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Preoperative Aspirin Use and Outcomes in Cardiac Surgery Patients

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Background: The effects of preoperative aspirin use on outcomes of cardiac surgery patients remain uncertain. This study was aimed to evaluate the effect of preoperative aspirin use on major outcomes in cardiac surgery patients.

Methods: An observational cohort study was performed on consecutive patients (n = 4256) undergoing cardiac surgery in 2 tertiary hospitals. Of all patients, 2868 patients met the inclusion criteria and were divided into 2 groups: those taking (n = 1923) or not taking (n = 945) aspirin within 5 days preceding surgery.

Results: Patients in the aspirin group presented significantly more with comorbidities including hypertension, diabetes, peripheral arterial disease, previous myocardial infarction, angina, cerebrovascular disease, older age, and male gender. With propensity scores adjusted and multivariate logistic regression, however, the results of this study showed that preoperative aspirin therapy (vs nonaspirin) significantly reduced the risk of 30-day mortality (3.5% vs 6.5%, OR: 0.611, 95% CI: 0.391–0.956, $P = 0.031$), postoperative renal failure (3.7% vs 7.1%, OR: 0.384, 95% CI: 0.254–0.579, $P < 0.001$), dialysis required (1.9% vs 3.6%, OR: 0.441, 95% CI: 0.254–0.579, $P < 0.001$), intensive care unit stay (mean 107.2 vs 136.1 h, $P < 0.001$) and a composite outcome-major adverse cardiocerebral events (8.7% vs 10.8%, OR: 0.662, 95% CI:: 0.482–0.909, $P = 0.011$) in the patients undergoing cardiac surgery. However, readmissions did not show a significant difference between the 2 groups (14.5% vs 12.8%, $P = 0.944$).

Conclusions: Preoperative aspirin therapy is associated with a significant decrease in the risk of major cardiocerebral complications, renal failure, intensive care unit stay and 30-day mortality but does not increase the risk of readmissions in patients undergoing cardiac surgery.

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Aspirin as an antiplatelet and anti-inflammatory agent has been one of cornerstones in prevention and treatment of cardiovascular disease (CVD) in nonsurgical settings. Accumulative evidence has demonstrated that aspirin significantly reduces all-cause mortality, myocardial infarction (MI), and stroke in patients with risk of CVD.[1–4] In surgical settings, antiplatelet and anticoagulant therapy is a key part of management of patients undergoing cardiac surgery. Early postoperative aspirin therapy has been reported to improve postoperative outcomes in patients undergoing coronary artery bypass graft (CABG), including improving graft patency,[5–8] a reduced risk of death and ischemic complications.[9,10] However, only few reports have evaluated whether preoperative aspirin improves outcomes for patients undergoing cardiac surgery; thus far, the findings of the reports have been inconsistent.[11–13]

Meanwhile, despite mounting evidence that aspirin is an effective drug in the field of cardiovascular medicine and increasing numbers of patients are treated with aspirin before cardiac surgery, whether aspirin should be continued or given until the day of surgery (preoperative aspirin therapy) remains controversy, and decisions are often made on the basis of individual and institutional experience.[14–16] As a matter of fact, the American Heart Association and American College of Cardiology (AHA/ACC)[17] the Society of Thoracic Surgeons,[18] and the European Association for Cardio-Thoracic Surgery[19] recommended that patients should stop aspirin several days (ranged from 2 to 10 days) before elective cardiac surgery, mainly due to concerns of perioperative bleeding. Thus, there is a need to investigate the efficacy and the safety of preoperative aspirin therapy in cardiac surgery patients. Also, although patients undergo different types of cardiac surgery (CABG, valve, and other cardiac surgery) due to different causes, they suffer common postoperative complications involving the brain, heart and kidneys; whereas aspirin, mainly due to its antithrombotic and anti-inflammatory effects, may break common final pathways of injury to multiple organ systems. We hypothesized that preoperative use of aspirin provides cardiovascular protection against major cardiac, cerebral, renal complications and death in patients undergoing cardiac surgery. Thus, this study was aimed to test the overall effect of preoperative aspirin use on cardiac surgery patients.

METHODS

Study Design

This study was an observational and cohort study involving consecutive patients (n = 4256) receiving cardiac surgery including CABG and/or valve surgery, and other cardiac surgery at 2 tertiary medical centers, Thomas Jefferson University hospital (Philadelphia, PA; dated from 2003 to 2009) and UC Davis Medical center (Sacramento, CA; dated from 2001 to 2009). The study was in compliance with Declaration of Helsinki and reviewed and approved by the local institution review board, and individual consent was waived. The patients excluded were those with preoperative anticoagulants, adenosine diphosphate receptor inhibitors, glycoprotein IIb/IIIa inhibitors, antiplatelets, or unknown aspirin use. Of all patients, 2868 patients met the inclusion criteria and were divided into 2 groups: using (n = 1923) or not using (n = 945) preoperative aspirin (Fig. 1).

Data Collection

The patient data were collected and organized to follow the template of the Society of Thoracic Surgeons national database, including demographics, patient history, medical record information, preoperative risk factors, preoperative medications, intraoperative data, postoperative cardiocerebral events, renal failure, and 30-day all-cause mortality. Independent investigators prospectively collected the data on each patient during the course of hospitalization for cardiac surgery. Preoperative use of aspirin indicates use of aspirin in the patient within 5 days preceding surgery.

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Disclosure: The authors declare that they have nothing to disclose.

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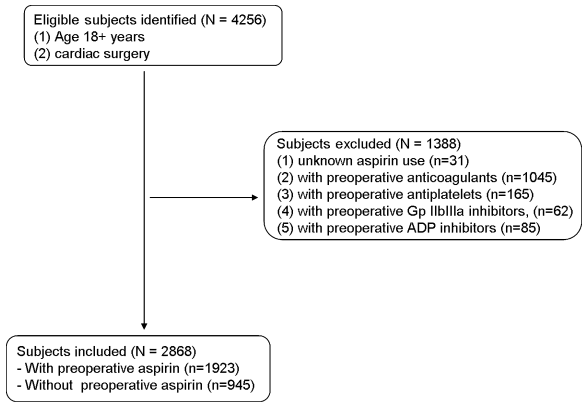

FIGURE 1. Selection of study sample.

Major outcomes of this study were 30-day all-cause mortality, postoperative renal failure/dialysis required, and a composite outcome—major adverse cardiocerebral events (MACE), the latter included permanent or transient stroke, coma, perioperative MI, heart block, and cardiac arrest. Other outcomes were readmission and intensive care unit (ICU) stay. On the basis of the Society of Thoracic Surgeons national criteria, *permanent stroke* is defined as a postoperative stroke (ie, any confirmed neurological deficit of abrupt onset caused by a disturbance in cerebral blood supply) that did not resolve within 24 hours; *transient stroke* or transient ischemic attack as loss of neurological function that was abrupt in onset but with complete return of function within 24 hours; *coma* as the patient had a new postoperative coma that persists for at least 24 hours secondary to anoxic/ischemic and/or metabolic encephalopathy, thromboembolic event or cerebral bleed; *perioperative MI* as documented by the following criteria (<24 hours postoperative): The creatine kinase isoenzyme MB (CK-MB) (or CK if MB is not available) must be greater than or equal to 5 times the upper limit of normal, with or without new Q waves present in 2 or more contiguous ECG leads, no symptoms required; or as documented by at least one of the following criteria (>24 hours postoperative): (1) evolutionary ST-segment elevations, (2) development of new Q-waves in 2 or more contiguous ECG leads, (3) new or presumably new LBBB pattern on the ECG, (4) The CK-MB (or CK if MB not available) must be greater than or equal to 3 times the upper limit of normal; heart block as a new heart block requiring the implantation of a permanent pacemaker of any type before discharge; postoperative renal failure as acute or worsening renal failure resulting in one or more of the followings: increase in serum creatinine more than 2.0 mg/dL and two times most recent preoperative creatinine level over baseline or new requirement for dialysis postoperatively; and readmission as the patient was readmitted as an in-patient within 30-days from the date of initial surgery for any reason. This includes readmissions to acute care, primary care institutions only, not to rehabilitation hospital or nursing home. The remaining definitions are available at http://www.sts.org/print/513 (accessed at September 22, 2011).

Statistical Analysis

Continuous and categorical variables were reported as mean ± SD or percentages, and compared with a 2-sample *t* tests or a χ^2 test (2-tailed), respectively. Univariate and multivariate logistic regression were performed to assess associations of demographic, therapeutic and clinical outcome variables. Missing data values for dichotomous variables were assigned the most frequent value, whereas continuous variables were assigned the median value, except for body surface area, which was assigned the sex-specific median value.[20]

As described previously,[21] because this was an observational study, a propensity score-adjusted analysis was performed to control for selection bias as result of nonrandom assignment to the 2 groups. A propensity score was derived, reflecting the probability that a patient would receive preoperative aspirin. This was accomplished by performing a multivariate logistic regression analysis using preoperative aspirin as the dependent variable and entering all baseline (preoperative) variables as in Table 1 that clinically would likely affect the probability of using preoperative aspirin.

In this study, the propensity score was used in regression (covariance) adjustment,[22] that is, using large set of preoperative variables as mentioned earlier to estimate the propensity score, and then the propensity score was subsequently regressed as an independent covariate in the multivariate logistic regression analysis, which was performed by using all relevant variables to identify independent predictors or risk factors for postoperative MACE, renal failure, and mortality. To achieve model parsimony and stability, the backward stepwise selection procedure was applied with the dropout criterion $P > 0.2$.

Potential preoperative confounding factors considered in this analysis were selected on the basis of a literature review, clinical plausibility, and variables collected in the database. These variables included (1) demographic characteristics such as age, gender, and body mass index (BMI); (2) patient history such as diabetes, hypertension, peripheral vascular disease, cerebrovascular disease, chronic lung disease, family history of coronary artery disease (CAD); (3) preoperative risk factors such as angina, congestive heart failure, previous MI, multiple CAD, left main CAD, and preoperative medications such as β-blockers, digitalis, diuretics, and rennin-angiotensin system inhibitors (inhibitors including angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers) in addition to aspirin. The preoperative lipid-lowering therapy was not included because of a large number of missing values (missing records were found 50.9%

TABLE 1. Demographic and Clinical Characteristics*

Characteristics	Aspirin Yes n = 1923	Aspirin No n = 945	*P*
Age, yrs	62.6 ± 13.0	60.4 ± 13.9	<0.001
Male gender, %	1455 (70.8)	599 (61.6)	<0.001
Body mass index, kg/m^2	29.3 ± 8.3	28.9 ± 6.7	0.211
Past medical history			
Diabetes	708 (36.8)	198 (20.9)	<0.001
Hypertension	1556 (80.9)	563 (59.6)	<0.001
Smoker	379 (19.7)	191 (20.2)	0.751
Cerebrovascular disease	295 (15.3)	90 (9.5)	<0.001
Peripheral vascular disease	254 (13.2)	71 (7.5)	<0.001
Chronic lung disease	410 (21.3)	161 (17.0)	0.007
Family history CAD	903 (47.0)	302 (32.0)	<0.001
Clinical pattern			
Angina	569 (29.6)	155 (16.4)	<0.001
Congestive heart failure	469 (24.4)	245 (25.9)	0.371
Previous MI	584 (30.4)	148 (15.7)	<0.001
Multiple CAD	1463 (76.1)	333 (35.2)	<0.001
Left main CAD	389 (20.2)	62 (6.6)	<0.001
Medical therapy			
β-blockers	1129 (58.7)	310 (32.8)	<0.001
Diuretics	368 (19.1)	150 (15.9)	0.033
Digitalis	56 (2.9)	27 (2.9)	0.934
ACE inhibitors or ARB	967 (50.3)	276 (29.2)	<0.001
Perfusion time (min)	154.5 ± 78.3	163.8 ± 83.2	0.003
Cross-clamp time (min)	118.2 ± 59.8	118.9 ± 63.6	0.781

*Values are n (%) for categorical variables and mean ± SD for continuous variables.

of all patients); and (4) intraoperative factors including perfusion time and cross-clamp time.

Models fit analysis was evaluated with the Hosmer-Lemeshow goodness-of-fit statistic. The C statistic was reported as a measure of predictive power. Results are reported as percentages and odds ratios (OR) and with 95% confidence intervals (CI). All reported *P* values were 2-sided, and $P < 0.05$ were considered to be statistically significant. Statistical analysis was performed with SPSS 17.0 software for Windows (SPSS Inc., Chicago, IL).

RESULTS

Baseline and Intraoperative Parameters

Of 4256 patients in the database, 2868 patients met the inclusion criteria and were divided into 2 groups: using (n = 1923) or not using (n = 945) preoperative (within 5 days preceding surgery) aspirin (Fig. 1). Most patients (88.4%) underwent CABG and/or valve surgery, including CABG (n = 1474), valve (n = 620), valve plus CABG (n = 442), and other cardiac surgery (n = 332). Demographic and clinical data of the patients who did and did not receive preoperative aspirin therapy are presented in Table 1. Between the 2 groups, there were no significant differences in body mass index, smoking, congestive heart failure, preoperative digitalis therapy, and cross-clamp time. However, the patients with aspirin were more frequent with history of hypertension, diabetes, peripheral vascular disease, previous MI, angina, cerebrovascular disease, chronic lung disease, and family history of CAD. Also, the patients with aspirin had more preoperative use of β-blockers, diuretics and rennin-angiotensin system inhibitors, and more left main and multiple CAD. The patients using aspirin were older and more likely to be males. Finally, perfusion time, a procedural characteristic, was shorter in the patients received aspirin (Table 1).

Postoperative Outcomes

Overall, the 30-day all-cause mortality rate was 129 of 2868 (4.5%). The unadjusted univariate analysis showed that the 30-day mortality was 3.5% (68/1923) for patients that received preoperative aspirin and 6.5% (61/945) for patients that did not take preoperative aspirin ($P < 0.001$ (Fig. 2). The 30-day mortality rate was 23.0% (62/269) for patients with MACE compared with 2.6% (67/2599) for patients without MACE ($P < 0.001$), indicating that postoperative cardiocerebral complications significantly contributed to the death associated with cardiac surgery.

The unadjusted univariate analysis also showed that a total of 9.4% of all 2868 patients undergoing cardiac surgery experienced at least one of MACEs, including permanent or transient stroke, coma, perioperative MI, heart block and cardiac arrest. The incidence of postoperative cardiocerebral events (MACE) in patients who received preoperative aspirin was 8.7% compared with 10.8% for patients who did not receive aspirin ($P = 0.069$; Fig. 2).

Among other outcomes through the unadjusted univariate analysis, preoperative use of aspirin (vs no aspirin preoperatively) also significantly reduced the risk of postoperative renal failure (3.7% vs 7.1%, $P < 0.001$) and dialysis required (1.9% vs 3.6%, $P = 0.007$), and ICU stay (total hrs in ICU 107.2 ± 179.9 vs 136.1 ± 238.2, $P < 0.001$). Importantly, the rates of readmissions did not show a significant difference between 2 groups (Fig. 2). The most common causes for readmissions in this study were deep stern infection, pericardial effusion and/or tamponade, pneumonia or respiratory complication, arrhythmia, etcetera, indicating that an obvious increase in postoperative bleeding requiring a readmission did not occur in patients taking aspirin preoperatively.

Figure 2 (the right 3 columns) presents the multivariate analysis to assess independent risk factors for postoperative complications, including 30-day all-cause mortality, renal failure, dialysis required, ICU stay, readmission and a composite outcome—MACE. The propensity score for preoperative aspirin therapy achieved an acceptable discrimination between 2 groups (C statistic: 0.815; 95% CI:, 0.798–0.831; $P < 0.001$). After adjusting for propensity score and covariates, preoperative aspirin did not show a significant effect on postoperative readmissions and cardiocerebral events including permanent stroke, transient ischemic attack, coma, heart block, and

	Outcome No.(% of incidence)							
	Preoperative aspirin		Univariate	*P*	Adjusted	95% CI	*P*	Adjusted Odd Ratio (95%)
	Yes	No	OR		OR			
No. of Patients	1923	945						
MACE	167(8.7)	102(10.8)	0.786	0.069	0.662	0.482–0.909	0.011	
Perioperative MI	22(1.1)	13(1.4)	0.830	0.595	0.331	0.151–0.725	0.006	
Permanent stroke	38(2.0)	25(2.6)	0.742	0.250	0.580	0.310–1.084	0.088	
TIA	11(0.6)	3(0.3)	1.806	0.358	1.012	0.223–4.600	0.988	
Coma	27(1.4)	12(1.3)	1.107	0.771	1.070	0.461–2.480	0.875	
Heart block	66(3.4)	42(4.4)	0.764	0.181	0.723	0.463–1.130	0.155	
Cardiac arrest	28(1.5)	22(2.3)	0.620	0.094	0.564	0.276–1.154	0.117	
Renal failure	71(3.7)	67(7.1)	0.502	<0.001	0.384	0.254–0.579	<0.001	
Dialysis required	37(1.9)	34(3.6)	0.526	0.007	0.441	0.245–0.790	0.006	
Total Hrs ICU	107.2 ± 179.9	136.1 ± 238.2		<0.001				
Readmission	279(14.5)	121(12.8)	1.114	0.360	0.990	0.756–1.298	0.944	
30-day mortality	68(3.5)	61(6.5)	0.531	<0.001	0.611	0.391–0.956	0.031	

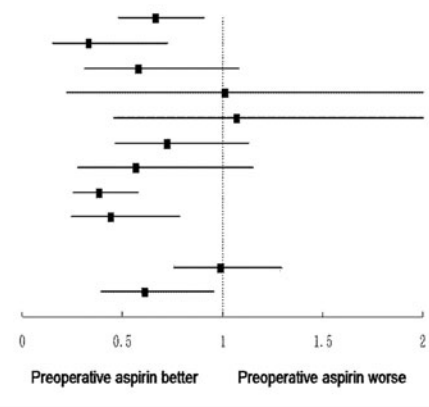

FIGURE 2. Effects of aspirin on postoperative complications and mortality in patients undergoing cardiac surgery. Values are n (%) for categorical variables and mean ± SD for continuous variables. OR indicates odd ratio; CI, confidence interval; MACE, major adverse cardiocerebral events; MI, myocardial infarction; TIA, transient ischemic attack.

cardiac arrest. However, patients who took preoperative aspirin had a significantly reduced the risk of MACE, perioperative MI, renal failure, dialysis required, and 30-day mortality (Fig. 2).

Independent Risk Factors for Postoperative 30-Day Mortality

Multivariate logistic regression analysis was adjusted for propensity scores and covariates to assess independent risk factors for postoperative 30-day mortality. After adjusting for propensity scores and covariates, preoperative aspirin was found to have a protective effect on 30-day mortality after cardiac surgery. Other independent predictors of postoperative 30-day mortality were history of hypertension, peripheral vascular disease, previous MI, multiple CAD, left main CAD, and cross-clamp time (Table 2).

Independent Risk Factors for MACE

Multivariate logistic regression analysis was adjusted for propensity scores and covariates to assess independent risk factors for postoperative MACE. After adjusting for propensity score and covariates, preoperative aspirin was found to have a protective effect on the incidence of MACE after cardiac surgery. Other independent predictors of MACE were male gender, age, history of peripheral vascular disease, angina, preoperative use of diuretics, and cross-clamp time (Table 3).

Independent Risk Factors for Postoperative Renal Failure

Multivariate logistic regression analysis was adjusted for propensity scores and covariates to assess independent risk factors for postoperative renal failure. After adjusting for propensity scores and covariates, preoperative aspirin was found to have a protective effect on the incidence of renal failure after cardiac surgery. Other independent predictors of postoperative renal failure were history of hypertension, family history CAD, previous MI, congestive heart failure, and perfusion time (Table 4).

The multivariate model (backward stepwise) significantly predicted the occurrence of postoperative 30-day mortality (model χ^2: 111.35; $P < 0.001$), MACE (model χ^2: 135.74; $P < 0.001$), and renal failure (model χ^2: 110.80; $P < 0.001$). The discriminatory ability of the logistic model was acceptable for 30-day mortality (C statistic: 0.743; 95% CI:, 0.701–0.786; $P < 0.001$), MACE (C statistic: 0.694; 95% CI:, 0.660–0.728; $P < 0.001$) and renal failure (C statistic: 0.750; 95% CI:, 0.707–0.793; $P < 0.001$). The model was well calibrated among deciles of observed and expected risk for 30-day mortality (Hosmer-Lemeshow χ^2: 4.742; $P = 0.785$, MACE (Hosmer-Lemeshow χ^2: 5.323; $P = 0.723$) and renal failure (Hosmer-Lemeshow χ^2: 10.345; $P = 0.242$).

TABLE 2. Multivariate Analysis of Risk Factors of Postoperative 30-day Mortality

Variable	Odds Ratio (95% CI)	*P*
Hypertension	1.682 (1.013–2.793)	0.045
Peripheral vascular disease	3.527 (2.138–5.818)	<0.001
Previous MI	2.855 (1.771–4.601)	<0.001
Multiple CAD	3.794 (1.677–8.582)	0.001
Left main CAD	3.948 (2.250–6.928)	<0.001
Aspirin	0.611 (0.391–0.956)	0.031
Cross-clamp time (min)	1.005 (1.001–1.009)	0.016

TABLE 3. Multivariate Analysis of Risk Factors of Major Cardiocerebral Adverse Events

Variable	Odds Ratio (95% CI)	*P*
Male gender	1.584 (1.166–2.153)	0.003
Age	0.986 (0.976–0.995)	0.003
Peripheral vascular disease	2.222 (1.541–3.203)	<0.001
Angina	1.765 (1.254–2.483)	0.001
Diuretics	1.487 (1.078–2.052)	0.016
Aspirin	0.662 (0.482–0.909)	0.011
Cross-clamp time (min)	1.008 (1.006–1.010)	<0.001

TABLE 4. Multivariate Analysis of Risk Factors of Renal Failure

Variable	Odds Ratio (95% CI)	*P*
Family history CAD	0.628 (0.421–0.937)	0.023
Hypertension	1.880 (1.199–2.947)	0.006
Previous MI	1.703 (1.152–2.517)	0.008
Congestive heart failure	1.879 (1.305–2.705)	0.001
Aspirin	0.384 (0.254–0.579)	<0.001
Perfusion time (min)	1.006 (1.004–1.008)	<0.001

DISCUSSION

This is an observational cohort study from 2 university hospitals in the United States to evaluate specifically effects of preoperative aspirin therapy on major clinical outcomes in patients undergoing cardiac surgery. This study provides new evidence that preoperative aspirin therapy (vs no preoperative aspirin) is associated with a significant decrease in the risk of 30-day mortality (3.5% vs 6.5%), renal failure (3.7% vs 7.1%), dialysis required (1.9% vs 3.6%), ICU stay (average 107.2 vs 136.1 h), and a composite outcome—MACE (8.7% vs 10.8%); and it is not associated with increased risk of readmissions (14.5% vs 12.8%).

Previous Studies

Aspirin or acetylsalicylic acid inhibits platelet aggregation and reduces inflammation through mechanisms, including suppressing the production of prostaglandins and thromboxanes, inducing the formation of NO-radicals and modulating NF-κB, a transcription factor complex or nuclear factor kappa-light-chain-enhancer of activated B cells.[3,23] The dual effects of aspirin, antiplatelet, and anti-inflammation, probably are key mechanisms responsible for its beneficial role in multiple diverse organs protection in cardiac surgery patients as found in this and a previous study,[9] though much remains to be investigated in this area, especially about anti-inflammatory effects of aspirin in the setting of cardiac surgery.

In clinical settings, several lines of evidence have well demonstrated the effectiveness of aspirin in the prevention and treatment of CVD. First, the Antiplatelet Trialists' Collaboration, a meta-analysis, has shown that among the high-risk patients for CVD, aspirin significantly reduced rates of MI, stroke, and death.[1] Second, in the setting of acute MI and stroke, aspirin therapy reduced cardiovascular morbidity and mortality, including recurrent ischemic stroke[24] and MI.[25] Third, the antiplatelet therapy with aspirin and clopidogrel (Plavix) has been recommended to be started before and continuously in percutaneous coronary intervention.[26] Fourth, aspirin, recommended by several professional societies, should be given postoperatively to all patients without contraindications after CABG or valve (mechanical) surgery to reduce thromboembolism and improve graft patency and survival.[17–19,27]

In 2000, Dacey et al[11] in a case-control study found that preoperative aspirin use was associated with a decreased risk of in-hospital mortality in CABG patients (vs nonusers, OR: 0.55, 95% CI: 0.3–0.98, $P = 0.04$) without significant increases in hemorrhage and

transfusion. Later (in 2005), Bybee et al[12] in a retrospective cohort study confirmed the findings mentioned previously in patients (n = 1636) undergoing first-time isolated CABG at a single institution, that is, preoperative aspirin (vs no preoperative aspirin) significantly lowered postoperative in-hospital mortality (1.7% vs 4.4%, $P = 0.007$), while without an increased risk of reoperation for bleeding (3.5% vs 3.4%, $P = 0.96$) or requirement for postoperative blood product transfusion (adjusted OR: 1.17, 95% CI: 0.88–1.54, $P = 0.28$).

In 2002, Mangano and research group[9] in a prospective multicenter study (n = 5065) showed that among patients who received aspirin within 48 hours (early postoperatively) after CABG, subsequent mortality was 1.3%, as compared with 4.0% among those who did not receive aspirin during this period. In addition, aspirin therapy was associated with a significant reduction in the incidence of MI (by –48%), stroke (by –50%), renal failure (by –74%), and bowel infarction (by –62%), while the risk of hemorrhage, gastritis, infection, or impaired wound healing was not increased with aspirin use.

Recently (in 2011), Jacob et al[13] reported in an observational single institution study that among patients undergoing nonemergent isolated CABG, late (within 5 days of the surgery) use of aspirin (vs discontinued aspirin ≥6 days before surgery) was associated with no significant difference in a composite outcome of in-hospital mortality, MI, and stroke (1.8% vs 1.7%, $P = 0.80$) and reoperations for bleeding (3.4% vs 2.4%, $P = 0.10$) but more intraoperative transfusions (23% vs 20%, $P = 0.03$) and postoperative transfusions (30% vs 26%, $P = 0.009$). The study of Jacob et al[13] showed that continuing preoperative aspirin increased transfusion requirement in patients undergoing isolated CABG but had no significant effect on major outcomes including mortality. The study of Jacob et al,[13] nonetheless, was not powered to determine the effect of aspirin on postoperative major complications and death rates. Given the complication and death rates showed in their study, an estimated sample size would be much larger than one in the study to detect a statistical difference. Also, although their study showed that preoperative aspirin was associated with a small increase in transfusion requirements (23% vs 20%), the patients with preoperative aspirin use (vs nonaspirin) were associated with increased anticoagulant use (49% vs 30%, $P < 0.0001$), which may cause/contribute to the increase in transfusion requirements. Finally, the technique of matching individual patients from the 2 exposure groups based on their respective propensity scores, as did in the study of Jacob et al,[13] may disregard individuals who cannot be matched but an effect modification may still exist, thus a potential important exposure effect may be ignored.[28]

Our Studies

This study showed the beneficial effects of preoperative aspirin use to cardiac surgery patients in "the real world," and the results are in line with our previous findings (one center study, n = 1879).[29] Notably, our studies showed that although the patients with preoperative aspirin were significantly older and with more comorbidities including hypertension, diabetes, cerebrovascular disease, peripheral vascular disease, previous MI, angina, left main and multiple CAD, and family history of CAD, preoperative aspirin protects the heart, brain, and kidneys against these major risk factors, indicating its efficacy (opposing the most important confounding factors—comorbidities) and potential application to these high-risk patients.

The extent and scope of the effect (multiple diverse organs protection) of preoperative aspirin in cardiac surgery patients as showed in this study were unexpected and are most likely a reflection of its anti-inflammatory effect rather than its antithrombotic effect. Although the findings from this study may overestimate the effect that might be achievable in clinical practice, the similar findings were also showed in a previous study of the early postoperative aspirin therapy by Mangano and research group,[9] as described earlier.

Ongoing Studies

At present, the Aspirin and Tranexamic Acid for Coronary Artery Surgery trial[30] is undergoing and this randomized clinical trial (RCT) was aimed to test the benefits and risks of preoperative aspirin (single dose of aspirin, 100 mg given 1 to 2 hours before the surgery) and intraoperative antifibrinolytic therapy in CABG patients. Although RCTs are considered to be the most reliable form of scientific evidence in the hierarchy of clinical evidence, RCTs' external validity may be limited. For example, the Aspirin and Tranexamic Acid for Coronary Artery Surgery trial will not answer the questions about continuing or discontinuing long-term use of aspirin before cardiac surgery because the aspirin use within 5 days of surgery is an exclusion criterion (the patient treated with long-term aspirin may also be excluded by this criterion). Thus, one may consider the evidence in 2 dimensions: internal validity (RCTs) and external validity (retrospective and/or observational studies) and recognize that different methods may complement one another.[31]

Bleeding remains a major concern for preoperative aspirin therapy, as reported recently.[13,15] However, in the current era of cardiac surgery, the potential bleeding may be avoided by using low dose of aspirin and/or giving antifibrinolytic therapy perioperatively.[15,32] Overall, the outcome benefits provided by preoperative aspirin therapy may override its possible risk of excess bleeding in patients undergoing cardiac surgery. Nonetheless, further studies are certainly needed to examine this potential side effect carefully.

Limitations of this Study

As in conducting any observational study, a major challenge for this study is to draw inferences that are acceptably free from influences by overt and/or potential hidden biases, including potential multiple and uncontrollable confounding factors, such as physician bias on selection of patients and medications. Although multivariate regression (included all plausible variables in the database) was used in this study to reduce overt biases, the potential flaws of a nonrandomized study may remain. Second, there are several different options of how propensity scores can be used to control confounding, including regression adjustment versus stratification versus matching based on the propensity scores. Each of these approaches has its advantages and shortcomings, as detailed in the literature.[22,28] Third, the latest version of our database on preoperative use of aspirin included "Aspirin: yes or no." There were no records of the duration of treatment or dosage of drug the patient was receiving, though preoperative aspirin use usually indicates chronic use of the drug in the patient. Finally, CABG and/or valve and other cardiac surgery were included in this study. We hypothesized that preoperative aspirin use benefits all types of cardiac surgery because of its broad cardiovascular protective effects, especially anti-inflammatory effect, thus the inclusion of all types of cardiac surgery would allow us to test the overall effect of preoperative aspirin use on cardiac surgery patients. The downside of this inclusion is that we do not know yet which type of surgeries contributes most to the overall effect, which would be solved when the sample size is large enough to parse the data. Thus, further studies to dissect different types of cardiac surgery (subgroup studies, such as CABG, valve, emergent, urgent or elective alone or various combinations) are needed and probably would provide more detail information about aspirin and cardiac surgery. As indicated before, nonetheless, the best overall estimate of the effect of a treatment probably comes from the average effect on all the patients and not from the individual subgroups.[33]

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ERRATUM

Fields RC, Busam KJ, Chou JF, et al. *Ann Surg.* 2011; 254:465-473; discussion 473-475. The published manuscript lists incorrect author affiliations. Only Ryan C. Fields should be listed as affiliated with Barnes-Jewish Hospital. All other authors are from Memorial Sloan-Kettering Cancer Center. Drs. Coit, Brady, Allen, and Kraus are all from the Department of Surgery at Memorial Sloan-Kettering. The published affiliations for the authors Busam, Chou, Panageas, and Pulitzer are correct.

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