

HEART Score Predicts Chest Pain Outcomes

BY BRUCE JANCIN

BARCELONA — A new scoring system for categorizing patients who present with chest pain to the emergency department—called the HEART score—proved to be a strong discriminator of acute coronary syndrome and the risk of major adverse cardiac events within the next 6 weeks in a Dutch multicenter validation study.

HEART is designed to be faster, simpler, and more intuitive than the acute coronary syndromes (ACS) risk scoring systems physicians now have, such as TIMI (Thrombolysis In Myocardial Infarction) and GRACE (Global Registry of Acute Coronary Events), Dr. Barbra Backus explained at the annual congress of the European Society of Cardiology.

“TIMI and GRACE ignore patient history, and are time consuming and complex. Although the use of the GRACE score in emergency rooms is recommended in the European guidelines, it’s not widely done,” according to Dr. Backus of St. Antonius Hospital, Nieuwegein, the Netherlands.

“The HEART score is analogous to the Apgar score for newborns. It’s easy to use, easy to remember, and easy to communicate,” she added.

The score takes less than 2 minutes to calculate and doesn’t require any costly, time-consuming imaging studies.

HEART is an acronym for the five elements that make up the score: History, ECG, Age, Risk factors, and Troponin level. Each element is assigned 0-2 points depending upon how abnormal it is. This yields a total HEART score ranging from 0 to 10.

For example, a patient who presents with a classic history that’s highly suspicious for ischemic chest pain gets 2 points for history; a somewhat suspicious history earns 1, and a nonsuspicious history for coronary heart disease gets 0 points.

Similarly, significant ST-segment deviation earns 2 points for the ECG element, nonspecific ECG changes get 1 point, and a normal ECG gets none. Patients get 2 points for being above age 65, 1 for being age 45-65, and 0 for being younger than age 45. An individual with three or more coronary risk factors or a history of treatment for atherosclerosis gets 2 points for the risk factor element; a patient with one or two risk factors earns 1 point.

Dr. Backus presented a retrospective HEART score validation study involving 910 consecutive patients who presented with chest pain to four Dutch emer-

gency departments. Thirty were lost to follow-up.

A major adverse coronary event—acute MI, percutaneous coronary intervention, coronary artery bypass surgery, or death—occurred in 18% of patients within 6 weeks of presentation. This was the case for just 3 of 303 patients (0.1%) with a HEART score of 0-3, 48 of 413 (12%) with a score of 4-6, and 107 of 164 (65%) with a score of 7 or higher.

The mean HEART score in patients who experienced a cardiac end point was 7.2, significantly more than the mean of 3.8 in individuals who did not.

“We believe it’s possible to base clinical decisions on the HEART score. Patients with a HEART score of 0-3 can be discharged from the emergency room immediately. Patients with a score of 4-6 require additional investigation. Patients with a HEART score of 7 or above should be admitted to the coronary care unit,” Dr. Backus continued.

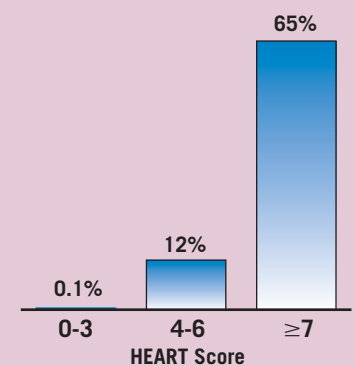
She and her coinvestigators performed subanalyses in diabetic patients, elderly patients above age 80, and in women. The HEART score performed as well in these groups as in the general population.

Asked if all five elements of the HEART score carry equal predictive power, Dr. Backus replied that actually

they don’t. The sensitivity and specificity of history, ECG, and troponin level were slightly stronger than age and risk factors, but not enough to warrant assigning those elements weighted values. That would make the HEART score more difficult to remember and to use in busy emergency departments, thus defeating the whole purpose of the new scoring system, she explained.

A prospective multicenter validation study of the HEART score is ongoing. ■

Coronary Event Rate Climbs With Higher HEART Scores



Note: Based on a study of 910 patients presenting with chest pain.

Source: Dr. Backus

Bosentan was teratogenic in rats given oral doses two times the maximum recommended human dose [MRHD] (on a mg/m² basis). In an embryo-fetal toxicity study in rats, bosentan showed dose-dependent teratogenic effects, including malformations of the head, mouth, face and large blood vessels. Bosentan increased stillbirths and pup mortality at oral doses 2 and 10 times the MRHD (on a mg/m² basis). Although birth defects were not observed in rabbits given oral doses of up to the equivalent of 10.5 g/day in a 70 kg person, plasma concentrations of bosentan in rabbits were lower than those reached in the rat. The similarity of malformations induced by bosentan and those observed in endothelin-1 knockout mice and in animals treated with other endothelin receptor antagonists indicates that teratogenicity is a class effect of these drugs [see **Nonclinical Toxicology**].

Nursing Mothers

It is not known whether Tracleer is excreted into human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Tracleer, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and efficacy in pediatric patients have not been established.

Geriatric Use

Clinical studies of Tracleer did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Clinical experience has not identified differences in responses between elderly and younger patients. In general, caution should be exercised in dose selection for elderly patients given the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy in this age group.

Hepatic Impairment

Because there is *in vitro* and *in vivo* evidence that the main route of excretion of bosentan is biliary, liver impairment could be expected to increase exposure (C_{max} and AUC) of bosentan. Mild liver impairment was shown not to impact the pharmacokinetics of bosentan. The influence of moderate or severe liver impairment on the pharmacokinetics of Tracleer has not been evaluated. There are no specific data to guide dosing in hepatically impaired patients; caution should be exercised in patients with mildly impaired liver function. Tracleer should generally be avoided in patients with moderate or severe liver impairment [see **Dosage and Administration, Warnings and Precautions**].

Renal Impairment

The effect of renal impairment on the pharmacokinetics of bosentan is small and does not require dosing adjustment.

Patients with Low Body Weight [see **Dosage and Administration**].

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis and Mutagenesis

Two years of dietary administration of bosentan to mice produced an increased incidence of hepatocellular adenomas and carcinomas in males at doses as low as 450 mg/kg/day (about 8 times the maximum recommended human dose [MRHD] of 125 mg twice daily, on a mg/m² basis). In the same study, doses greater than 2000 mg/kg/day (about 32 times the MRHD) were associated with an increased incidence of colon adenomas in both males and females. In rats, dietary administration of bosentan for two years was associated with an increased incidence of brain astrocytomas in males at doses as low as 500 mg/kg/day (about 16 times the MRHD). In a comprehensive battery of *in vitro* tests (the microbial mutagenesis assay, the unscheduled DNA synthesis assay, the V-79 mammalian cell mutagenesis assay, and human lymphocyte assay) and an *in vivo* mouse micronucleus assay, there was no evidence for any mutagenic or clastogenic activity of bosentan.

Reproductive and Developmental Toxicology

Bosentan was teratogenic in rats given oral doses ≥60 mg/kg/day. In an embryo-fetal toxicity study in rats, bosentan showed dose-dependent teratogenic effects, including malformations of the head, mouth, face and large blood vessels. Bosentan increased stillbirths and pup mortality at oral doses of

60 and 300 mg/kg/day. Although birth defects were not observed in rabbits given oral doses of up to 1500 mg/kg/day, plasma concentrations of bosentan in rabbits were lower than those reached in the rat. The similarity of malformations induced by bosentan and those observed in endothelin-1 knockout mice and in animals treated with other endothelin receptor antagonists indicates that teratogenicity is a class effect of these drugs.

Impairment of Fertility/Testicular Function

The development of testicular tubular atrophy and impaired fertility has been linked with the chronic administration of certain endothelin receptor antagonists in rodents.

Treatment with bosentan at oral doses of up to 1500 mg/kg/day (50 times the MRHD on a mg/m² basis) or intravenous doses up to 40 mg/kg/day had no effects on sperm count, sperm motility, mating performance or fertility in male and female rats. An increased incidence of testicular tubular atrophy was observed in rats given bosentan orally at doses as low as 125 mg/kg/day (about 4 times the MRHD and the lowest doses tested) for two years but not at doses as high as 1500 mg/kg/day (about 50 times the MRHD) for 6 months. Effects on sperm count and motility were evaluated only in the much shorter duration fertility studies in which males had been exposed to the drug for 4-6 weeks. An increased incidence of tubular atrophy was not observed in mice treated for 2 years at doses up to 4500 mg/kg/day (about 75 times the MRHD) or in dogs treated up to 12 months at doses up to 500 mg/kg/day (about 50 times the MRHD).

PATIENT COUNSELING INFORMATION

Advise patients to consult the Medication Guide on the safe use of Tracleer.

Important Information

• Monthly monitoring of serum aminotransferases

The physician should discuss with the patient the importance of monthly monitoring of serum aminotransferases.

• Pregnancy testing and avoidance of pregnancy

Patients should be advised that Tracleer is likely to cause birth defects based on animal studies. Tracleer treatment should only be initiated in females of childbearing potential following a negative pregnancy test. Females of childbearing potential must have monthly pregnancy tests and need to use two different forms of contraception while taking Tracleer and for one month after discontinuing Tracleer. Females who have a tubal ligation or a Copper T 380A IUD or LNG 20 IUS can use these contraceptive methods alone. Patients should be instructed to immediately contact their physician if they suspect they may be pregnant and should seek contraceptive advice from a gynecologist or similar expert as needed.

• Drug Interactions

The physician should discuss with the patient possible drug interactions with Tracleer, and which medications should not be taken with Tracleer. The physician should discuss the importance of disclosing all concomitant or new medications.

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