Patients Over 80 Do Well After Cardiac Surgery

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — Old age is not a reason to deny cardiac surgery to patients.

Patients aged 80 and older who underwent cardiac surgery had a life expectancy that was as good as the current average survival rate for similarly aged people in the U.S. population, according to three separate reports presented at annual scientific sessions of the American Heart Association.

Cardiac surgery "is a viable option for selected patients" aged 80 and older," Dr. Paul Kurlansky said at the meeting. Chronologic age alone should not be a criterion for deciding whether an elderly patient should be offered cardiac surgery, added Dr. Kurlansky, a cardiothoracic surgeon and director of research at the Florida Heart Research Institute in Miami, who presented one of the meeting reports.

His report reviewed the experience of 1,062 consecutive patients aged 80-99 years who underwent on-pump coronary artery bypass grafting (CABG) during 1989-2001 at Mount Sinai Medical Center, a community hospital in Miami Beach. The average age of these patients was 83. During a mean follow-up of 6 years, actuarial survival following surgery was about 6 years, closely matching the current life expectancy for people aged 80 in the United States.

"Without surgery, their survival would be very short. If survivorship is 5 or 6 years [with surgery], you are offering these patients something that they wouldn't otherwise have," Dr. Kurlansky said.

In addition, a "very remarkable" finding was how they were doing overall and how they perceived their health. The Short Form–36 health-status questionnaire was completed by 545 of the patients during an in-person or telephone interview an average of 3 years after hospital discharge. The results showed that their self-rated physical- and mental-health scores very closely matched the scores of aged-matched

norms for the U.S. population, he reported.

His analysis also showed that during the 12-year period reviewed, the rate of in-hospital mortality in patients undergoing CABG at Mount Sinai steadily fell from a high of nearly 15% in 1989 to a rate of just over 2% by 2001. It is not clear what led to this dramatic increase in perioperative safety, but possible factors are reduced perfusion times, improved anesthesia techniques, and overall better patient care, he said.

The second report at the meeting reviewed 8,796 patients who underwent aortic valve surgery, with or without concurrent CABG, at eight medical centers in northern New England during 1989-2006. This included about 1,000 patients aged 80-84, and about 350 patients aged at least 85.

The median survival rate following surgery was about 7 years in both patients aged 80-84 and those aged 85 and older. Expected survival rates in the general U.S. population inpeople 80-84 is also 7 years, and 5 years for those aged 85 and older, said Donald S. Likosky, Ph.D., a health policy analyst at Dartmouth Medical School in Lebanon, N.H. The survival rates in the elderly cardiac surgery patients were similar whether they underwent valve surgery only or had combined valve surgery and CABG.

Actuarial survival following surgery closely matched the current life expectancy for people aged 80 in the United States.

DR. KURLANSKY

The third report at the meeting reviewed 203 patients aged 80 or older (average age 83) who underwent aortic-valve surgery at the Methodist-DeBakey Heart Center in Houston during 1977-2008. A third of the patients also had concurrent CABG. The average perioperative mortality in these patients was about 6%, not significantly different from the average 4% perioperative mortality in 1,020 patients aged 79 or younger (average age 63) who also had aortic valve surgery, and in some cases CABG, at the Methodist-DeBakey Heart Center during the same period, Dr. Gerald M. Lawrie reported in a poster. Dr. Lawrie and his associates did not compare long-term mortality rates in their octogenarian, postsurgical patients with those of age-matched norms.

To see an interview with Dr. Kurlansky, go to www.youtube.com/watch?v=rr-dzV_epv0. ■

---

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Hemorrhage

The incidence of major hemorrhagic complications during Lovenox treatment has been low.

The following rates of major bleeding events have been reported during clinical trials with Lovenox Injection [see Tables 2 to 7].

Table 2
Major Bleeding Episodes Following Abdominal and Colorectal Surgery[1]

	Dosing Regimen	
	Lovenox	Heparin
Indications	40 mg q.d. SC	5000 U q8h SC
Abdominal Surgery	n = 555 23 (4%)	n = 560 16 (3%)
Colorectal Surgery	n = 673 28 (4%)	n = 674 21 (3%)

[1] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥ 2 g/dL or transfusion of 2 or more units of blood products. Retroperitoneal, intraocular, and intracranial hemorrhages were always considered major.

Table 3
Major Bleeding Episodes Following Hip or Knee Replacement Surgery[1]

	Dosing Regimen		
	Lovenox	Lovenox	Heparin
	40 mg	30 mg	15,000
Indications	q.d. SC	q12h SC	U/24h SC
Hip Replacement Surgery Without Extended Prophylaxis[2]		n = 786 31 (4%)	n = 541 32 (6%)
Hip Replacement Surgery With Extended Prophylaxis			
Peri-operative Period[3]	n = 288 4 (2%)		
Extended Prophylaxis Period[4]	n = 221 0 (0%)		
Knee Replacement Surgery Without Extended Prophylaxis[2]		n = 294 3 (1%)	n = 225 3 (1%)

[1] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥ 2 g/dL or transfusion of 2 or more units of blood products. Retroperitoneal and intracranial hemorrhages were always considered major. In the knee replacement surgery trials, intraocular hemorrhages were also considered major hemorrhages.

[2] Lovenox 30 mg every 12 hours SC initiated 12 to 24 hours after surgery and continued for up to 14 days after surgery.

[3] Lovenox 40 mg SC once a day initiated up to 12 hours prior to surgery and continued for up to 7 days after surgery.

[4] Lovenox 40 mg SC once a day for up to 21 days after discharge.

NOTE: At no time point were the 40 mg once a day pre-operative and the 30 mg every 12 hours post-operative hip replacement surgery prophylactic regimens compared in clinical trials.

Injection site hematomas during the extended prophylaxis period after hip replacement surgery occurred in 9% of the Lovenox patients versus 1.8% of the placebo patients.

Table 4
Major Bleeding Episodes in Medical Patients With Severely Restricted Mobility During Acute Illness[1]

	Dosing Regimen		
	Lovenox[2]	Lovenox[2]	Placebo[2]
Indications	20 mg q.d. SC	40 mg q.d. SC	
Medical Patients During Acute Illness	n = 351 1 (<1%)	n = 360 3 (<1%)	n = 362 2 (<1%)

[1] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, (2) if the hemorrhage caused a decrease in hemoglobin of ≥ 2 g/dL or transfusion of 2 or more units of blood products. Retroperitoneal and intracranial hemorrhages were always considered major although none were reported during the trial.

[2] The rates represent major bleeding on study medication up to 24 hours after last dose.

Table 5
Major Bleeding Episodes in Deep Vein Thrombosis With or Without Pulmonary Embolism Treatment[1]

	Dosing Regimen[2]		
	Lovenox	Lovenox	Heparin
	1.5 mg/kg	1 mg/kg	aPTT Adjusted
Indication	q.d. SC	q12h SC	IV Therapy
Treatment of DVT and PE	n = 298 5 (2%)	n = 559 9 (2%)	n = 554 9 (2%)

[1] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥ 2 g/dL or transfusion of 2 or more units of blood products. Retroperitoneal, intraocular, and intracranial hemorrhages were always considered major.

[2] All patients also received warfarin sodium (dose-adjusted according to PT to achieve an INR of 2.0 to 3.0) commencing within 72 hours of Lovenox or standard heparin therapy and continuing for up to 90 days.

Table 6
Major Bleeding Episodes in Unstable Angina and Non-Q-Wave Myocardial Infarction

	Dosing Regimen	
	Lovenox[1]	Heparin[1]
	1 mg/kg q12h SC	aPTT Adjusted
Indication		IV Therapy
Unstable Angina and Non-Q-Wave MI[2,3]	n = 1578 17 (1%)	n = 1529 18 (1%)

[1] The rates represent major bleeding on study medication up to 12 hours after dose.

[2] Aspirin therapy was administered concurrently (100 to 325 mg per day).

[3] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease by ≥ 3 g/dL or transfusion of 2 or more units of blood products. Intraocular, retroperitoneal, and intracranial hemorrhages were always considered major.

Table 7
Major Bleeding Episodes in acute ST-segment Elevation Myocardial Infarction

	Dosing Regimen	
	Lovenox[1]	Heparin[1]
	Initial 30-mg IV bolus followed by 1 mg/kg q12h SC	aPTT Adjusted IV Therapy
Indication		
acute ST-segment Elevation Myocardial Infarction	n = 10176 n (%)	n = 10151 n (%)
- Major bleeding (including ICH)[2]	211 (2.1)	138 (1.4)
- Intracranial hemorrhages (ICH)	84 (0.8)	66 (0.7)

[1] The rates represent major bleeding (including ICH) up to 30 days

[2] Bleedings were considered major if the hemorrhage caused a significant clinical event associated with a hemoglobin decrease by ≥ 5 g/dL. ICH were always considered major.

Thrombocytopenia:

[See *Warnings and Precautions (5.5)*]

Elevations of Serum Aminotransferases

Asymptomatic increases in aspartate (AST [SGOT]) and alanine (ALT [SGPT]) aminotransferase levels greater than three times the upper limit of normal of the laboratory reference range have been reported in up to 6.1% and 5.9% of patients, respectively, during treatment with Lovenox. Similar significant increases in aminotransferase levels have also been observed in patients and healthy volunteers treated with heparin and other low molecular weight heparins. Such elevations are fully reversible and are rarely associated with increases in bilirubin.

Since aminotransferase determinations are important in the differential diagnosis of myocardial infarction, liver disease, and pulmonary emboli, elevations that might be caused by drugs like Lovenox should be interpreted with caution.

Local Reactions

Mild local irritation, pain, hematoma, ecchymosis, and erythema may follow SC injection of Lovenox.

Other

Other adverse effects that were thought to be possibly or probably related to treatment with Lovenox, heparin, or placebo in clinical trials with patients undergoing hip or knee replacement surgery, abdominal or colorectal surgery, or treatment for DVT and that occurred at a rate of at least 2% in the Lovenox group, are provided below [see Tables 8 to 11].