Incremental Risk of Prior Coronary Arterial Stents for Pulmonary Resection

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Background. **Many patients requiring lung cancer resection have concomitant coronary artery disease. Preoperative coronary artery stenting has been associated with increased risk of cardiac events after noncardiac surgery. Our aim was to determine the incidence of major adverse cardiac events (MACE) in patients undergoing pulmonary resection for lung cancer after percutaneous coronary stenting.**

Methods. **This study uses Surveillance, Epidemiology, and End Results-Medicare data (1998 to 2005). Patients undergoing lung cancer resection within 1 year after coronary stenting were compared with patients without preoperative coronary intervention. The incidence and predictors of MACE within 30 days after surgery were determined.**

Results. **Five hundred nineteen patients underwent lung cancer resection after coronary stenting (stent), and 21,892 patients underwent lung cancer resection without a preceding coronary intervention (no stent). The stent group had higher comorbidity scores ($p < 0.0001$) and more males (66% versus 50%; $p < 0.0001$). There were no differences in age (74 versus 74 years), tumor size (33.7 versus 33.6 mm), stage (53% versus 54% stage I), and resections of lobectomy or greater (83% versus 80%) between stent and no-stent groups (all $p > 0.05$). Thirty-day MACE and mortality rates were 9.3% and 7.7% in the stent group and 4.9% and 4.6% in the no-stent group (both $p < 0.0001$). Multivariable predictors of MACE were coronary stent, age, male sex, comorbidity score, tumor size, and stage.**

Conclusions. **Patients undergoing lung cancer surgery within 1 year of coronary stenting are at high risk for perioperative MACE. The presence of a coronary stent should be an important component of risk assessment before resection for lung cancer.**

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Patients with coronary artery disease (CAD) requiring pulmonary resection for non-small cell lung cancer (NSCLC) can present difficult management problems. A major pulmonary resection may lead to an increased risk of perioperative myocardial infarction (MI) in patients with severe untreated CAD. Coronary revascularization before noncardiac surgery may decrease risk in selected groups of patients [1]. Percutaneous coronary intervention (PCI) with a stent is commonly performed in patients with CAD requiring noncardiac surgery. After stent placement, patients are generally maintained on dual antiplatelet therapy (aspirin and clopidogrel or equivalent) to decrease the risk of stent thrombosis [1–4]. Current practice guidelines recommend continuation of dual antiplatelet therapy for 4 to 6 weeks after bare-metal stent (BMS) placement and 12 months for a drug-eluting stent (DES) [1–3]. Discontinuation of dual antiplatelet therapy for noncardiac surgery before these time points is associated with a high risk of major adverse cardiac events (MACE) [5–7]. Operating in the presence of dual anti-platelet therapy may increase the risk of perioperative bleeding complications [4, 8].

The risk of MI in all patients undergoing lung resection for NSCLC is 0.36% according to The Society of Thoracic Surgeons (STS) General Thoracic Surgery Database (GTSD) [9]. A retrospective report from the Mayo Clinic found a MACE rate of 5.4% for noncardiac surgery after PCI with DES [10]. Another study from the same group reported a 5.2% rate of MACE after PCI with a BMS before noncardiac surgery [11]. Finally, Brichon and colleagues [12] found that major lung resection within 3 months of coronary stenting with a BMS was associated with an incidence of 9% of MI and a 3% mortality rate.

In this study, we aim to determine the incidence and risk of perioperative MACE in patients undergoing preoperative coronary intervention with a stent before surgical resection of NSCLC. We also compare long-term survival in these patients with those patients not having had a preoperative coronary stent placed. Such data will help risk stratify patients with severe coronary disease requiring intervention before surgical resection of NSCLC.

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Abbreviations and Acronyms

BMS = bare-metal stents
CAD = coronary artery disease
DES = drug-eluting stents
GTSD = General Thoracic Surgery Database
MACE = major adverse cardiac event
MI = myocardial infarction
NSCLC = non-small cell lung cancer
PCI = percutaneous coronary intervention
SEER = Surveillance, Epidemiology, and End Results
STS = The Society of Thoracic Surgeons

Patients and Methods

We performed a retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database to evaluate outcomes in patients with NSCLC treated with pulmonary resection after percutaneous placement of a coronary stent from 1998 through 2005. Patients undergoing pulmonary resection without prior placement of a coronary stent within 1 year of surgery served as the control group. The SEER database is a tumor registry sponsored by the National Cancer Institute capturing roughly 14% to 25% of incident tumors in the United States. Medicare beneficiaries within the registry have had their tumor records linked to all their claims data. The quality, validity, and generalizability of the SEER-Medicare data have been described previously [13]. The Washington University Medical Center Human Studies Committee reviewed this study and found it not to constitute human subject research based on the regulatory definition of a human subject; therefore, subsequent review by the Human Studies Committee was not deemed necessary.

Among all lung cancer patients from 1998 through 2005 in the SEER-Medicare dataset, the following sequential exclusions were made: patients younger than 66 years, patients treated with therapy other than surgery, and patients with partial fee-for-service or concurrent health maintenance organization enrollment, or both, 1 year before lung cancer diagnosis. Only full fee-for-service beneficiaries not enrolled in other insurance programs would have complete claims records; therefore, all other patients were excluded. Patients who were 65 years old at the time of diagnosis were excluded because they do not have Medicare claims data in the year before diagnosis of lung cancer.

Patient, disease, and treatment information were available through the SEER registry and Medicare database. Specifically, placement of a percutaneous coronary stent was determined by querying the Centers for Medicare and Medicaid Services data files for Healthcare Common Procedure Coding System Current Procedural Terminology codes 92980 and 92981. We considered any coronary stent placed within 1 year preceding lung cancer resection, as our cohort selection criteria described above included patients with complete Medicare claims data for at least 1 year preceding surgery. This period was selected as clinically relevant also, as American College of Cardiology/American Heart Association guidelines recommend that elective surgery in patients with coronary stents be delayed from 4 to 6 weeks to 12 months, dependent on stent type (BMS versus DES, respectively) [1]. To reduce confounding, any patient undergoing coronary artery bypass grafting after coronary stenting was excluded from analysis. Because DES were approved by the US Food and Drug Administration in 2004, making BMS the most common stent placed during the study period, we consider all types of cardiac stents together in this analysis [14].

For analysis of patient characteristics, indicators of low income or education were based on the lowest quartiles of median income and proportion with a high school education within a given zip code from Census Tract data. Area of residence is stratified into metropolitan, urban, and rural based on population size. Medicare claims within the Physician/Supplier and Outpatient files in the year before diagnosis were used to calculate a Klabunde-modified Charlson Comorbidity Index, which was used for risk adjustment [15]. Tumor size, stage (American Joint Committee on Cancer, 7th edition), and histologic identification were all based on information within 4 months of diagnosis. All tumors were restaged to the American Joint Committee on Cancer, 7th edition.

The primary outcome measure was development of perioperative MACE. Major adverse cardiac events were defined as death, ST-elevation MI, non–ST-elevation MI, stent thrombosis, and repeat revascularization with either coronary artery bypass grafting, stenting, or angioplasty, as done is prior studies [10, 11]. The perioperative period was defined as from the day of surgery to 30 days postoperative. Occurrence of MACE was determined by the presence of *International Classification of Diseases, 9th revision* (ICD-9) or Current Procedural Terminology codes within the Medicare Analysis Provider and Review, Outpatient and Physician/Supplier files (Appendix).

SAS version 9.3 (SAS Institute, Cary, NC) was used to perform all statistical analysis. Continuous and categorical variables were compared by a Kruskal-Wallis test and the χ test, respectively. Kaplan-Meier curves were generated that provide unadjusted survival estimates at postoperative points for patients overall and across strata of other variables. Differences among strata were determined by log-rank tests. Cox proportional-hazards models were used to evaluate the relationships between percutaneous coronary stents and MACE while adjusting for patient and tumor characteristics. Variables in Table 1 were selected a priori and examined by means of univariate analysis. Variables with a probability value of less than 0.20 were included in the multivariable analysis. All statistical tests were two-sided using a level of significance of 0.05 for α.