

# Infection Risk Poses Blood Transfusion Dilemma

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PHILADELPHIA — For a transfusion, fresher blood is better.

Patients who received a first unit of packed red blood cells that had been stored for at least 26 days following donation were twice as likely to develop a nosocomial infection than were patients who received more recently donated blood, Dr. Raquel Nahra said at the annual meeting of the

American College of Chest Physicians.

But the practical implication of the finding is not to simply discard old blood sooner. "From our results, it's clear that the younger the blood the less the risk of infection, but it's hard to say we should just use fresher blood for all patients. We can't just discard blood that is older than 26 days," said Dr. Nahra, an infectious diseases physician at Cooper University Hospital in Camden, N.J. Current practice in the United States is to discard

blood once it is 42 days old, she noted.

An alternative response is to limit blood transfusions to those that are absolutely necessary, thereby relieving pressure on the banked blood supply.

"If a more restrictive transfusion strategy were applied, it would skew the blood supply to a younger age," said Dr. David R. Gerber, associate director of the ICU at Cooper University Hospital and senior investigator for the study.

Standard practice at most U.S. hospitals

has moved to a more restrictive transfusion approach in recent years, commented Dr. Mark J. Rosen, chief of the divisions of pulmonary, critical care, and sleep medicine at North Shore-University Hospital and Long Island Jewish Medical Center in New Hyde Park, N.Y. "We used to transfuse everyone to a hemoglobin of 10 g/dL. Now, if a patient has a hemoglobin of 7 g/dL or higher and is doing okay and does not have coronary disease or another reason to get better oxygen delivery,

## ADVERTISEMENT

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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.<sup>14</sup> 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.<sup>15</sup> 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).<sup>15</sup>

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).<sup>15</sup>

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.<sup>15</sup>

### Incidence of DVT/PE in patients undergoing cancer surgery<sup>15</sup>

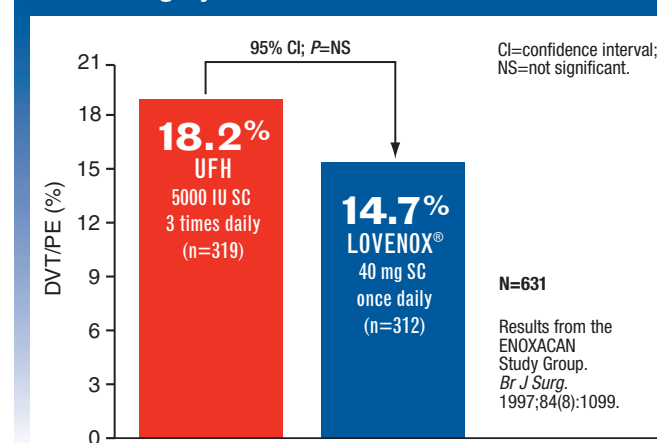


Figure 3. Incidence of DVT/PE in patients undergoing cancer surgery.

### 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).<sup>16</sup>

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

### Incidence of DVT in patients undergoing hip-replacement surgery<sup>16</sup>

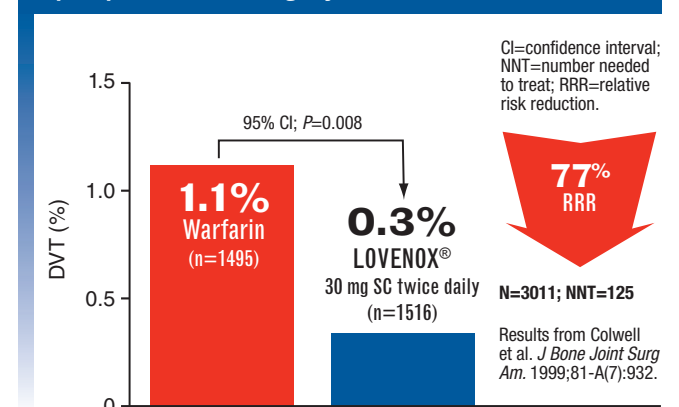


Figure 4. Incidence of DVT in patients undergoing hip-replacement surgery.

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).<sup>17</sup>

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

### Incidence of DVT/PE in patients undergoing knee-replacement surgery<sup>17</sup>

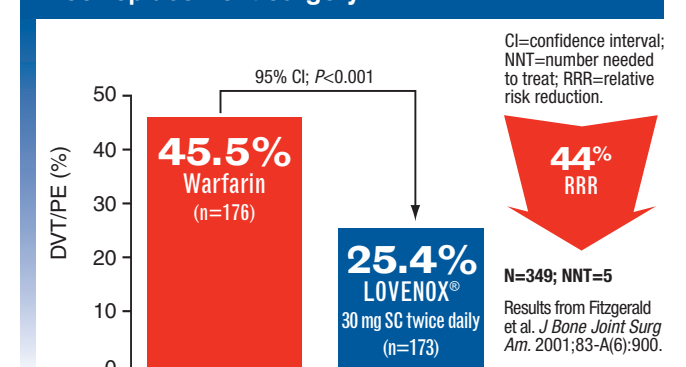


Figure 5. Incidence of DVT/PE in patients undergoing knee-replacement surgery.

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we generally don't transfuse," he said.

The new finding "is consistent with a large body of information that indicates that the shelf life [of blood] really does matter," Dr. Rosen added. "In the best possible world, blood would be safe and free from complications, but we're not there. We need to deal with the supply we have, and the best we can do is use it responsibly."

The study by Dr. Nahra, Dr. Gerber, and their associates reviewed 421 patients who received one or more units of packed red blood cells at Cooper University Hospital from July 2003 to September 2006. The median age of the patients was 66 years, and they spent a median of 5 days in the ICU

and a median of 17 days in the hospital. The analysis looked at the age of the oldest unit of blood they received, the age of the first unit of blood, and the total number of units received. Those parameters were analyzed relative to mortality rates, hospital length of stay, ICU length of stay, and infection rate while in the hospital.

The average age of the blood they received was 26 days. Eleven patients died,



and 57 developed nosocomial infections.

In addition to showing a doubled risk for infection when the first unit of blood was at least 26 days old, the analysis also showed that patients had a 2.9-fold increased risk for infection when they received any unit that was at least 29 days old.

Both of those were statistically significant associations, Dr. Nahra reported.

The analysis failed to find any significant

link between the age of blood transfused and the rate of death or length of stay in the hospital or ICU. Patients who received five or more units of packed red cells were significantly more likely to develop at least one nosocomial infection, compared with patients who received less blood.

Red cells that are stored for more than 2 weeks begin to release increased amounts of proinflammatory cytokines, which may underlie an increased susceptibility to infection, Dr. Nahra said. The amount of cytokine released increases with time, peaking at 42 days, which is when unused stored blood is discarded. ■

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.

Authored by Frank Michota, MD; Cleveland Clinic; sanofi-aventis consultant.

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/mm<sup>3</sup>, 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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