

Medical, Surgical Therapies Yield Similar Outcomes

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MUNICH — Surgical repair did not show a clear survival advantage over medical management of patients with anomalous aortic origins of the coronary arteries, in a review of 54 patients.

A review of 35 years' worth of case experiences of patients undergoing coronary catheterization at the Cleveland Clinic through the mid-2000s identified 54 pa-

tients as having anomalous aortic origins of coronary arteries that had an interarterial course. Of them, 28 were managed by surgical repair, and 26 were managed medically. But the split between these two options over time showed a dramatic shift, with most of the surgical repairs occurring since 2000, while medical management was preferred before then, Dr. Richard A. Krasuski said at the annual congress of the European Society of Cardiology.

The results of his new analysis, showing

no added survival benefit from surgical repair, led him to rethink his approach to treating these patients.

"My attitude about 4 years ago, when I got to Cleveland, was that you had to convince yourself why they shouldn't be sent to surgery. But I now think that I need to be convinced that the patient needs surgery," said Dr. Krasuski, director of the adult congenital heart disease service at the Cleveland Clinic. Although the concept of repairing a clear structural defect is ap-

pealing, physicians also have to be wary of potential morbidity from surgery, he said.

During the 35 years reviewed, slightly more than 210,000 patients underwent coronary catheterization at the Cleveland Clinic. Of these, 301 (0.14%) could be clearly identified with an anomalous aortic origin of a coronary artery, either a right coronary artery coming out of the left cusp, or a left coronary coming out of the right cusp. Of the 54 of these patients who had an interarterial course and who un-

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THE-PRINCE (Thromboembolism Prevention in Cardiac or Respiratory Disease With Enoxaparin) was a multicenter, controlled, randomized, open-label trial that assessed the efficacy and safety of unfractionated heparin (UFH) and LOVENOX® (enoxaparin sodium injection) in patients with CHF or severe respiratory disease.¹⁴ LOVENOX® was shown to be at least as effective as UFH in the prevention of thromboembolic events in patients with heart failure or severe respiratory disease. The overall VTE rate for LOVENOX® was 8.4% vs 10.4% for UFH.

LOVENOX® Was Effective in Reducing the Incidence of DVT/PE in Patients Undergoing Abdominal or Pelvic Surgery for Cancer

In ENOXACAN (Enoxaparin and Cancer), patients undergoing abdominal or pelvic surgery for cancer were randomized to either LOVENOX® 40 mg subcutaneously (SC) once daily or UFH 5000 IU 3 times daily given 2 hours before surgery and continued for 10 ± 2 days.¹⁵ There was no significant difference in thromboembolic events comparing LOVENOX® 40 mg SC once daily with UFH 5000 IU SC 3 times daily (14.7% vs 18.2%, respectively).¹⁵

Overall, there was no difference in the incidence of major hemorrhagic events between LOVENOX® 40 mg SC once daily and UFH 5000 IU SC 3 times daily (4.1% vs 2.9%, respectively).¹⁵

LOVENOX® was demonstrated to be as safe and effective as UFH given 3 times daily for prophylaxis of DVT/PE in patients undergoing abdominal or pelvic surgery for cancer.¹⁵

Incidence of DVT/PE in patients undergoing cancer surgery¹⁵

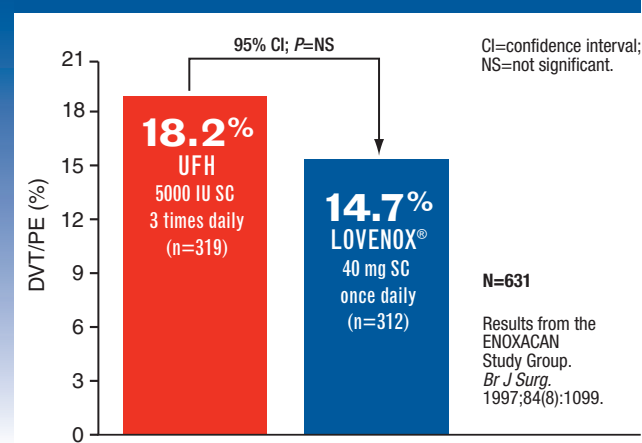


Figure 3. Incidence of DVT/PE in patients undergoing cancer surgery.

In Patients Undergoing Hip- or Knee- Replacement Surgery, LOVENOX® Reduced the Incidence of DVT/PE Compared to Warfarin

In a large, randomized, multicenter, open-label, parallel-group clinical trial with over 3000 patients undergoing total hip arthroplasty, LOVENOX® significantly reduced DVT risk versus warfarin during hospitalization (0.3% vs 1.1%, respectively).¹⁶

The incidence of major bleeding episodes was comparable between LOVENOX® and warfarin-treated patients (0.6% vs 0.3%, respectively).¹⁶

Incidence of DVT in patients undergoing hip-replacement surgery¹⁶

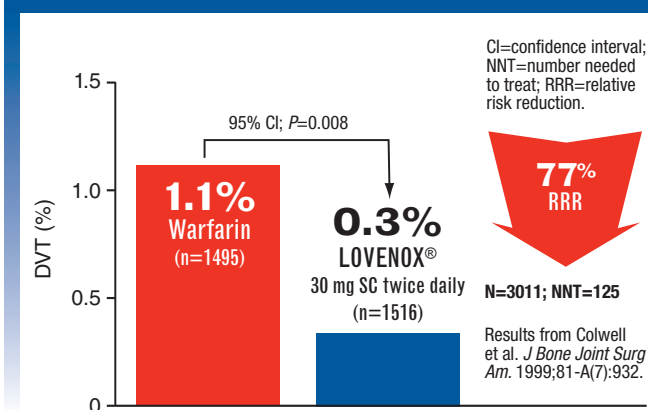


Figure 4. Incidence of DVT in patients undergoing hip-replacement surgery.

In patients undergoing total knee arthroplasty, a randomized, multicenter, open-label, parallel-group study demonstrated that LOVENOX® was able to significantly reduce the incidence of DVT/PE compared to warfarin (25.4% vs 45.5%, respectively).¹⁷

There was no significant difference in the number of major bleeding episodes between both treatment groups.¹⁷

Incidence of DVT/PE in patients undergoing knee-replacement surgery¹⁷

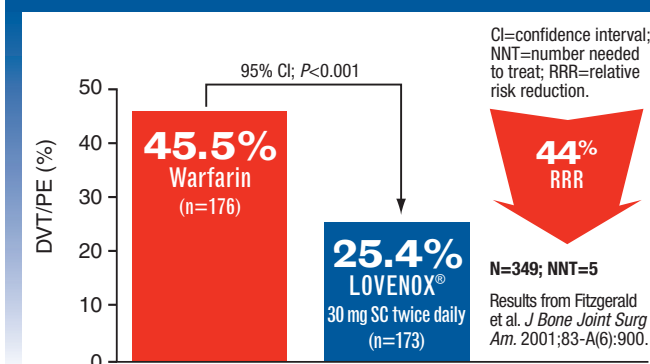


Figure 5. Incidence of DVT/PE in patients undergoing knee-replacement surgery.

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derwent treatment, 26 were managed medically, and 28 underwent surgical repair.

The average age of all patients was about 53, and about two-thirds were men. The anomalous vessel was a left main coronary artery in about a third of patients. About three-quarters of the patients had chest pain at the time of treatment. Stress tests were done in slightly more than half of the patients, and patients who underwent surgery had a 94% prevalence of a stress-test abnormality, significantly higher than the 46% prevalence among the medically treated patients. The surgery patients also had significantly more atherosclerosis, with an average of 1.3 atherosclerotic coronary

arteries, compared with an average of 0.8 affected coronaries in the medical group.

No surgical patients had diabetes, compared with a 30% prevalence of diabetes in the medically treated patients.

The most common surgery used was coronary artery bypass grafting with arterial grafting, in 40% of the surgery patients, either as an isolated procedure or with coronary ligation. Coro-



nary bypass with a vein graft was used in 32%, also either as an isolated procedure or with ligation.

Surgery may not always be the best option for patients with an anomalous aortic origin of a coronary artery.

DR. KRASUSKI

(totals more than 100% because of rounding). No patients died during surgery.

During follow-up, the survival rate was

82% in the surgery patients and 54% in the patients treated medically, but the two subgroups had a marked difference in the duration of follow-up. The median follow-up interval was 61 months in the surgery patients and 137 months in the medical patients. When the analysis examined actuarial 10-year survival, the rates were similar in the two treatment arms, Dr. Krasuski said.

A major limitation of this study is that it was confined to patients who had undergone coronary catheterization. The findings do not address the prevalence of anomalous aortic origins of the coronary arteries in the general population. ■

Despite evidence-based clinical practice guidelines for the prophylaxis of DVT and PE, recommendations are underutilized and many patients are not receiving proper anticoagulation. This is not only detrimental to patient care but also increases the burden on the health care system.

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The first step in reducing the incidence of DVT/PE is to increase public and physician awareness of these devastating conditions, and to ensure that all hospitalized patients are adequately assessed for risk of DVT and treated accordingly.

Important Safety Information

WARNING: SPINAL/EPIDURAL HEMATOMAS

When neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with low-molecular-weight heparins or heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis.

The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of drugs affecting hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.

Monitor patients for signs and symptoms of neurological impairment. If neurologic compromise is noted, urgent treatment is necessary.

Consider the potential benefit versus risk before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis (see *Warnings and Precautions* [5.1] and *Drug Interactions* [7]).

- LOVENOX® (enoxaparin sodium injection) cannot be used interchangeably with other low-molecular-weight heparins or unfractionated heparin (UFH), as they differ in their manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage
- As with other anticoagulants, use with extreme caution in patients with conditions that increase the risk of hemorrhage. Dosage adjustment is recommended in patients with severe renal

impairment. Unless otherwise indicated, agents that may affect hemostasis should be discontinued prior to LOVENOX® therapy. Bleeding can occur at any site during LOVENOX® therapy. An unexplained fall in hematocrit (HCT) or blood pressure should lead to a search for a bleeding site. (See WARNINGS and PRECAUTIONS)

- In the ST-segment elevation myocardial infarction (STEMI) pivotal trial, the rates of major hemorrhages (defined as requiring 5 or more units of blood for transfusion, or 15% drop in HCT or clinically overt bleeding, including intracranial hemorrhage [ICH]) at 30 days were 2.1% in the LOVENOX® group and 1.4% in the UFH group. The rates of ICH at 30 days were 0.8% in the LOVENOX® group and 0.7% in the UFH group. The 30-day rate of the composite endpoint of death, myocardial infarction (MI), or ICH (a measure of net clinical benefit) was significantly lower in the LOVENOX® group (10.1%) as compared to the UFH group (12.2%)
- Thrombocytopenia can occur with LOVENOX®. In patients with a history of heparin-induced thrombocytopenia (HIT), LOVENOX® should be used with extreme caution. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm³, LOVENOX® should be discontinued. Cases of HIT have been observed in clinical practice. (See WARNINGS and PRECAUTIONS)
- The use of LOVENOX® has not been adequately studied for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves. (See WARNINGS and PRECAUTIONS)
- LOVENOX® is contraindicated in patients with hypersensitivity to enoxaparin sodium, heparin, or pork products, and in patients with active major bleeding

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