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To cut CHF, caregivers should get a handle on hypertension

Get aggressive; treat to goal, experts say

(Editor's note: This is the first of a two-part series on managing hypertension. This month, we will examine the problems associated with hypertension and CHF. Next month, we'll learn techniques and treatment options for dealing with hypertension and CHF. Our series will incorporate current medication options, alternative therapies, and suggestions on tailoring patient education programs to specific patient groups.)

As a health care professional, you know that hypertension is the most common reason for a patient to visit a doctor; it affects more than 50 million Americans; and it's a major risk factor for stroke, kidney disease, and of course, heart disease, including CHF.

But you may not know that hypertension is largely to blame for the increase in CHF in recent years. Only about one-fourth of hypertensive patients have their blood pressure adequately controlled, and the problem will only get worse as improving life expectancy increases the number of elderly people in the United States.

Hypertension is a huge problem, and it's specifically the caregiver's responsibility to handle it. Getting blood pressure rates controlled to below 140/90 mm Hg is one of the few ways to make a positive impact on CHF, experts say.

KEY POINTS

- Hypertension is largely to blame for the increase in CHF in recent years.
- To reduce CHF, work to get patients' blood pressure to the goal level of 130/85 mm Hg or better.
- Evidence suggests that systolic hypertension is more important than diastolic in predicting cardiovascular disease.

But according to the Bethesda, MD-based National Heart, Lung and Blood Institute (NHLBI), which supplied those statistics, dramatic improvements in the treatment of hypertension seen from 1976 to 1991 have slowed and even decreased. During that period, the percentage of patients who were aware of their high blood pressure rose from 51% to 73%, and treatment increased from 31% to 55%, according to the National Health and Nutrition Examination Survey (NHANES).

> *"Hypertension control in the United States is abysmal. . . . We are only controlling 16% of hypertensive patients despite the fact that we have in excess of 100 drugs for treating this disease."*

The number of patients with high blood pressure controlled to below 140/90 mm Hg rose from 10% to 29%. The next round of NHANES, in 1994, found those numbers slipping: Only 68.4% were aware they had hypertension, 53.6% were being treated, and 27.4% were being controlled.[1]

A recent Mayo Clinic study found that downward trend continuing in a community that is socioeconomically prosperous with easy access to both primary and tertiary medical care. Out of 636 randomly selected Olmsted County, MN, residents studied, 53% had hypertension, 39% were unaware of that fact, and only 16% were being treated and controlled.[2]

"We are seeing a definite leveling off, even a deterioration, in our level of awareness, treatment, and control of hypertension, possibly because we aren't paying enough attention to it," says **Irene Meissner**, MD, the researcher who led the study and a neurologist at the Mayo Clinic in Rochester, MN.

"This suggests that instead of making progress in combating the health threat posed by high blood pressure, we may actually be backsliding. People aren't as aware as they should be, and control rates are quite low. This is happening despite solid clinical evidence that proper detection and treatment can dramatically reduce the number of deaths and disabilities caused by uncontrolled high blood pressure," she adds.

The trend is even worse when you consider that the NHANES surveys define adequate control as less than 140/90 mm Hg, while the current report from the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) recommends 130/85. Also, the NHANES surveys don't include people over age 75, the most rapidly growing segment of hypertensive patients, says hypertension expert **Joel Neutel**, MD.

Neutel is chief of clinical pharmacology and hypertension at the Veterans Affairs Medical Center in Long Beach, CA, and assistant clinical professor of medicine at the University of California, Irvine. When the over-75 age group is included, the control rate for U.S. hypertensive patients drops from 27% to 16%.

"Hypertension control in the United States is abysmal, and we are amongst the very best in the world," Neutel says. "We are only controlling 16% of hypertensive patients despite the fact that we have in excess of 100 drugs for treating this disease."

He points out that the CHF problem will only get worse since there are more hypertensive people in general, more older hypertensive people, and more survivors of heart attacks. "In order to make an impact on congestive heart failure, we have to take a much more preventive kind of approach," he says.

"Heart failure is a difficult disease to treat, and certainly, it's not a disease we can cure. We can only try to control it. The essence of treating congestive heart failure is to protect patients from developing the actual disease process of which heart failure is a consequence. Blood pressure control is the most important thing we can do to protect people from developing heart failure," explains Neutel.

It's not enough just to treat hypertension; you have to make sure the treatment is dropping the

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patient's blood pressure to the goal level of 130/85 or better to prevent stroke, preserve renal function, and prevent or slow the progression of heart failure, Neutel says. "Treated but uncontrolled hypertensive patients remain at risk for cardiovascular disease.

"It's not a golden bullet that if you treat hypertensive patients you'll completely protect them from developing heart disease. The vast majority of hypertensive patients who develop cardiovascular disease have diastolic blood pressure somewhere between 90 and 104 and systolic blood pressure between 130 and 160. It's not OK to accept inadequate control. We have to control them to the levels that we know are cardioprotective," he says.

Focus on systolic hypertension

Not only do physicians need to treat to goal, but they need to make sure they don't ignore the systolic pressure, many experts say. Diastolic pressure accurately predicts heart disease and stroke risk in younger patients but doesn't do as well with the elderly. There is overwhelming evidence to suggest that systolic hypertension is more important than diastolic in predicting cardiovascular disease, Neutel says.

"For all these years, we've really focused on diastolic blood pressure," he says. "Now that we have much more older patients who predominantly have systolic blood pressure, we've learned how important systolic is. If you bring systolic blood pressure down, that is associated with a dramatic impact on heart disease."

The JNC-VI guideline stresses this point, and recent studies underscore the risks of ignoring the systolic reading. New evidence from the NHLBI's Framingham Heart Study[3] found that systolic blood pressure — far more than diastolic blood pressure — identifies patients with hypertension, determines their blood pressure stage, and indicates the need for treatment.

Researchers found that systolic pressure alone correctly classified the JNC-VI blood pressure stage in about 96% of patients, compared to 68% using the diastolic pressure alone. In patients over age 60, the systolic pressure correctly classified 99% of patients, compared to 47% using diastolic alone.

Several studies presented at the American College of Cardiology's 49th Annual Scientific Session held in March in Anaheim, CA, also focused on systolic pressure. One study from the University of California, Irvine examined the relative importance of the individual components of blood pressure in determining cardiovascular risk in more than 6,700 men and women in the Framingham Heart Study.

The researchers found that with age, the best predictors of cardiovascular risk shift from diastolic to systolic as well as to pulse pressures, perhaps because those are indicators of large vessel stiffness.[4]

A second related study[5] presented at the conference found a more accurate way of using blood pressure to assess risk: tracking naturally occurring changes in diastolic and systolic blood pressure over a long period of time.

Researchers put two cohorts of men (15,561 men ages 20 to 82 and 6,246 men ages 42 to 53) into groups according to changes in their blood pressure, then kept track of deaths in each group for up to 17 years. Men with an increase in systolic and decrease in diastolic blood pressure had twice the risk of dying of cardiovascular disease than men whose blood pressure remained unchanged.

A third study[6] found that most older patients with high blood pressure have higher than normal readings of systolic pressure but normal diastolic readings, challenging assumptions that high diastolic pressure is the more pervasive problem among people with high blood pressure.

Traditional focus is on diastolic data

The researchers analyzed blood pressure data on nearly 20,000 patients who took part in NHANES III. They found that 80% of participants over age 50 who had hypertension had systolic readings higher than 140 but had diastolic pressures below 90. Three-fourths of both treated and untreated hypertensive patients were more than 50 years old; only 26% were less than age 50. In both untreated and treated patients over age 50, there was a greater prevalence of systolic than diastolic hypertension.

Pablo LaPuerta, MD, one of the researchers on the NHANES study, says physicians have traditionally focused on diastolic blood pressure because the first clinical trials on hypertension recruited patients based on diastolic readings and because increasing systolic pressures had been thought to be a natural part of the aging process that couldn't be controlled. But in the last four

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Don't pick doxazosin for first-line therapy

Physicians should carefully reassess the use of the alpha blocker drug doxazosin for the treatment of hypertension, say researchers. A large clinical trial has found patients taking the drug were twice as likely to be hospitalized for CHF as those taking a diuretic.

The trial's sponsor, the Bethesda, MD-based National Heart, Lung and Blood Institute, halted the doxazosin arm in March after investigators announced that the approximately 9,000 study participants who took doxazosin had 25% more serious complications from hypertension than the group taking the diuretic chlorthalidone.

The risk of developing CHF was 1% per year in the diuretic group and doubled to 2% per year for those in the doxazosin group, says **Curt Furberg**, MD, PhD, chairman of the study's steering committee from Wake Forest University Baptist Medical Center in Winston-Salem, NC.

The study, known as ALLHAT (Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) is the largest ever to compare the efficacy of newer drugs against the standby diuretics for the treatment of hypertension. More than 42,000 high-risk antihypertensive patients at 623 clinical sites in the United States, Puerto Rico, the Virgin Islands, and Canada are participating to see if the drugs reduce the incidence of coronary artery disease.

In addition to doxazosin (Cardura, Pfizer Inc., New York City), ALLHAT is also looking at the calcium antagonist amlodipine (Norvasc, Pfizer) and the ACE inhibitor lisinopril (Prinivil, Merck & Co., Whitehouse Station, NJ, and Zestril, AstraZeneca Pharmaceuticals, Wilmington, DE). Only the doxazosin portion of the study will stop.

A total of about 900 patients developed heart failure during the study, Furberg says. "It's not clear why there was an increased risk of heart failure. This was a surprise finding. Right now, one can only speculate."

After the researchers presented their findings[1] at the American College of Cardiology's 49th Annual Scientific Session in March in Anaheim, CA, the organization issued a clinical alert on alpha blockers for hypertension that urged physicians to reassess their use of doxazosin.

"The diuretic remains the drug of choice because it's effective, safe, and cheap," he says. "ALLHAT is a test to see how newer, much more expensive drugs compare to standard treatment with diuretics. One drug lost, and on the other two, we'll have to see. Until we have that information, the diuretic is the drug of choice."

Furberg says that Cardura was shown to be inferior overall to chlorthalidone, a cheaper drug, for hypertension control, drug compliance, and reduction of cardiovascular complications. Cardura should be at the bottom of the list of drugs from which physicians choose to treat hypertension, he says. It should not be considered as first-line therapy for hypertension.

"Heart failure is the most common reason for hospitalization of older people, and it's the most costly. This is serious. You don't want to double the risk and pay 10 times more for it," he adds.

The drugs in the study were similarly effective in preventing heart attacks and in reducing the risk of death from all causes; the heart failure outcome was the only major difference.

"The assumption has been, for quite a while, that the entire benefit of blood pressure lowering drugs is lowering blood pressure, but that is not the case anymore," Furberg says. "We have more and more data showing that drugs have other effects. There must be some other mechanism at work because of the difference in heart failure. We are beginning to understand more and more that we can't look at blood pressure reduction and say we know all the clinical effects. It varies with the drugs."

Patients in the doxazosin group had slightly higher systolic blood pressures than the chlorthalidone group, although the diastolic pressures were the same. The doxazosin group also had poorer compliance with treatment. Only 75% were still on the drug or another alpha blocker after four years, compared with 86% still taking chlorthalidone or another diuretic.

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years, the clinical evidence has been mounting that systolic blood pressure shouldn't be ignored.

"Systolic blood pressure increases with age so a lot of patients in their 70s and 80s have hypertension," says LaPuerta, who is a clinical assistant professor at the Robert Wood Johnson Medical School and director of outcomes research at the Bristol-Myers Squibb Pharmaceutical Research Institute in Princeton, NJ. "We found in this study that patients with isolated systolic hypertension are frequently very far from their target blood pressure goals, as much as 15 mm to 20 mm or more from their target goal. Most medications can't lower systolic blood pressure to that degree."

The researchers concluded that selection and treatment biases favored diastolic blood pressure and that greater efforts must be made to identify and effectively monitor treatment regimens in high-risk patients.

One of the problems with treating that population is that many of them don't even know they need help. A survey of 1,500 Americans over age 50, which was released in March by The National Council on Aging, found that nearly half did not know their own systolic and diastolic blood pressure. Sixty-nine percent said they had not discussed the physical consequences of high blood pressure with a doctor or nurse in the past year, and only 27% knew the importance of the systolic number as an indicator of high blood pressure. Forty-six percent incorrectly believed that stress is the main cause of high blood pressure.

Manage hypertension and CHF

It's not an easy task to manage elderly patients with systolic hypertension, but those are exactly the people who need help, says **Martin LeWinter**, MD, a cardiologist with a special interest in CHF. LeWinter is professor of medicine and director of the cardiology unit at the University of Vermont College of Medicine and Fletcher Allen Health Care in Burlington. "There needs to be more emphasis on controlling blood pressure to prevent heart failure in elderly people with systolic hypertension."

LeWinter says management of heart failure is much easier when the blood pressure is down and that it's fairly easy to achieve that goal for the 60% or so of CHF patients with decreased ejection fraction. "There are well-publicized guidelines for treating those patients, and those treatments — ACE inhibitors, diuretics, beta-blockers — will almost always control blood pressure also.

"But patients with normal ejection fraction are frequently the elderly patients with systolic hypertension who tend to get acutely ill with heart failure. With that group, there are no large studies available to guide therapy," LeWinter says.

"The importance of the group has been slow to get out there. People are somewhat reluctant to treat hypertension in older folks because they are more concerned about side effects. But you need to tailor the therapy to the older patient and find drugs they can tolerate," he adds.

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CHF drug trials are highlight of ACC 2000

Omapatrilat looks promising

The results of two separate late-breaking CHF-related clinical trials presented at the American College of Cardiology's 2000 meeting held in March in Anaheim, CA, found no benefit in either of the drugs studied. But a third presentation comparing the investigational drug omapatrilat with lisinopril found that the new drug appears to be more effective in preventing death or hospitalization in CHF patients.

PRAISE-2 (Prospective Randomized Amlodipine Survival Evaluation), presented by **Milton Packer**,

MD, of Columbia University College of Physicians and Surgeons in New York City, did not confirm the survival benefit of the calcium channel blocker amlodipine seen in nonischemic cardiomyopathy in the PRAISE-1 trial.

Packer said in his presentation that there was one significant benefit from PRAISE-2, and that was to emphasize the need for replication, even when the results of a trial define a mortality benefit and are associated with low P values.

David Roffman, PharmD, BCPS, associate professor in the University of Maryland School of Pharmacy in Baltimore, agrees with Packer that there is an important lesson to be learned from the trial. "PRAISE-1 basically gave some hint that nonischemic cardiomyopathies might benefit from calcium channel blockers," Roffman explains to *CHF Disease Management*.

"What often happens is that people implement that kind of data in their clinical practice before the definitive trial, like PRAISE-2, has the chance to be done. I think that's an important lesson for people not to run with the results of preliminary data until the definitive data are in. The PRAISE-2 trial demonstrates that really nicely."

PRAISE-2 was conducted as a follow-up to test a hypothesis generated by PRAISE-1 that amlodipine could prolong life in patients with nonischemic cardiomyopathy. In PRAISE-1, all-cause mortality was reduced by 46%. PRAISE-2 enrolled 1,652 patients by January and found that there were no significant differences in all-cause mortality between the two arms of the study (31.7% in placebo and 33.7% with amlodipine).

The combined results of PRAISE-1 and PRAISE-2 show that long-term treatment with amlodipine is neither beneficial nor harmful in patients with severe chronic heart failure, Packer said in his presentation. The favorable survival benefit of amlodipine seen in PRAISE-1 was most likely due to chance, he said.

OPTIME-CHF, a study presented by **Mihai Gheorghiade**, MD, of Northwestern University in Evanston, IL, found that an infusion of intravenous milrinone had few beneficial effects in hospitalized patients with CHF. Milrinone did not cut hospital days or mortality, and the results showed milrinone should not be incorporated as routine therapy for all patients admitted with CHF.

OPTIME-CHF (The Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure) was designed to look for a new indication for milrinone by examining the role of the drug in patients hospitalized with CHF who would not normally receive this therapy.

A total of 951 patients were randomized within 48 hours of admission to intravenous milrinone. Patients had to have ejection fraction of less than 40%, chronic heart failure, no myocardial infarction, no significant hypertension or hypotension, and no need, in the opinion of the investigator, for milrinone therapy. But at 60 days, there was no significant difference in hospital days or mortality (35% event rate) between the placebo and milrinone groups.

"In effect, the study is not changing current practice," Gheorghiade explains. "The importance of this study is that it is the first large trial that is placebo-controlled and randomized to be conducted in this patient population.

> *"The major implication of these trials is that this new agent may be better than the gold standard for heart failure treatment, the ACE inhibitor."*

"Although we have 1.5 million admissions for heart failure per year in the United States, there have been no studies to address this population. It's really interesting how there are so many studies for acute MI, one after another, but none for heart failure. I hope many more studies will come on how to manage, how to develop a strategy in patients admitted with exacerbation of their heart failure," he says.

Mike Cuffe, MD, an OPTIME researcher from Duke University in Durham, NC, says a lot of people were very optimistic that the trial, the largest ever done with milrinone, would show a reduced length of stay.

"There's enormous pressure in health care right now to find strategies to improve outcomes and simultaneously reduce length of stay and cut costs," Cuffe says. "We were pleasantly surprised that the drug appeared safe but disappointed that it didn't appear to have efficacy in this broader population."

A third study[1] to come out of the annual meeting that has implications for CHF treatment is one on the investigational drug omapatrilat, a member of a new class of cardiovascular medications called vasopeptidase inhibitors.

These drugs simultaneously inhibit two key enzymes that regulate heart function and blood pressure — neutral endopeptidase and angiotensin-converting enzyme.

A combined analysis of two Phase II studies comparing omapatrilat with the ACE inhibitor lisinopril found that the new drug was more effective in preventing death or hospitalization in the 1,242 participating CHF patients.

The relative risk of the combined endpoint of death or hospitalization was 78% with omapatrilat and 95% with lisinopril. Both drugs were well-tolerated.

"Omapatrilat is the first and most clinically advanced vasopeptidase inhibitor," says **John Kostis**, MD, principal investigator of the study and chair of the department of medicine at the University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School in New Brunswick, NJ. "The major implication of these trials is that this new agent may be better than the gold standard for heart failure treatment, the ACE inhibitor."

Other studies are ongoing to compare omapatrilat with enalapril and to evaluate the drug's efficacy in treating patients with isolated systolic hypertension. The drug is under priority review at the U.S. Food and Drug Administration. Princeton, NJ-based Bristol Myers-Squibb, which is marketing omapatrilat under the name Vanlev, expects a decision by June 20.

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Beta-blockers are not so bad after all

Study shows one drug reduces death by 34%

Contrary to conventional wisdom, certain beta-blockers actually ease the symptoms of patients in heart failure.

Rather than worsening patients' conditions, these medications helped reduce the need for hospitalization — and in a number of cases — extended lives.

A new international study, which specifically involved the beta-blocker metoprolol, followed 3,991 heart failure patients in the United States and thirteen European countries for one year. In June, researchers reported that the drug reduced deaths by 34%. Those findings sharply contradicted the longstanding belief that, because they slow down the heart rate, beta-blockers, in general, should be judiciously avoided in treating heart failure.

As a result of the study's findings as well as those of similar studies, the American Heart Association plans to update its treatment guidelines to include recommendation of beta-blockers' use for most heart failure patients, says **Sharon Hunt**, MD, a Stanford University cardiologist in Palo Alto, CA, and chairwoman of the updating committee.

Sidney Goldstein, MD, co-author of the study and a cardiologist at Henry Ford Hospital in Detroit, has long been a proponent of beta-blockers' use in treating heart failure. He was the principal investigator in the Beta Blocker Heart Attack Trials, published in the *Journal of the American Medical Association* in the early 1980s.

"What's most significant is that it illustrates the major impact metoprolol has in treating sudden death, which represents about two-thirds of the mortality rate of heart failure patients," Goldstein says. From that standpoint, the drug is superior to ACE inhibitors, mainstays in heart failure treatment, which, although successful in reducing symptoms, do little in terms of modifying the sudden death rate, he adds.

Hospitalizations reduced by one-third

The study was funded by Wilmington, DE-based Astra Zeneca, manufacturers of metoprolol, which is sold in the United States under the name Toprol XL. The study was led by **Ake Hjalmarson**, MD, of Sahlgrenska University Hospital in Gothanburg, Sweden. Of the patients followed, all were given conventional medication. Metoprolol, in an extended-release form, was administered to about a half, and the rest received a placebo.

Along with a significant reduction in the number of deaths, there were about a third fewer hospitalizations in the beta-blocker group. In addition, symptoms improved in 28% of the group treated with beta-blockers, compared with 25.8% of the

placebo group, and 50% of the beta-blocker group reported feeling better.

"Twenty years ago, the common wisdom was that beta-blockers were the worst thing you could possibly use in a failing heart. Now, rather than being looked at as last-ditch, experimental, or cutting-edge therapy, they're considered a standard, routine treatment that should be used in most cases of heart failure," says **Robert E. Safford**, MD, professor of medicine and chairman of internal medicine at Mayo Clinic in Jacksonville, FL.

One reason acceptance of the drugs in the United States has been slow in coming is that, initially, they were available only in doses that were too strong for heart failure patients just beginning to take the drug to tolerate, he says. Even though they were directed to break the pills into quarters, "Unless a pill is scored, when you try to break it, it turns to dust. So first, pharmaceuticals had to develop a pill with a dosage low enough to be tolerated by people in heart failure," Safford says.

Slowing down the 'revs'

But the primary reason for their belated endorsement was the concern that beta-blockers would reduce the heart rate to a level so low that it could prove fatal for patients who already were in a debilitated condition.

"Looking at the heart as a pump, the thinking was, 'If you slow it down, it's going to pump even less effectively.' But, as it turns out, sometimes the heart [can] get in trouble from overstimulation. If, for example, it's beating at 120-130 beats per minute, sometimes, to use the analogy of a automobile engine, it is better to put a 'rev' limit on it, of 90-100 beats per minute," says **Charles Inman Wilmer**, MD. Wilmer is director of angioplasty, cardiac disease specialist, and director of data management at the Fuqua Heart Center of Piedmont Hospital in Atlanta.

There are, of course, patients for whom beta-blocker therapy is too risky — such as those with a tendency to wheeze, or those with severe bronchospasms or asthma, he says.

"Patients with the fastest heart rate may have the worst cardiomyopathy and therefore be unable to tolerate them. In addition, those with the most severe heart failure, either because their heart doesn't squeeze well or their blood pressure is too low, cannot tolerate them. . . . More likely are patients with mild to moderate heart failure, and those who are more tachycardic," Wilmer explains.

"If their blood pressure [has] fallen, they'll need to decrease their dosages of diuretics or ACE inhibitors," says Safford, adding that as the beta-blocker dosage is gradually increased over several months, with adjustments every couple of weeks, close contact with the physician should be maintained.

As it takes a while for the drug to begin taking effect, he cautions against delaying beta-blocker therapy until the last possible minute. "Since it does take some time to show improvement, [that therapy] needs to be added early on, and not late, as a last-ditch effort," he points out.

Safford has treated patients who have experienced significant improvement in pump function, from "dramatically reduced, to mildly or moderately reduced. On an average, their symptoms improve — and, in many cases, the progression of the disease is attenuated. At the very least, I think, the patient can expect his pump function to stabilize."

As far as side effects, "Most patients should be prepared to experience quite a bit of fatigue. Generally, that can last for a couple of weeks, on up to several months. . . . As reduced blood pressure is one of the side effects, they will at some point need to decrease their diuretics or ACE inhibitors, especially if their blood pressure has fallen," Safford says. ■

Drugs overlooked, underused for elderly

Routine therapies not part of treatment plans

If a recent study of elderly patients living in long-term care facilities is any indication, too little attention is being focused on how to treat the very old and frail — a rapidly growing segment of the country's population.

The study used the Systematic Assessment of Geriatric Drug Use via Epidemiology (SAGE) database to study the cases of 86,094 patients with congestive heart failure admitted to any of 1,492 long-term care facilities in five states from 1992 to 1999.

The study indicated that although drugs now

used in treating the elderly may play a role in reducing deaths, other medications are vastly underutilized. These drugs not only could reduce hospitalizations and enhance their quality of life, but otherwise would be a routine component of drug therapy in treating heart failure.

"Because it is a disease process that arises almost naturally with the aging process, heart failure is at epidemic proportions among older people. This becomes even more apparent in a nursing-home environment, where people are the right age to be vulnerable," says **Daniel E. Forman**, MD, a member of the research panel and assistant professor at Boston University and director of cardiovascular services for Boston Health Net.

The patients' average age was 84.9 years. Eighty-nine percent were 75 and older, and 55% were older than 85. An overwhelming majority (80%) of patients was women. More than two-thirds underwent frequent hospitalizations related to CHF in the year preceding admission to the long-term facility. The most common causes were coronary heart disease and hypertension.

"Our understanding of heart failure has become much more sophisticated, and we are now recognizing that medications like ACE inhibitors are very important. Yet, their [use] lags significantly behind that of digoxin and lasix."

Half of all patients received digoxin and 45% a diuretic, regardless of background or cardiovascular comorbidities. Only 25% had a prescription for ACE inhibitors.

The intent of the study was threefold:

1. to describe patients' clinical and functional characteristics;

2. to characterize specific pharmacologic regimens and the extent to which they vary depending on comorbid conditions;

3. to evaluate predictors of appropriate pharmacologic care, including specific facility characteristics.

Most troubling to researchers was the disparity among treatments. There was a "dramatic underuse" of drugs such as ACE inhibitors, a virtual staple in recent years that according to Forman "[has] proved to be so effective" in treating heart failure.

Jane Geraci, MD, MPH, an assistant professor at the Baylor College of Medicine in Houston, agrees with Forman's view.

"There is every reason to believe that older, and even much older patients, especially if they have normal or minimal physical or cognitive impairment could benefit from ace inhibitor treatment, and an attempt should be made to treat them." Geraci is treating a 90 year-old man with coronary artery disease, diabetes, and severe osteoarthritis of the knees with an ACE inhibitor.

A lot more data needed

"I am slowly trying to titrate his dose to as high as he can tolerate. I would expect this to be an easier task in a long-term setting than in the outpatient area, because patients could be watched more closely and with greater ease in a nursing home," she explains.

Geraci also expressed a concern regarding the amount of aspirin used in long-term care facilities. "I was concerned that, even though one-third of the patients were diagnosed with coronary heart disease, only 19% are getting aspirin," she says.

As a whole, Forman says, it became apparent from the study that "in addition to the fact that treatment modalities lag, there are not a lot of data available, and what are available are ambiguous."

A large part of the problem may be the fact that clinicians only now are really beginning to establish a true definition of heart failure.

"In the past 10 years, the idea of what heart failure really is has undergone dramatic changes. At one time, it was thought that the most important thing was to treat inappropriate fluid accumulation. As a result, everyone was given lasix. The other thrust of treatment focused on systolic dysfunction, and people were given digoxin in an effort to make their hearts squeeze properly," he adds.

Why is ACE inhibitor use lower?

"Our understanding of heart failure has become much more sophisticated, and we are now recognizing that medications like ACE inhibitors are very important. Yet, their [use] lags significantly behind that of digoxin and lasix," says Forman, who speculates that the fact that patients in long-term care facilities are not seen on a regular basis may partly explain clincians' reluctance to try new treatments.

The study only pointed up what researchers already had recognized. Heart failure trials, almost invariably, have excluded elderly patients, especially the oldest ones. In addition, they have all but ignored women — which is ironic, as women account for the vast majority of the older population, he adds.

"The literature that's so predominant focuses on younger people, and men specifically — yet, women tend to live longer. We don't have a clear treatment on older people — and we certainly don't have a clear treatment on women," Forman says.

> *"Women tend to live longer. We don't have a clear treatment on older people — and we certainly don't have a clear treatment on women."*

Minireum Data Set (MDS) data were linked to a drug utilization file listing all drugs consumed by each resident during the seven days preceding the assessment. Up to 18 different drugs were coded according to the National Drug Codes. Information included brand and generic name, dose, route and frequency of administration, and whether the prescription was standing or administered as needed.

Drug codes were matched to the Master Drug Data Base (MediSpan Inc., Indianapolis), which contains complete records for prescription drug products in the retail pharmacy environment.

The MDS and pharmacologic data were linked to Medicare enrollment files. Residents then were cross-linked with MDS data to the Medicare inpatient claims database that contains information for all health services for which a claim had been filed between 1991 and 1997.

From 478,508 residents, all patients who had a diagnosis of CHF as their initial MDS assessment were identified. Staff physicians coded a diagnosis of heart failure using information obtained from the medical record, including the physical examination of the resident, medication and other treatment orders, and hospital discharge documentation (available for 78% of patients). Of 89,174 patients with CHF, those younger than 65 or in a vegetative state were excluded, leaving a sample population of 86,094 patients. ■

New options decrease transplant rejection odds

Medications offer alternative to cyclosporine

Clinicians treating heart transplant rejection have little choice but to subject their patients to drugs known to produce a variety of side effects, some of which are potentially fatal.

In the near future, however, that may well cease to be a problem. The new drugs being studied reportedly not only prevent transplant rejection, but eliminate potential side effects as well.

Avoiding dangerous side effects

Among them are two new intravenous drugs used acutely following transplant in lieu of cyclosporine. Cyclosporine can cause numerous side effects, including kidney failure.

With the advent of the new drugs, "You don't even have to use cyclosporine for the first few weeks," says **Reynolds Delgado**, MD, assistant medical director, department of cardiopulmonary transplantation, St. Luke's Episcopal Hospital/Texas Heart Institution in Houston.

Also being considered are two new pill form medications that can either be used instead of or in combination with cyclosporine. The pills' primary advantage is that "it allows us to cut the (cyclosporine) dosage way down," Delgado says. Rapaycin, one of the medications in consideration, is successful in kidney transplants and is showing promise with heart transplantation as well, he adds.

Largely as a result of improved medications, the incidence of heart transplant rejection has decreased considerably in recent years. "We're doing a lot better with coronary artery disease because we are using staten drugs [to lower cholesterol] after all the transplants," says Delgado.

Thousands could be helped by advances

In spite of the advances, of the approximately 2,000 heart transplants performed every year in the United States alone, "it is estimated that a number in excess of 40,000 could benefit from them," Delgado says. "We need to find a way to help these people — and that is where the

new artificial heart devices we are working on come in."

For treatment of heart transplant rejection, "There's also an increased interest in percutaneous myocardial revascularization, which basically is a laser that makes small holes in the heart to stimulate angiogenesis," according to **Charles Inman Wilmer**, MD, director of angioplasty and cardiac disease specialist and director of data management at the Fuqua Heart Center of Piedmont Hospital in Atlanta.

Also being studied are various revolutionary devices such as a new battery-powered pump that does not require a wire connection to the patient and an enhanced extra corporeal counterpulsation for inoperable patients with angina who otherwise would require transplantation, says Wilmer. ■

NEWS BRIEF

Study stopped early due to survival benefit

A major international study of carvedilol (sold under the name Coreg, manufactured by Hoffman-LaRoche in Basel, Switzerland) in patients with advanced chronic heart failure has

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been stopped early by its steering committee due to a significant survival benefit seen with the drug. Based on the size and consistency of the mortality benefit seen in the trial, known as Copernicus (Carvedilol Prospective Randomized Cumulative Survival Trial), the committee believed it would be inappropriate for physicians to further withhold treatment with the drug.

Copernicus enrolled more than 2,200 patients in 21 countries with advanced heart failure who had symptoms at rest or on minimal exertion but who did not require hospitalization in the intensive care unit or intravenous drug support.

Half the patients received Coreg, and half received a placebo, which were both added to the heart failure medications the patients were already taking. The mortality rate in the Coreg group was significantly lower than in the placebo group, and serious adverse effects were more common in the placebo group. The data from the study will be submitted to the U.S. Food and Drug Administration for review. ■

SourceKit

The following sources were featured in this month's *CHF Disease Management:*

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CE objectives

After reading *CHF Disease Management*, health care professionals will be able to:

1. Identify management, clinical, educational, and financial issues relevant to the care of CHF patients.
2. Explain how those issues affect CHF patients and the providers who care for them.
3. Describe practical ways to solve problems commonly encountered by care providers in their daily activities. ■