Pulmonary Embolism After Coronary Artery Bypass Grafting

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Case Presentation: A 76-year-old man developed increased fatigue during his daily 40-lap swim and daily 3-mile walk. His past medical history included use of hydrochlorothiazide for hypertension. His physical examination and baseline ECG were normal. An exercise treadmill test demonstrated ischemia, and cardiac catheterization showed left main and 3-vessel obstructive coronary artery disease. Echocardiography revealed normal left ventricular function.

He underwent a 3-vessel coronary artery bypass grafting (CABG) with the left internal mammary artery grafted to the left anterior descending, and separate saphenous vein grafts, harvested endoscopically from the left leg, to the obtuse marginal branch and posterior descending coronary artery. The surgery was uncomplicated, with an aortic cross clamp time of 73 minutes and cardiopulmonary bypass time of 89 minutes.

On the first postoperative day, he was transferred out of the intensive care unit. By the fifth postoperative day, he was walking 100 feet steadily without use of any assist device. He was discharged home on the sixth postoperative day on enteric-coated aspirin, hydrochlorothiazide, metoprolol, and atorvastatin.

He presented to his community hospital on the 30th postoperative day, complaining of 5 days of increasing fatigue and 1 day of markedly increased shortness of breath. The ECG showed a heart rate of 79 beats per minute and nonspecific ST and T wave abnormalities. The D-dimer level was elevated (>8000 ng/mL). Contrast-enhanced spiral computed tomography (CT) of the pulmonary arteries, including additional sections of the lower extremities, acquired during venous phase of contrast enhancement (“indirect CT venography”) showed a large bilateral central pulmonary embolism (PE) and a right leg deep vein thrombosis (DVT), without DVT in the leg from which the saphenous vein had been harvested (Figure 1). He was transferred to Brigham and Women’s Hospital for further management, where he was hospitalized for 6 days, received enoxaparin as a “bridge” to warfarin, and was discharged uneventfully.

Discussion
Challenges in Prediction and Detection of PE After CABG
Asymptomatic venous thromboembolism (VTE) occurs after CABG with surprisingly high frequency. Though not clinically important in most instances, it serves as a harbinger for massive symptomatic DVT and PE, including life threatening and fatal events. Unfortunately, there is no foolproof way of determining who will develop VTE or who will suffer a rare but deadly complication. The patient who we present deceptively appeared to be at low risk of postoperative PE because he had only mild hypertension as a comorbidity and was in excellent physical shape. He illustrates the teaching point that predicting who will have a PE is difficult and, therefore, universal measures to prevent postoperative VTE are of paramount importance.

The low detection rate of symptomatic VTE after CABG is understandable. Shortness of breath is often ascribed to deconditioning, atelectasis, or preexisting left ventricular dysfunction. The patient who we discuss had a normal heart rate, normal blood pressure, normal ECG, and vague symptoms. His presentation could have been ascribed to pericarditis, costochondritis, or anxiety. Undoubtedly, some of the patients who “die suddenly” within 30 days of CABG succumb to PE without any clear warning signs and...
without the diagnosis of PE being established. DVT is also difficult to detect clinically because leg discomfort and swelling may be attributed to trauma from the vein harvest site, excessive hydration during cardiopulmonary bypass, or muscle cramping due to perioperative immobility. Rarely is DVT suspected in the contralateral leg after vein harvest for CABG.

Scope of the Problem
At Brigham and Women’s Hospital, we performed predischarge venous ultrasonography in 330 patients who had undergone CABG. Overall, 67 (20%) had DVT diagnosed by ultrasonography. Clots were found as often in the leg contralateral to the saphenous vein graft harvest site as in the ipsilateral leg. Of those with DVT, 56 (84%) had thrombi isolated to the calf, and 11 (16%) had DVT in proximal leg veins. Two patients had symptomatic PE, including a 51-year-old man who died from massive PE despite emergent pulmonary embolectomy. Only 1 patient had symptomatic DVT, which was proximal. Thus, the ratio of isolated calf DVT to proximal leg DVT was approximately 5–to–1, and the ratio of all DVT to symptomatic PE or DVT exceeded 20–to–1. These findings indicate that almost all DVT after CABG is asymptomatic and most often is confined to the calf veins. However, we found that although symptomatic VTE occurred in only about 1% of CABG patients, it can result in fatal PE.

Our observations at Brigham and Women’s Hospital are consistent with those of the California Patient Discharge Data Set, in which 66 180 records were surveyed for symptomatic VTE within 91 days after CABG. Overall, 736 patients (1.1%; 95% confidence interval 1.1 to 1.2) were detected with symptomatic DVT or PE. Two thirds (0.7%) were diagnosed after hospital discharge.

If we extrapolate these findings to the entire United States, based on 500 000 CABG operations annually, then each year, approximately 100 000 patients develop DVT, with about 84 000 isolated to the calf and 16 000 with proximal disease. Only about 10 000 have disease that is symptomatic and diagnosed definitively. Because of short hospitalizations, about 7000 of the diagnosed cases are recognized after hospital discharge. Assuming a mortality rate of 1% among asymptomatic patients and 2% to 4% among symptomatic patients with overt DVT and PE, there are between 1100 and 1300 potentially preventable postoperative deaths each year in the United States alone, including patients who die from PE in which the death is ascribed to other etiologies, such as arrhythmia or myocardial infarction.

In addition to death from PE and disability from chronic thromboembolic pulmonary hypertension, VTE...
increases health care costs because it contributes to hospital readmissions after CABG. In New York State in 1999, 16,325 patients were discharged after CABG, and 2111 (12.9% of live discharges) were readmitted within 30 days for complications directly related to CABG. PE and DVT constituted the fifth most common cause of readmission, 6.3% of all readmissions, and were exceeded in frequency only by infections, heart failure, myocardial ischemia, and arrhythmia. The median length of time until readmission was 9 days, with an interquartile range of 4 to 17 days.

**Rationale for Universal Prophylaxis**

PE and DVT are easier and less expensive to prevent than to diagnose or treat. Therefore, virtually all CABG patients should receive prophylactic measures against VTE. CABG is particularly well suited for protocols that proactively prevent anticipated potential complications. However, primary prevention of perioperative VTE with standard mechanical or pharmacological prophylactic measures is often not routine practice.

In a registry of 5451 US patients with ultrasound-confirmed DVT, only 42% of the inpatients had received prophylaxis within 30 days before diagnosis. Various theses are proposed to justify omission of specific VTE prophylaxis protocols after CABG. Administration of tens of thousands of units of heparin during cardiopulmonary bypass has traditionally been considered protective, though an increasing proportion of patients are undergoing off-pump CABG. Aspirin, used universally after CABG, may have a very weak but measurable effect in reducing the frequency of postoperative VTE. Thus, the use of aspirin is at times claimed to be sufficient for prevention of VTE after CABG. Early ambulation and routine hospital discharge within 4 to 5 days minimize the period of immobility and lower the risk of DVT or PE. However, hospitalized patients may be much more mobile when prodded by nurses and physical therapists than they are after discharge home.

**Strategies to Prevent PE After CABG**

To prevent VTE after CABG, cardiac surgeons can utilize mechanical prophylaxis, pharmacological prophylaxis, or a combination of both strategies. Most concerning to the cardiac surgeon is the possibility of doing harm with pharmacological prophylaxis. Bleeding complications are immediately apparent, but PEs prevented by heparin remain invisible. Routine heparin injections increase the pharmacy expenditures and are perceived as an additional annoyance or minor discomfort by some patients.

The two principal mechanical prophylaxis measures are graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) devices. GCS increase venous blood flow and prevent perioperative venodilation of the legs. They are inexpensive, simple, and free of serious complications such as hemorrhage. In randomized trials evaluating GCS for VTE prevention after non-orthopedic surgery, there was an overall reduction of 72% in DVT.

IPC devices ("pneumoboots") provide intermittent inflation of air-filled cuffs, prevent venous stasis in the legs, and compress the veins more forcefully than GCS; they also stimulate the endogenous fibrinolytic system. Their main drawback is lack of use due to poor patient compliance, especially after transfer out of the intensive care unit.

Subcutaneous administration of fixed-dose unfractionated or low molecular weight heparin helps prevent perioperative VTE. The most comprehensive randomized, controlled trial of low-dose unfractionated heparin ("mini-dose heparin") as prophylaxis against fatal postoperative PE was performed in the pre-CABG era, enrolled 4121 patients, and was published in 1975 as the International Multicenter Trial. Prophylaxis consisted of 5000 U of heparin administered subcutaneously, 2 hours preoperatively and every 8 hours thereafter for 7 days. Eligible patients were over age 40 and were scheduled to undergo elective major surgery. Sixteen patients in the control group versus 2 in the heparin group died of PE confirmed by autopsy.

Collins and colleagues pooled the data from 78 randomized controlled mini-dose heparin trials with 15,598 surgical patients. There was a 40% reduction in nonfatal PE and 64% reduction in fatal PE among patients treated prophylactically with heparin 5000 U every 8 to 12 hours. Patients assigned to heparin had about one-third as many DVTs as control patients, regardless of whether they had undergone general, urological, elective orthopedic, or trauma surgery. Overall, there was a 2% increase in the rate of excessive bleeding, especially common after urological procedures.

Low molecular weight heparins have several advantages over unfractionated heparin, but they have not been tested extensively in CABG patients. Low molecular weight heparins exhibit less binding to plasma proteins and to endothelial cells than unfractionated heparin. Consequently, they tend to have a more predictable dose response, a more dose-independent mechanism of clearance, and a longer plasma half-life than unfractionated heparin. Furthermore, osteoporosis and heparin-induced thrombocytopenia seem to be less common with low molecular weight heparins than with unfractionated heparin. In most prevention trials, low molecular weight heparins are administered as once daily subcutaneous injections in low, fixed doses, without laboratory monitoring or dose adjustment.

What is a practical approach to preventing PE after CABG? Both GCS and IPC devices can be used immediately postoperatively in the leg contralateral to the saphenous vein harvest. GCS reduces the frequency of venous thrombosis and
should therefore be considered first-line prophylaxis against PE, except for those with peripheral arterial occlusive disease whose condition may be worsened by vascular compression. IPC devices are most effective in the intensive care unit, where compliance can readily be monitored and enforced.

Pharmacological prophylaxis should be considered as a routine prevention measure after CABG. The strategy least likely to cause excessive bleeding is administration of 5000 U of unfractionated heparin subcutaneously twice daily. Patients with additional VTE risk factors are candidates for more intensive prophylaxis, either with heparin 5000 U three times daily, enoxaparin 40 mg once daily, or dalteparin 5000 U twice daily; TID, thrice daily. Patients with additional VTE risk factors are candidates for more intensive prophylaxis, either with heparin 5000 U three times daily, enoxaparin 40 mg once daily, or dalteparin 5000 U twice daily.

Future Perspectives

Future clinical trials should investigate VTE prophylaxis among patients undergoing CABG. In addition to unfractionated heparin and low molecular weight heparin, novel anticoagulants such as fondaparinux, a direct factor Xa inhibitor, and ximelagatran, an oral direct thrombin inhibitor, appear promising for the prevention of VTE and should be studied in patients undergoing CABG. Finally, computer-generated prompting may increase the utilization of prophylaxis orders. The results of these trials will contribute to continuous quality improvement.

References

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