, 792–793. [CrossRef]

10. Cronin, M.; Dengler, N.; Krauss, E.S.; Segal, A.; Wei, N.; Daly, M.; Mota, F.; Caprini, J.A. Completion of the Updated Caprini Risk Assessment Model (2013 Version). *Clin. Appl. Thromb. Hemost.* 2019, 25, 1076029619838052. [CrossRef]

11. Rogers, S.O., Jr.; Kilariu, R.K.; Hosokawa, P.; Henderson, W.G.; Zinner, M.J.; Khuri, S.F. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: Results from the patient safety in surgery study. *J. Am. Coll. Surg.* 2007, 204, 1211–1221. [CrossRef]

12. Afshari, A.; Ageno, W.; Ahmed, A.; Duranteau, J.; Faroani, D.; Kozek-Langenecker, S.; Llau, J.; Nizard, J.; Solca, M.; Stensballe, J.; et al. European guidelines on perioperative venous thromboembolism prophylaxis: Executive summary. *Eur. J. Anaesthesiol.* 2018, 35, 77–83. [CrossRef]

13. Gould, M.K.; Garcia, D.A.; Wren, S.M.; Karanickolas, P.J.; Arcelus, J.L.; Heit, J.A.; Samama, C.M. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *CHEST* 2012, 141, e227S–e277S. [CrossRef]

14. Caprini, J.A. Thrombosis risk assessment as a guide to quality patient care. *Dis. Mon.* 2005, 51, 70–78. [CrossRef]

15. Bahl, V.; Hu, H.M.; Henke, P.K.; Wakefield, T.W.; Campbell, D.A., Jr.; Caprini, J.A. A validation study of a retrospective venous thromboembolism risk scoring method. *Ann. Surg.* 2010, 251, 344–350. [CrossRef]

16. Geahchan, N.; Basile, M.; Tohmeh, M.; on behalf of the DIONYS registry. Venous thromboembolism prophylaxis in patients undergoing abdominal and pelvic cancer surgery: Adherence and compliance to ACCP guidelines in DIONYS registry. *SpringerPlus* 2016, 5, 1541. [CrossRef]
29. Galante, M.; Languasco, A.; Gotta, D.; Bell, S.; Lancelotti, T.; Knaze, V.; Saubidet, C.L.; Grand, B.; Milberg, M. Venous thromboprophylaxis in general surgery ward admissions: Strategies for improvement. *Int. J. Qual. Health Care* 2012, 24, 649–656. [CrossRef]

30. Kearon, C.; Akl, E.A.; Ornellas, J.; Blaivas, A.; Jimenez, D.; Bounameaux, H.; Huisman, M.; King, C.S.; Morris, T.A.; Sood, N.; et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *CHEST* 2016, 149, 315–352. [CrossRef]

31. Ortel, T.L.; Neumann, I.; Ageno, W.; Beyth, R.; Clark, N.P.; Cuker, A.; Hutten, B.A.; Jaff, M.R.; Manja, V.; Schulman, S.; et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: Treatment of deep vein thrombosis and pulmonary embolism. *Blood Adv.* 2020, 4, 4693–4738. [CrossRef]

32. Kanchanabat, B.; Stapanavatr, W.; Meknavin, S.; Soorapanth, C.; Sumanasrethakul, C.; Kanchanasuttirak, P. Systematic review and meta-analysis on the rate of postoperative venous thromboembolism in orthopaedic surgery in Asian patients without thromboprophylaxis. *Br. J. Surg.* 2011, 98, 1356–1364. [CrossRef]

33. Yhim, H.Y.; Jang, M.J.; Bang, S.M.; Kim, K.H.; Kim, Y.K.; Nam, S.H.; Bae, S.H.; Kim, S.H.; Mun, Y.C.; Kim, I.; et al. Incidence of venous thromboembolism following major surgery in Korea: From the Health Insurance Review and Assessment Service database. *J. Thromb. Haemost.* 2014, 12, 1035–1043. [CrossRef]

34. Lewis-Lloyd, C.A.; Pettitt, E.M.; Adiamah, A.; Crooks, C.J.; Humes, D.J. Risk of postoperative venous thromboembolism after surgery for colorectal malignancy: A systematic review and meta-analysis. *Dis. Colon Rectum* 2021, 64, 484–496. [CrossRef]

35. Moubayed, S.P.; Eskander, A.; Mourad, M.W.; Most, S.P. Systematic review and meta-analysis of venous thromboembolism in otolaryngology-head and neck surgery. *Head Neck* 2017, 39, 1249–1258. [CrossRef]

36. Dong, Y.; Cao, W.; Cheng, X.; Fang, K.; Zhang, X.; Gu, Y.; Leng, B.; Dong, Q. Risk factors and stroke characteristic in patients with postoperative strokes. *J. Stroke Cerebrovasc.* Dis. 2017, 26, 1635–1640. [CrossRef]

37. Blacker, D.J. In-hospital stroke. *Lancet Neurol.* 2003, 2, 741–746. [CrossRef]

38. Sellers, D.; Srinivas, C.; Djaiani, G. Cardiovascular complications after non-cardiac surgery. *Anaesthesia* 2018, 73 (Suppl. S1), 34–42. [CrossRef]

39. Sahara, K.; Ishibe, A.; Yabuno, T.; Kondo, H.; Nakayama, G.; Yasuda, S.; Nishida, T.; Watanabe, J.; Uranaka, Y.; Akiyama, H.; et al. Acute iliac arterial thrombosis during laparoscopic abdominoperineal resection. *J. Surg. Case Rep.* 2019, 2019, rjz20. [CrossRef]