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Left Main Coronary Artery Angioplasty

ABSTRACT & COMMENTARY

As techniques, equipment, and adjuvant therapy have evolved in the 25 years since the first balloon angioplasty was performed, the application of percutaneous coronary intervention (PCI) has expanded widely. While once reserved for uncomplicated lesions in patients with single vessel disease and limited comorbidity, PCI is now performed in a wide variety of clinical and pathoanatomic scenarios. For example, the current generation of coronary stents, with the addition of atheroablative therapy, intravascular ultrasound imaging catheters, and glycoprotein IIb/IIIa inhibitors, in particular, have contributed to make previously high-risk, low success rate lesions, such as those with heavy calcium, large thrombus burden, eccentricity or tortuosity, safely approachable by the experienced interventionalist, even in the setting of acute myocardial infarction, multivessel disease, or severely reduced left ventricular systolic function. In contrast, the presence of left main coronary artery (LMCA) stenosis remains a relative contraindication to PCI in most clinical settings. In fact, the most recent ACC/AHA Guidelines for PCI,[1] list left main disease (particularly in the patient who is a candidate for coronary artery bypass graft surgery) as a class 3 condition for PCI (condition for which there is evidence and/or general agreement that the procedure is not useful/effective, and in some cases may be harmful) with level of evidence B (data derived from a single randomized trial or nonrandomized studies). However, despite these recommendations, there is some evidence that PCI of the unprotected LMCA might be effective and appropriate therapy in certain subsets of patients in need of coronary revascularization.

Tan and colleagues present the long-term results of the ULTIMA multicenter registry of patients undergoing unprotected LMCA PCI. This paper describes the outcomes of 279 consecutive patients between July 1993 and July 1998 at 25 high-volume clinical centers. Forty-six percent of these patients were believed to be inoperable or at high risk for poor surgical outcomes, and the majority of the remaining patients received PCI due to patient preference. Eighty nine (32%) patients were characterized as low risk, defined as age < 65 years, left ventricular ejection fraction (LVEF) > 30%, and

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absence of acute MI or cardiogenic shock. Of these, 65.2% of patients received stenting as primary therapy, and an additional 3.6% received stenting for a bailout indication. Almost 30% received atheroablative therapy (rotational atherectomy or directional atherectomy) and 46% of procedures were performed with intra-aortic balloon counterpulsation support. Of note, only 4.3% of patients received treatment with a glycoprotein IIb-IIIa inhibitor (abciximab).

Thirty-eight patients died in-hospital. At 1 year of follow-up, the rate of total mortality was 24%, cardiac death was 20%, MI was 9.8%, CABG was 9.4%, and repeat PCI was 24%. After the index hospitalization, the majority of adverse events occurred within the first 3 months of follow-up. By multivariate analysis, significant predictors of mortality were LVEF < 30% (hazard ratio [HR] = 4.21), severe mitral regurgitation (HR = 3.66), cardiogenic shock (HR = 3.56), creatinine > 2 mg/dL (HR = 3.1), and severe lesion calcification (HR = 2.32). In contrast, there were no in-hospital deaths among patients in the low-risk subgroup, the 1-year actuarial incidence of death was 3.4% and of MI was 2.3%, with no deaths or MI occurring beyond 4 months after hospital discharge. Among low-risk patients, repeat revascularization rates were comparable with 11.4% undergoing CABG and 20.4% undergoing repeat PCI within 1 year.

Tan et al comment that patient selection remains of utmost importance for both the surgeon and the interventional operator, but that the low-risk patients are likely to have good outcomes with either LMCA PCI or CABG. They conclude that, despite the limitations of a study based on a registry population, LMCA PCI might be considered in low-risk patients as already outlined, in addition to those patients deemed inoperable. Due to the clustering of adverse events early in the follow-up period, they also recommend routine surveillance angiography be performed in all patients at 2 and 4 months after LMCA PCI to evaluate for restenosis (Tan WA, et al. *Circulation*. 2001;104:1609-1614).

COMMENT BY SARAH M. VERNON, MD

PCI for LMCA disease remains controversial in part due to well-established data demonstrating survival benefit for patients with LMCA disease undergoing CABG, with overall low rates of in-hospital and 1 year mortality. In addition, earlier reports from the ULTIMA registry, raised concern because of high rates of procedural complications and early mortality.[2] However, as in the present report, these outcomes are at least in part attributable to extremely high-risk patient subsets including advanced age, acute MI, cardiogenic shock, and patients deemed to be inoperable, making comparison between the 2 methods of revascularization difficult, particularly for high-risk patients. In these patients, particularly those felt not to be surgical candidates, LMCA PCI, while high risk, remains by definition "the lesser of 2 evils." The present report suggests that, in lower-risk patients, PCI using more contemporary therapy (albeit infrequent use of platelet inhibitors) may represent a truly viable alternative to bypass surgery. Further evidence that PCI might be an acceptable approach in low-risk patients also comes from a recent publication by Park and associates, who report a 2-year survival rate of 97% and angiographic restenosis in 19% in 127 patients undergoing LMCA stenting.[3] They also suggest that angiographic outcomes can be optimized using IVUS guidance and atheroablative debulking prior to stent implantation. While it is unlikely that the use of LMCA PCI will ever be clearly established in a randomized clinical trial, accumulating evidence suggests that in time PCI may ultimately prove to be the procedure of choice in some subsets of patients with LMCA stenosis. ❖

References

1 Smith SC, et al. *J Am Coll Cardiol*. 2001;37:2215-2238.

2 Ellis SG, et al. *Circulation*. 1997;96:3867-3872.

3. Park S, et al. *J Am Coll Cardiol*. 2001;38:1054-1060.

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Interesting New Developments in Hypertension

ABSTRACTS & COMMENTARY

Synopsis: These studies call for trials to see whether pharmacologic treatment of high-normal blood pressure will reduce cardiovascular events.

Sources: Vasan RS, et al. *N Engl J Med.* 2001;345: 1291-1297; Panza JA. *N Engl J Med.* 2001;345:1337-1340; Staessen JA, et al. *Lancet.* 2001;358:1305-1315.

The framingham heart study investigators have reported on the relationship between gradations of normal blood pressure (BP) and cardiovascular events during long-term follow-up of a large cohort of the original subjects as well as participants in the Framingham Offspring Study, followed for up to 12 years. Subjects were stratified on the basis of optimal, normal, or high-normal BP. The results indicate that high-normal BP imparts significant risk, particularly in older men and women. A total of 6859 subjects were included in this observational report. Examinations were carried out every 2 years. Baseline BP was recorded at one of the Framingham biannual examination cycles. Based on JNC VI and WHO-ISH criteria, optimal BP was defined as less than 120/80; a normal BP as 120-129/80-84; and high-normal as 130-139/85-89 mm HG. Hypertension was defined as a BP of > 140/90 mm HG or use of antihypertensive therapy. The primary outcome was time to occurrence of cardiovascular death, myocardial infarction, stroke, or congestive heart failure during the 11- to 12-year follow-up. A variety of statistical methods were used, including separate tracking of subjects who progressed to higher levels of BP during follow-up, and calculation of a theoretical number needed to treat for 5 years to prevent one major event. At baseline, one third of the cohort had normal BP, one quarter had high-normal BP, and the rest had optimal BP levels. The high-normals were older, had higher cholesterol levels, and greater BMI than those with optimal BP.

Results: The mean follow-up was 11 years; 397 cardiovascular events were documented, of which approximately half were myocardial infarction. There was an increasing risk of cardiovascular events in the middle and highest categories of BP (*see Figure*). Furthermore, in subjects < 65 years of age with high-normal BP, the 10-year cumulative incidence of cardiovascular events was only 4% in women and 8% in men. In contrast, in those individuals between 65 and 90 years, the event rates were 18% in women and 25% in men (a 3- to 4-fold increase), confirming that advanced age plus high-normal BP is a particularly lethal combination. Compared to optimal BP, the high-normal cohort had an adjusted hazard ratio of 2.5 in women and 1.6 in men. The normal BP cohort had an adjusted hazard ratio of 1.5 for women and 1.3 for men. In individuals whose BP increased over follow-up, there was a greater risk of cardiovascular disease. Vasan et al estimated that the number needed to treat to prevent 1 cardiovascular event in older subjects ranges from 24-71 in men and 34-102 in women, substantially higher than in younger subjects. NHANES III and other data indicate that the prevalence of high-normal BP is comparable to that of mild hypertension in the United States. Thus, the findings indicate a continuous and increased cardiovascular risk across 3 nonhypertensive BP cohorts, more so in men than women. The 10-year absolute event rate in older subjects was > 20% in men and close to 20% in women, thus meeting criteria for moderate to high risk for primary prevention interventions. Vasan and colleagues call for clinical trials to see whether pharmacologic treatment of high-normal BP will reduce cardiovascular events. They emphasize that risk in the high-normal cohort may not be solely related to the BP levels, as other studies have shown increased carotid IMT and LV diastolic abnormalities in such individuals.

COMMENT BY JONATHAN ABRAMS, MD

In an accompanying editorial, Panza discusses the evidence for endothelial dysfunction in hypertensive patients, related to decreased nitric oxide availability and increased endothelin-1 levels. It is not known whether such abnormalities are present in individuals with high-normal BP, but based on the literature, it is likely that this is the case. Further, it is possible that many of the high-normal BP subjects have or are more likely to develop the insulin-resistance syndrome over time. The increase in other CAD risk factors, particularly higher cholesterol and BMI in the high-normal subjects, further confounds the issue. The issue of therapy for such individuals is speculative, but the Framingham observations are of real importance because of the clear and consistent gradient of increased cardiovascular end points as BP goes from the lowest to the highest levels, yet all within the normal range. This gradation of risk is similar to that with total LDL cholesterol levels, as well as glycemic control in diabetics. In all these conditions, less is more.

Another publication appearing in the *Lancet* examines the question as to whether sepecific pharmacologic

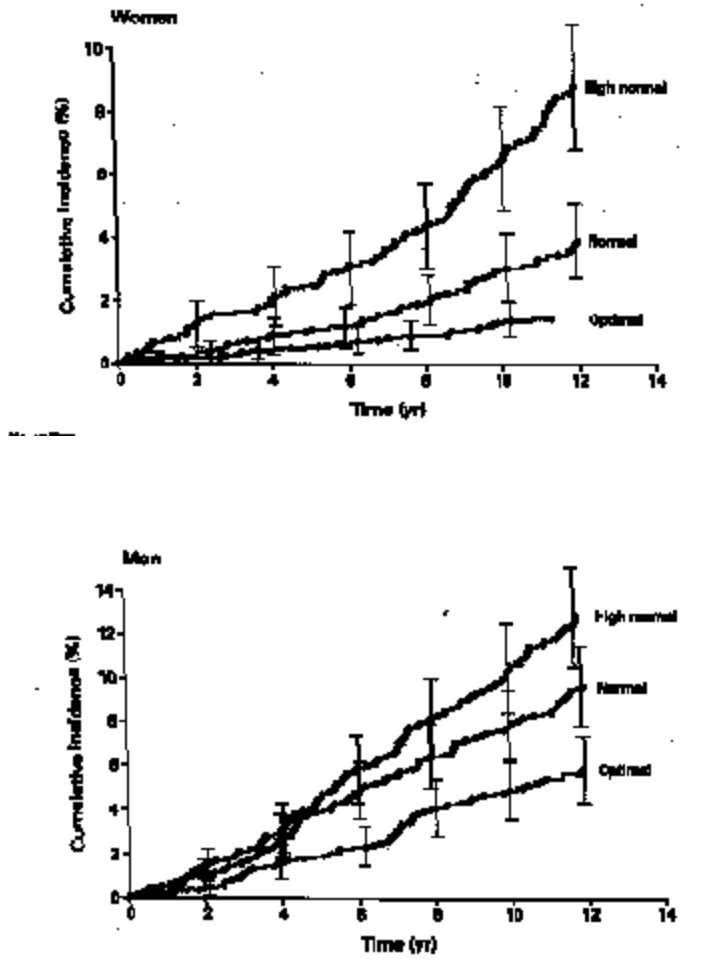
therapy for hypertension has salutary effects beyond BP lowering. This is a new meta-analysis of antihypertensive drugs from Belgium. The data focus on systolic BP in middle-aged and older individuals. Two different analyses were carried out. One compared outcome results in trials that used "old" agents, such as diuretics and beta blockers, with new agents, including calcium channel blockers (CCB), ACE inhibitors, and alpha blockers. Eleven trials were included. The second component was to examine the relationship between treatment groups and the corrected baseline BP differences, ie, was the effectiveness in reducing events in part related to non-BP lowering actions of a given class of therapy. A total of 27 studies were included in this meta-analysis, which compared older drugs to each other and newer classes compared to other newer compounds. The trials included more than 33,000 subjects randomly assigned old drugs and 29,000 given new drugs.

Results: 1) New antihypertensive drugs (CCB, ACE inhibitors) were as effective as older ones (diuretics, beta blockers) for prevention of cardiovascular death, stroke, fatal, and nonfatal myocardial infarction; 2) patients randomized to diuretics or beta blockers had similar outcomes to those receiving initial treatment with a CCB or ACE inhibitor; 3) overall risk of stroke was decreased with CCB, but CCB increased the risk of myocardial infarction; 4) in an analysis of the degree of BP reduction to cardiovascular end points, there was a reduction in events directly related to gradations of BP. Thus, BP differences during follow-up accounted for all differences in outcomes between treatments. Staessen and colleagues conclude that "results of outcomes trials for anti-hypertensive drugs can be explained by BP differences between randomized groups;" 5) all antihypertensive drugs had similar long-term efficacy and safety; 6) this analysis could not confirm that non-antihypertensive actions of various agents are of importance in influencing cardiovascular end points as opposed to the actual degree of BP lowering; the lower the BP, the greater reduction in cardiovascular complications.

Staessen et al point out that this relationship has been shown previously in isolated systolic hypertension, with substantial reductions in stroke and myocardial infarction attributable to relatively modest differences in BP reduction between groups. Even after adjustment for baseline BP, the conclusions remained the same. The analysis suggests that for all outcomes combined, a 5 mm HG difference in systolic pressure was clinically important. Furthermore, "all possible benefits" of therapy were seen at systolic BP gradients or differences of about 15 mm HG. (However, this degree of BP difference was achieved in only 4% of patients in the entire analysis). Staessen et al discuss the HOPE trial and the hypothesis of these investigators and others that the benefits from ramipril were unrelated to BP lowering; there was a 3.3 mm HG difference in systolic pressure between ramipril in HOPE and placebo. They conclude that BP lowering itself could have accounted for most of the benefits in HOPE in those allocated to ramipril. In summary, the conclusions of this "quantitative overview" of many thousands of patients suggests that CCB and ACE inhibitors are equally effective as diuretics and beta blockers in decreasing multiple fatal and nonfatal cardiovascular outcomes, and offer comparable protection. CCB appear to reduce the risk of stroke more than other agents but impart a lesser protection for

Figure

Cumulative Incidence of Cardiovascular Events Without Hypertension



Adapted from: *Vasan RS, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med. 2001;345:1291-1297.*

myocardial infarction. Similar conclusions have been made in 2 recently published meta-analyses of hypertensive therapy emphasizing CCBs.[1,2] Staessen et al stress that this analysis emphasizes "the desirability of BP control," and that any suggestion that a given class of drugs may have clinically relevant actions over and above BP lowering remains an unproven hypothesis.

■ COMMENT BY JONATHAN ABRAMS, MD

This is another significant contribution to the mega hypertension meta-analysis industry. The conclusions are concordant with other analyses, although this publication represents the largest number of patients analyzed (27 trials). As Staessen et al point out, the various published BP trials are disparate and not homogenous in design, use of statistical analysis, and methodology in measuring end points. Also, this meta-analysis uses combined or summary data; individual patient data were not entered, as is the case in a more formal meta-analysis. This may result in somewhat less reliability and validity. As in other meta-analyses, researchers pick and choose among the studies selected for analysis. The controversy about safety of calcium channel blockers will linger. It does appear, based on several different meta-analyses of contemporary antihypertensive therapy, that CCBs have a greater effect on lowering stroke rates than other agents but are less protective regarding reduction in myocardial infarction. This does not necessarily mean that CCBs are hazardous but may indicate only that they are somewhat less potent than other agents, particularly beta blockers and ACE inhibitors, in reducing infarction rates. This analysis strongly supports that the optimal BP lowering target is as low as is feasible without producing limiting side effects. One might not have thought small differences in mean systolic BP levels between 2 study cohorts, such as 2-5 mm HG, would have a significant effect on cardiovascular event rate gradients, but this appears to be the case. Thus, the arguments of Peter Sleight and the HOPE investigators that the modest BP differences in that study between ramipril and placebo are not important must be reconsidered in light of this meta-analysis. High-risk populations, such as the elderly (*see first review on page 91*), diabetics, and those with established vascular disease, are particularly vulnerable to the effects of hypertension. Such individuals demand even more vigorous and aggressive efforts to lower BP. In conclusion, more is better with respect to BP lowering. All commonly used agents are effective, well tolerated, and have excellent safety profiles. There is no excuse for physicians not to effectively use these data in daily practice. ❖

References

1. Lees, K, et al. *Lancet*. 2000;355:1949-1954.
2. Neoptolemos J, et al. *Lancet*. 2000;355:1955-1960.

Mechanism of Syncope in Patients With Bundle Branch Block

ABSTRACT & COMMENTARY

Synopsis: Intermittent AV block may occur in patients with pre-existing bundle branch block even if they have a negative electrophysiologic study.

Source: Brignole M, et al. *Circulation*. 2001;104: 2045-2050.

Brignole and colleagues, on behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators, describe the use of implantable loop recorders (ILRs) in patients with recurrent syncope, bundle branch block, and a negative conventional evaluation that included electrophysiologic (EP) studies. ISSUE is a multicenter, international, prospective study to determine the optimal methods for evaluating patients with syncope of uncertain origin. The data concern patients with a baseline bundle branch block in whom syncope was still suspected to be due to bradycardia despite a negative EP study. Patients could be entered into the trial if they had recurrent syncope. They underwent a careful history, physical examination, baseline ECG, carotid sinus massage, echocardiogram, 24-hour ambulatory ECG monitoring, and a complete EP study including atrial and ventricular stimulation. The criteria for a positive EP study were as follows: sinus bradycardia and an abnormal sinus node recovery time; a baseline HV interval 70 msec or greater; high degree His-Purkinje block after intravenous ajmaline, induction of sustained monomorphic ventricular tachycardia, or a supraventricular arrhythmia with hypotension. Patients also underwent a tilt-table study but because of the presence of bundle branch block, the tilt-table study results were not regarded as being adequate for diagnosis.

Patients who had completed these evaluations with no etiology for their syncope determined received an ILR (Reveal, Medtronic). They were then followed, and the results of monitoring are reported in this paper.

Fifty-two patients are included in the study. Their age was 71 ± 8 years and 33/52 were male. The mean QRS duration was 134 ± 18 msec. Twenty-eight of 52 had some form of associated heart disease. However, only 5 of 52 had an ejection fraction less than 40%. At baseline EP study, the mean HV interval was 55 ± 9 msec and the maximum HV interval after ajmaline infusion was 79 ±

19 msec. Tilt-table studies had been positive for hypotension in 7 of 51 but none had asystole or severe bradycardia.

An ILR-documented syncopal event occurred in 19 patients after a median of 48 days. One or more prolonged asystolic pauses attributed to atrioventricular (AV) block or sinus arrest were the most frequent findings observed in 17 patients. In 2 patients, only sinus rhythm or sinus tachycardia was documented at the time of syncope. In addition to these 19 patients, another 9 patients had clinical events during the study. Three patients developed persistent third-degree AV block without syncope; 3 patients had syncope but did not activate the ILR; 2 patients had AV block associated with presyncope and 1 patient died suddenly during a medical procedure after he developed atrial fibrillation that progressed to bradycardia.

AV block was the most frequent finding at the time of recurrent syncope. The actuarial estimates of AV block occurrence were 24%, 34% and 34% at 3, 9, and 15 months' follow-up, respectively. Tilt-table testing results were not predictive of bradyarrhythmias. Three of the 15 patients with AV block and 1 of the 4 patients who had sinus arrest associated with syncope had manifest hypotension without bradycardia during their tilt-table study. No other clinical finding or test results predicted the occurrence of AV block during follow-up. Brignole et al conclude that intermittent AV block may occur in patients with preexisting bundle branch block even if they have a negative EP study. An ILR-based strategy seems a safe and appropriate approach for documentation of the need for pacing in these patients.

■ COMMENT BY JOHN P. DiMARCO, MD, PhD

Recurrent unexplained syncope is often a frustrating condition to evaluate, and this becomes particularly true when it occurs in patients with baseline conduction defects. It was recognized many years ago that pacemaker therapy often failed to prevent recurrent syncope in such patients, and guidelines were developed to prevent the overuse of pacemakers. These guidelines were based on longitudinal studies of patients with bundle branch blocks but without syncope or other symptoms. These studies showed that the rate of progression to clinical AV block was slow in such patients. In addition, it was recognized that patients with bundle branch block were also likely to have ventricular arrhythmias or even supraventricular arrhythmias as the cause of syncope. Unfortunately, the data presented in this paper by Brignole et al illustrate how little we know about the development of AV block in patients with bundle branch block.

A few comments should be made about Brignole et al's methodology. In this paper, they considered patients to have positive EP studies if they manifest inducible ventricular or supraventricular tachyarrhythmias or an HV interval of greater than 70 msec. An HV interval longer than 70 msec was considered an indication for pacing in these patients with recurrent syncope. In the new ACC-AHA guidelines for pacemaker implantation,[1] however, only the finding of an HV interval greater than 100 msec was an indication for pacing. This is an extreme value that is rarely seen in patients unless they have had documented AV block. Several years ago, Englund and associates also reported that programmed ventricular stimulation in patients with bifascicular block could also be only a nonspecific finding.[2] Therefore, significant questions still remain about the value of EP study in these patients.

The current paper is part of a large international study on syncope. When the final study results are reported, it would be interesting to see how many patients fell into in which of Brignole et al's 4 classifications. Data from this study should clarify the optimal approaches for diagnosis in patients with different clinical characteristics and presentations. ❖

References

1. Gregoratos G, et al. *Circulation*. 1998;97:1325-1335.
2. Englund A, et al. *J Am Coll Cardiol*. 1995;26: 1508-1515.

In-Hospital vs. Out-of-Hospital Nonsustained Ventricular Tachycardia

ABSTRACT & COMMENTARY

Synopsis: The setting in which nonsustained VT is identified is an important diagnostic factor and is associated with a greater likelihood for inducing sustained ventricular tachycardia and lower overall survival.

Source: Pires LA, et al. *J Am Coll Cardiol.* 2001;38: 1156-1162.

The multicenter unsustained tachycardia trial (MUSTT) was a study designed to evaluate the predictive value of electrophysiologic (EP) studies and the efficacy of EP-guided therapy in post-MI patients with low ejection fractions and nonsustained ventricular tachycardia (VT). In this report, Pires and colleagues describe the influence of the clinical setting (in-hospital

vs out-of-hospital) during which the index episode of nonsustained VT was recorded on the inducibility of VT, the rates of arrhythmic events, total mortality, and the effects of treatment. For the purpose of this paper, enrolled patients were classified as "in-hospital" if their nonsustained VT for entry into the trial had been recorded on hospital telemetry, and as "out-of-hospital" if it had been documented during an outpatient ambulatory electrocardiogram. Cumulative event rates were estimated using the Kaplan-Meier method. Estimated relative risks were expressed as hazard ratios based on the Cox proportional hazards model.

A total of 2202 patients were enrolled in MUSTT, and data regarding the clinical setting in which the index nonsustained VT was documented were available for 2190 of these patients. Of this latter group, 1631 (74.5%) were classified as "in-hospital" patients and 559 (25.5%) were classified as "out-of-hospital" patients.

There were many differences between the out-of-hospital and the in-hospital groups. The in-hospital group was slightly older and included a higher proportion of non-Caucasians. The mean cycle length of nonsustained VT was slightly shorter (410 vs 440 msec), and of longer mean duration (5 beats vs 4 beats) in the in-hospital group. In-hospital patients were more likely to have 2- and 3-vessel coronary disease, a myocardial infarction within either 1 month or 1 year, a history of congestive heart failure, and class III New York Heart Association Functional Class. Thirty-eight percent of the patients in the in-hospital group had an inducible VT vs. 32% of the patients in the out-of-hospital group. Event rates during follow-up were first analyzed among the untreated patients. The 2- and 5-year rates for cardiac arrest or arrhythmic death were 14% and 28% among in-hospital patients and 11% and 21% for out-of-hospital patients. Total mortality rates at 2- and 5-year follow-ups for the 2 groups were 24% and 48% for the in-hospital group and 18% and 38% for the out-of-hospital group. Rates for cardiac arrest or arrhythmic death and overall mortality were then adjusted for multiple risk factors. The adjusted hazard ratio was 1.24 for the in-hospital group vs. the out-of-hospital group for both arrhythmic events and total mortality.

Pires et al conclude that the setting in which nonsustained VT is identified is an important diagnostic factor. It is associated with a greater likelihood for inducing sustained VT and lower overall survival. Clinical factors that led to the initial hospitalization, however, explained much of these differences.

■ COMMENT BY JOHN P. DiMARCO, MD, PhD

In 2 previous reports, the MUSTT investigators have described a benefit of implantable cardioverter defibrillator (ICD) therapy in patients after myocardial infarction with depressed left ventricular ejection fractions and nonsustained VT and slightly higher rates of arrhythmic events and death among untreated patients based on ability to induce VT.[1,2] This follow-up analysis of the MUSTT database points out that the MUSTT study patients often had their nonsustained VT detected in-hospital during an admission for another cardiac or noncardiac condition. Patients who require hospitalization are usually at higher risk for future events than are stable outpatients. This study therefore supports other trials that have shown the greatest benefit of therapy in highest-risk patients. These include patients with advanced age, the lowest ejection fractions, and the most severe congestive heart failure. The data also argue against the value of periodic ambulatory ECG screening in out-patients who are otherwise doing well. These patients would have a lower probability of having an inducible VT and a lower event rate whether they had inducible VT. ❖

References

1. Buxton A, et al. *N Engl J Med*. 1999;341:1882-1890.
2. Buxton A, et al. *N Engl J Med*. 2000;342:1937-1945.

Blood Transfusion in Acute Myocardial Infarction

ABSTRACT & COMMENTARY

Synopsis: Blood transfusion is associated with a lower short-term mortality in elderly patients with acute myocardial infarction and hematocrit < 30%.

Source: Wu WC, et al. *N Engl J Med*. 2001;345: 1230-1236.

There is little objective evidence concerning when to transfuse blood in patients with acute myocardial infarction. Thus, Wu and associates examined the Cooperative Cardiovascular Project database of 78,974 medicare beneficiaries aged ≥ 65 years who were hospitalized for acute myocardial infarction to assess the prognostic importance of anemia and the effect of transfusion. In this cohort, 43% had a low hematocrit (< 39%), and, in general, they had more comorbidities compared to those with normal hematocrits. Also, they had more complications and progressively higher mortality as the hematocrit fell. Only 5% of the total cohort received a transfu-

sion, and transfusion was more likely the lower the hematocrit. Transfusion was associated with a lower 30-day mortality in patients with hematocrits below 33%, but a higher mortality if the hematocrit was above 36%. Subgroup analysis among patients who survived at least 2 days showed that there was no mortality benefit of transfusion with hematocrit values > 30%. Wu et al concluded that blood transfusion is associated with a lower short-term mortality in elderly patients with acute myocardial infarction and hematocrit < 30%.

■ COMMENT BY MICHAEL H. CRAWFORD, MD

The most striking finding in this study was the high prevalence of anemia in this elderly, acute myocardial infarction population. Almost half had hematocrits below 39% and one tenth were below 33%. Also, low hematocrit was associated with a higher mortality at 30 days (*see Table 1*).

Table 1

30-Day Mortality by Hematocrit Range

Hematocrit	5-24%	24-27%	27-30%	30-33%	33-36%	36-39%
Mortality	39%	35%	36%	30%	26%	21%

In those patients who were not transfused with a hematocrit < 27%, the mortality was near 50%. Naturally, those with anemia had significant comorbidities, so it could be argued that anemia was just a marker for a more ill individual who was not going to do well postinfarction. However, if this were the case, one would not expect the excellent results of transfusion. Relative risk of death in 30 days was significantly reduced by transfusion for hematocrits below 33% even when adjusted for other clinical factors (*see Table 2*).

Interestingly, at hematocrits > 36% relative risk of death actually increased in those transfused.

The major problem with this report is that it is a retrospective, observational study in which only one quarter of patients with hematocrits < 33% got transfusion.

On the other hand, this rate falls within the range in other studies of 0.2-27%. Also, two thirds of the patients in the original database were excluded for a variety of reasons. This figure is actually low for this type of study, in which 95% often are rejected. In addition, it is not known if these results are transferable to younger patients with less comorbidities. Such patients may be able to tolerate a lower oxygen carrying capacity of the blood and could derive less benefit from transfusion.

Table 2

Relative Risk of Mortality by Initial Hematocrit Range in Transfused vs. Untransfused Patients

	5-24%	24-27%	27-30%	30-33%	33-36%	36-39%
Unadjusted	.37	.42	.49	.62	1.01	1.43
Adjusted	.31	.48	.54	.64	1.05	1.25

The low rate of transfusion is undoubtedly due to the almost complete lack of data in this situation. Older studies of hospitalized patients in general suggested that adverse clinical events do not occur more frequently until the hematocrit is below 27%. Some guidelines acknowledge that patients with coronary occlusions may need more blood cells, and suggest a cut-off of 30% in the acute myocardial infarction setting. The latter expert opinion comes close to the data presented in this study. Wu et al recommend transfusion for hematocrits < 30%, but the accompanying editorial urges transfusion at 33% or less.[1] Despite this study's flaws, it is valuable to have a definite cut-off point to confidently tell our patients and colleagues when the acute myocardial infarction patient needs a blood transfusion. ❖

Reference

1. Goodnough LT, Bach RG. *N Engl J Med*. 2001;345: 1272-1344.

CME Questions

23. Blood transfusion should be considered in elderly acute MI patients if the hematocrit is:

a. < 39%.
b. 36-39%.
c. 33-36%.
d. < 33%.

24. Syncope in patients with bundle branch block and a negative evaluation including electrophysiologic studies is usually due to:

a. sinus arrest.
b. high-grade AV block.
c. supraventricular tachycardia.
d. a and b

25. The detection of nonsustained VT in the hospitalized patient vs. an outpatient:

a. is benign.
b. has a worse prognosis.
c. is usually due to drug toxicity.
d. is an indication for ambulatory ECG monitoring.

26. A progressive gradation in risk of cardiac events over the high-normal to abnormal range has been shown for:

a. blood pressure.
b. LDL cholesterol.
c. blood glucose.
d. All of the above