



# MEDICAL FRONTIERS

I N T E R N A T I O N A L

---

New Frontiers in

## HEART FAILURE

### From Pathophysiology to Clinical Practice

A report from the

**9th Annual Toronto International Heart Failure Summit**

Toronto, Ontario / June 14-16, 2006

---

**Toronto** - The past year has been one of consolidation of knowledge about the diagnosis and management of heart failure. At the 9th Annual Conference of the Toronto International Heart Failure Summit, key opinion leaders met to discuss the newest findings on the optimal pharmacological and non-pharmacological methods of treating heart failure, a disease which is fast becoming an epidemic as the population ages. Held in collaboration with the Canadian Cardiovascular Society (CCS) and the Canadian Institutes of Health Research (CIHR) Institute of Circulatory and Respiratory Health, the conference participants discussed issues of emerging importance, such as the management of elderly heart failure patients, new tools for accurate and rapid diagnosis of heart failure, epidemiological trends in pharmacotherapy and heart failure outcomes, and finally end-of-life care. The highlight of the Summit was an interactive workshop which gave delegates an opportunity to review the 2006 CCS Heart Failure Consensus Recommendations and discuss ways to implement these new guidelines into their daily practice.

---

---

**The 2006 Canadian Cardiovascular Society  
Heart Failure Consensus Recommendations**

---





Each year, advances and new knowledge about the clinical management of heart failure continue to emerge and although there were no landmark trials with the potential to change medical practice in heart failure during the year since the last International Heart Failure Summit, four sets of guidelines were published, which made the past year “remarkable,” confirmed Dr. Malcolm Arnold, Program Director for Cardiology Research, Lawson Health Research Institute, Research Affairs Director, London Health Sciences Centre, and Professor of Medicine, University of Western Ontario, London, Ontario.

“Some years we are blessed with many major trials that change the way we practice, but the past year seems to have been more of consolidation of knowledge. The year has been notable for the publication of these guidelines,” he told delegates.

Guidelines for the treatment of heart failure were issued by the European Society of Cardiology (ESC), the American Heart Association/American College of Cardiology (AHA/ACC), the Canadian Cardiovascular Society (CCS) and the Heart Failure Society of America (HFSA). Although they were all published in the same year and based on the same evidence, the four guidelines offer dissimilar recommendations.

As an example, according to the ESC guidelines, biventricular pacing for heart failure, also known as cardiac resynchronizational therapy (CRT), “can be considered” in patients with reduced ejection fraction and ventricular dyssynchrony (a QRS >120 ms) who remain New York Heart Association (NYHA) class III to IV despite optimal medical therapy. However, the AHA/ACC guidelines, in reviewing the same evidence for the same population of patients, recommend that these individuals “should receive CRT, unless contraindicated,” Dr. Arnold indicated. The CCS and the HFSA are more in line with the ESC guidelines, he added, “although the HFSA adds a clear statement that CRT is not recommended in asymptomatic or mildly symptomatic patients.” The nuances among these four sets of guidelines indicate that the clinician can use clinical judgment and apply those that most suit the individual patient with regard to biventricular pacing for heart failure.

Yet there is consistency across the board among all four sets of guidelines with regard to medical therapy, Dr. Arnold noted. He reviewed several of the most notable trials from the past year that were particularly relevant to the medical management of heart failure.

---

### **The CCS Heart Failure Guidelines: Keeping Current**

“The Canadian Cardiovascular Society has made a commitment to knowledge translation and the venue which has been chosen is heart failure, because it is a rapidly evolving field, there are a lot of recommendations, there are multiple opportunities to improve care, and it is a high burden illness, with a large public health cost,” commented Dr. Jonathan Howlett, Medical Director, Cardiac Transplant and Heart Function Clinic, Queen Elizabeth II Health Sciences Centre, and Associate Professor of Medicine, Dalhousie University, Halifax, Nova Scotia.

Given the importance of these issues, the CCS has decided to offer practical, implementable, usable and updated heart failure guidelines on a yearly basis. “We do not plan to totally revamp the guidelines but to simply add or make changes where the situation warrants. These guidelines will have a carefully thought-out strategy of knowledge translation, which will include a plan of assessment to determine their impact so that we can better plan future knowledge translation activities. The idea is to make a difference,” emphasized Dr. Howlett, who was also a member of the writing committee of the 2006 CCS consensus conference recommendations on heart failure.

Whereas various associations and societies issue guidelines for heart failure, the ones that are most relevant to Canadians are the Canadian guidelines, “because they recognize the reality that we live in, and that the way we practice medicine is perhaps different than the way the other jurisdictions practice medicine,” Dr. Howlett indicated. Referral patterns, expectations of patients and costs are all completely different between the US and Canada, he noted.

“We spend a very small proportion of our health care money on administration compared to America. We have more consistent coverage by and large, as opposed to the US system, where they may have highly aggressive strategies that are fully covered, and where wait times and access are not issues, but in Canada, we have to make do with the resources that we have and our guidelines flow from that,” explained Dr. Howlett.

One important difference between the Canadian and other guidelines is the Canadian emphasis on end-of-life and elderly care. “These are extremely important issues. Everyone with heart failure will eventually succumb, either to heart failure or something else, and they all have the same right to proper end-of-life care and palliative care,” he observed.

The Canadian guidelines also make a strong statement that heart failure is a collaborative care effort and have tailored their recommendations so that all health care professionals will derive the information that is relevant to their roles in the health care system, Dr. Howlett indicated, “We are very aggressive in trying to include all of the major stake holders. We are publishing the guidelines in multiple specialty journals, not just cardiology.”

### **From Bench to Bedside**

Dr. Malcolm Arnold, chaired the 2006 CCS consensus recommendations on heart failure. He noted that there are some gaps when it comes to putting what physicians know into their practice. In outlining some of the more notable gaps, he told his audience, “If the trials and guidelines we have been seeing for the past 25 years are so good, why are we still seeing a gap in terms of what we are able to achieve? Perhaps we are not as good as we think we are in terms of what we do.”

Heart failure is often treated inappropriately, at least initially, he qualified. “There is a tendency for us to look for something we can quickly reverse and deal with and get the patient out of the office, and then move on to things we enjoy doing. So that physician perhaps does not have the skills or the knowledge or is unaware of the evidence in the guidelines and the impact that the therapies we do have can make,” Dr. Arnold observed.

Some physicians may be uncomfortable managing a complex illness such as heart failure, he added. “This is understandable. As we have sat here for the last few days, each of us has a new understanding and appreciation of the complexity of heart failure, and that each year, we are learning more about it. For example, diastolic heart failure—surely, that is simple. But when you get into the physiology and pathophysiology, it is remarkable how complex diastolic heart failure is.”

Adding to the complexity are patients who do not fit a specific clinical trial profile, or individuals who delay seeking help until their heart failure is more advanced, or they do not comply with treatment, Dr. Arnold suggested.

Right now, Canada’s annual average in hospital mortality rate is about 9.5 deaths per 100 hospitalized patients over the age of 65. This climbs to 12.3 deaths per 100 hospitalizations for patients over the age of 75. Heart failure patients overall have a poor prognosis, with an average one-year mortality rate of 33% after hospital discharge. “These are results from trials. In Ontario, a 65-year-old white male, after the first heart failure

---

hospitalization, has greater one-year mortality than that shown in most of the clinical trials, so the reality is worse than in the selected patients within clinical trials,” he noted.

The situation is projected to get worse in the future, Dr. Arnold cautioned. “Johansen et al. [*Can J Cardiol* 2003; 19(14):430-5] has analyzed and predicted that over the next few decades, there is going to be at least a threefold increase in the incidence of heart failure cases.”

However, he emphasized, “We have the tools and the skills. The CCS is committed to provide papers, and not just the general guideline article that is published yearly in the *Canadian Journal of Cardiology*. We are going to be publishing other papers in *Canadian Nurse*, *Canadian Pharmacist*, *Canadian Geriatrics* and others, to give a breadth of dissemination of the guidelines, not just to the cardiovascular community.”

The CCS also has two Web sites from which can be downloaded more information about the heart failure guidelines: [www.ccs.ca](http://www.ccs.ca) and <http://hfcc.ccs.ca> The CCS is also planning several symposia and workshops to discuss the guidelines which will be taking place in New Brunswick, Vancouver and Quebec City.

### Highlights of the Heart Failure Guidelines

Dr. Howlett began the discussion of the 2006 CCS Heart Failure Consensus Recommendations by telling delegates that the consensus recommendations were categorized by class, according to the level of evidence for or against a specific therapy. This system is more in accordance with the AHA/ACC guidelines for heart failure, he noted.

Table 1. Class Recommendations and Grade of Evidence

Level of Evidence A	Data derived from multiple randomized trials or meta-analyses
Level of Evidence B	Data derived from a single randomized clinical trial or nonrandomized studies
Level of Evidence C	Consensus of opinion of experts and/or small studies

Arnold JMO et al. *Can J Cardiol* 2006;22(1):23-45.

Class I recommendations are generally made after a review of the evidence-based literature where there is a wide consensus that they are the most beneficial and effective. Class III recommendations, on the other hand, indicate those treatments that have not been shown to be effective,

and in some cases, might even do harm, Dr. Howlett remarked.

However, he added, in some cases, class III evidence is listed after a recommendation, because it is sometimes difficult to carry out randomized clinical trials of some treatments due to ethical concerns. In such cases, the recommendations have been based on “considerable experience and practice patterns that have a similar weight as evidence from multiple randomized trials.”

Dr. Howlett cited eight key recommendations in the guidelines:

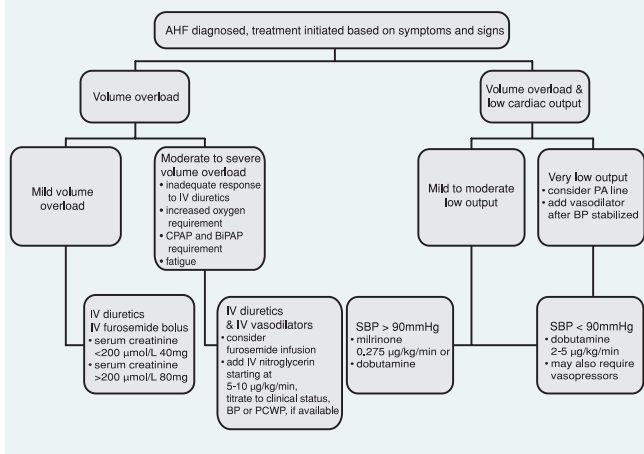
- Begin with an accurate diagnosis. “If you don’t know what you are treating, you will likely not have optimal outcomes.”
- Aggressive treatment of all known risk factors, e.g. diabetes, hypertension. “If the patient has hypertension, treat that as well. Treatment should be based on the patient characteristics in front of you.”
- Treatment requires rational combination drug therapy.
- Care should be individualized for each patient based on symptoms, clinical presentation, disease severity and underlying cause.
- Patient and caregiver education should be individualized and communicated. “This is critical because if (patients) don’t have this information, they cannot implement the changes in their lives. Heart failure is a life-altering disease. Almost every aspect of how patients behave is changed.”
- Mechanical interventions (e.g. revascularization devices) should be available. “This is something we used to think only applied to a tiny proportion of patients, but is now probably appropriate for upwards of 10 to 20% of heart failure patients. They are now in the mainstream and they are something that should go through your mind. Appropriate centres and individuals who specialize in these areas should be consulted.”
- Collaboration is required among health care professionals. “This is something that we are very proud of. We espouse the notion that collaborative care is extremely important. Quite frankly, if all members of the health care community are not participants in the treatment of our heart failure patients, then we can expect a suboptimal outcome.”
- Accessibility to primary, emergency and specialist care must be timely.

### Some Pearls to Remember

Upwards of 40 to 50% of heart failure patients will not have an obvious diagnostic / symptom presentation. Subtle findings that are apparent, either in the patient's history or upon physical examination, will help in making the diagnosis, Dr. Howlett confirmed. “Five years ago, we

used to tell patients that they couldn't possibly have heart failure if the ejection fraction was normal. This is no longer true, so only measuring the ejection fraction will not give you the information you need."

Figure 1. Treatment Algorithm for Acute Heart Failure



With regard to timely care, it is recommended that heart failure treatment be initiated within two hours. Unfortunately, in Canada, “we’re not even close,” Dr. Howlett told listeners. “That is a very tall order. It’s in line with the door-to-needle time and door-to-balloon times that the AHA/ACC tell us about. Initially, we are not going to be able to match that. Our time to diagnosis in Canada is three to four hours and in many cases, it is likely to be a lot longer than that.”

**Diastolic Heart Failure**

Diastolic heart failure is beginning to emerge as “the new picture of heart failure,” according to Dr. Peter Liu, Scientific Director, Institute of Circulatory and Respiratory Health, CIHR, and Heart & Stroke/Polo Chair Professor, University of Toronto, Ontario.

“This is heart failure with preserved systolic function. We now realize that the traditional definition of heart failure—the patient with symptoms whom we always associated with a big, dilated heart that is weakened—is not the whole picture. The reality is actually shifting, because it looks like more and more patients with heart failure may not actually have the classic dilated heart. Their heart may actually be normal-sized, and yet they have just as many of the complications that are associated with heart failure,” Dr. Liu related.

The heart in diastolic failure may contract well, but it will be very stiff and will not accommodate fluid, he explained. “The patient will end up with pulmonary edema and be very difficult to manage. The challenge is, physicians don’t always recognize this as heart failure. They may think it is lung disease or something else. But we have to recognize that this is heart failure and that it is as bad as the classic systolic heart failure.”

Dr. Liu added that physicians must use the correct combination of medications and treat these patients with diastolic heart failure aggressively, “because otherwise they are going to end up with the same fate as systolic heart failure patients.”

Dr. Howlett added that the guidelines recommend that ACE inhibitors, ARBs and beta blockers “in varying combinations” be considered for most patients with diastolic heart failure.

Patients who present with severe volume overload should be treated with assisted breathing techniques, such as continuous pulmonary airway pressure (CPAP) and vasodilator therapy early on, as opposed to waiting a few hours, Dr. Howlett said.

Patients with low cardiac output are likely to require inotropes and other advanced forms of care, and are more difficult to treat, he noted.

Mechanical interventions can make a very big difference for the better in patients who have very low ejection fractions (i.e. less than 30%) and significant dyssynchrony on ECG. The guidelines recommend that after a period of optimal medical management, such patients should be considered for an implantable cardioverter defibrillator (ICD) therapy. Cardiac resynchronization therapy (CRT) has the added benefit of improving heart failure symptoms, reducing hospitalizations and mortality, “particularly if patients have a wide QRS and are NYHA function class III to IV as opposed to NYHA function class II,” Dr. Howlett indicated.

**Cautionary Notes**

The guidelines also contain a number of caveats, Dr. Howlett noted. The consensus committee has been very careful to ensure appropriate medications are suggested for specific conditions and that mechanical therapies are not to be employed unless the patient has a reasonable quality of life and life expectancy. “It is probably not a good idea to put an ICD in a patient who is bed-bound,” he advised, adding that there is ongoing research that hopefully will give more answers about this issue in patients who are currently on CRT therapy.

The guidelines offer few recommendations for surgery and revascularization simply because there is not enough evidence for their utility as yet, Dr. Howlett told the audience. However, if surgery is to be considered—for example, to replace a mitral valve or to use a left ventricular assist device or even for heart transplantation—it is essential that an experienced surgical team be employed to minimize surgical mortality. “There is quite a variation in outcomes, depending on the degree of experience that your team has and how patients are selected,” he remarked.

Elderly patients with heart failure often present a conundrum for the diagnostician. Not only can they come into the emergency room or office with a confusing array of symptoms, including affective problems such as confusion and depression, they also have atypical features, such as delirium, falls, sudden functional decline with rales, and personality changes, Dr. Howlett noted.

These patients are difficult to medicate and doses should be titrated with care. For example, “digoxin should be given at half of whatever dose you use in a younger person,” Dr. Howlett suggested.

### End-of-Life Care

An important and distinctive aspect to the CCS consensus guidelines is its emphasis on end-of-life issues. Vaska Micevski, RN, PhD, Heart Failure Clinic, Toronto General Hospital, offered insights into managing heart failure patients as they progress through the continuum of their disease.

She began her talk with the case of a 75-year-old woman with end-stage heart failure who had been followed in the clinic for five years and had had an ICD implanted two years previously. Despite being on optimized medical therapy, she was deteriorating, had been hospitalized three times for heart failure in the last year, and had symptomatic hypotension, deteriorating renal function and hyponatremia. In addition, she had suffered two ICD shocks within the past three months. She presented to Micevski asking for her ICD to be turned off.

After consultation with the woman’s family and a reassessment of her wishes, the decision was made to accede to her request. “She died 53 days later, at home, of sudden cardiac death, after she had had breakfast with her husband,” Micevski recounted.

It is important to discuss end-of-life issues with patients before they arrive at the end stage of their disease. However, some physicians may not feel comfortable in so doing, Micevski said. To help them, the CCS guidelines have made the following Class I recommendations:

- A living will should be discussed with patients to clarify wishes for end-of-life care.
- Patients with heart failure should be approached early in their disease process regarding their prognosis, advanced medical directives and wishes for resuscitation.
- As patients near end-of-life, physicians should reassess all the therapies with the shift of focus to quality of life.
- Psychosocial issues, including depression, fear, isolation, support and the need for respite care, should be re-evaluated routinely.

According to Dr. Gary Newton, Assistant Professor of Medicine, University of Toronto, heart failure patients are often relieved when they are asked about end-of-life issues.

“This is the sort of patient whom I will routinely ask, in front of the family, if they have thought of end-of-life. Heart failure is different from cancer. In cancer, families are emotionally keyed up for their loved ones to die and a lot of discussions occur, but in heart failure, it’s years of denial because our therapy works, they get sick, but they get better,” Dr. Newton commented.

He added that often, when they are asked whether they feel that they are “close to the end,” patients experience a palpable sense of relief. “They’ve been trying to talk with their family and nobody will let them. So there is a sense of relief when they are finally allowed to talk about dying.”

Dr. Arnold added: “One of the greatest privileges of being in the health care profession as a physician or a nurse is being able to talk to patients and their families about the process of dying and about death itself. I feel very privileged whenever I am able to enter into those discussions. It is a remarkably tender time and it can be one of the most rewarding times in medical practice, to help the patient and their family come to a decision that they are all comfortable with. I think that’s a real privilege.”

### Recommendations and Practical Tips

In the end, the CCS guidelines consist of 111 recommendations and 65 practical tips developed to be comprehensive yet compact, readable, relevant, evidence-based and practical, Dr. Arnold continued.

“We trust that they are helpful to you as you apply them and also that many of you will consider using common sense because this is what we are all doing already. I hope that some other recommendations will help you make changes in your practice,” he addressed his listeners.

The CCS has also produced aids to make the guidelines more “user-friendly.” These include slide sets which can be

downloaded from the CCS Web site, pocket cards that can be easily carried about that offer reminders about treatment, as well as a simple algorithm and doses of drugs that have been proven to be of benefit, Dr. Arnold explained.

#### KEY RECOMMENDATIONS

- ACCURATE DIAGNOSIS
- AGGRESSIVE TREATMENT OF ALL KNOWN RISK FACTORS
- (RATIONAL) COMBINATION DRUG THERAPY
- INDIVIDUALIZED CARE BASED ON:
  - SYMPTOMS
  - CLINICAL PRESENTATION
  - DISEASE SEVERITY
  - UNDERLYING CAUSE
- TAILORED EDUCATION TO PATIENT AND CAREGIVER
- AVAILABILITY OF MECHANICAL INTERVENTIONS
- COLLABORATION AMONG HEALTH CARE PROFESSIONALS
- TIMELY ACCESSIBILITY TO PRIMARY, EMERGENCY AND SPECIALIST CARE

#### Complicating Factors in Diagnosis

A low ejection fraction after a myocardial infarction identifies a patient at high risk for heart failure, as does atrial fibrillation, ECG abnormalities and left bundle branch block, Dr. Arnold observed.

Renal dysfunction not only makes it difficult to titrate medications correctly and safely, it is also an independent indicator of worsening and subsequent poor outcomes in heart failure. Dr. Arnold cited a study by Hillege et al. (*Circulation* 2006;113:671-8) where patients who had the lowest estimated glomerular filtration rate (eGFR) had the worst heart failure risk. “Yet these are the patients in whom we have the greatest difficulty for increasing the doses of ACE inhibitors, ARBs and spironolactone. This is a high-risk population who are difficult to treat. I think that many of us are beginning to make the calculation of eGFR as part of our management of patients,” he noted.

Anemia and unexplained weight loss are each “very strong markers” of patients with heart failure who are at very high risk for poor outcomes, Dr. Arnold added.

Dr. Thomas Force, Clinical Director, Jefferson Center for Translational Medicine, Jefferson Medical College, Philadelphia, Pennsylvania, told delegates that certain cancer treatments can cause heart failure, even in younger patients with no history of cardiovascular disease.

He referred to a recent study which was presented at this year’s annual meeting of the American Society of Clinical Oncology by Dr. Sharon Giordano, Assistant Professor of Medicine, Department of Breast Medical Oncology, University of Texas M.D. Anderson Cancer Center, Houston. She and colleagues found that

postmenopausal women with breast cancer who were treated with adjuvant anthracycline chemotherapy were significantly more likely to develop heart failure five and 10 years after their treatment. This was especially true in women aged 66 to 70.

“The development of heart failure in patients receiving anti-cancer drugs will become an increasing problem,” Dr. Force predicted.

Currently it is difficult, if not impossible, to predict which patients are at risk. Dr. Force cautioned: “There are many of these agents coming down the road and we are going to be seeing more and more of them. One of them (sunitinib) has just been approved by the Food and Drug Administration, which is used for renal cell cancer, and it causes heart failure as well. The problem is, we don’t know the incidence. But if you see patients who are on a novel tyrosine kinase inhibitor and they develop heart failure, a trial of medical therapy is warranted.”

Dr. Force also told attendees of two new experimental approaches to heart failure in animal models. One is a substitution of a single amino acid in the cardiac troponin I protein which protects the ischemic and failing heart. The second is a chemical-based membrane sealant which has been found to reverse the progressive cardiomyopathy in animal models of Duchenne muscular dystrophy. “These exciting advances from Dr. Joseph M. Metzger’s laboratory at the University of Michigan School of Medicine in Ann Arbor won’t be ready for prime time for a while, but they are remarkable and show a lot of promise against heart failure,” Dr. Force observed.

In addition, there have been recent advances in understanding the genetics of cardiomyopathies and sudden death. These have focused on cardiac hERG channels. Mutations in cardiac hERG channels can cause long QT syndrome and lethal arrhythmias. Certain compounds, such as the atypical antidepressant trazodone, have been found to inhibit cardiac hERG potassium channels.

“These discoveries are, or may be in the future, most relevant to clinical science in heart failure,” he concluded.

#### Continuing the Search for Improved Outcomes

Dr. Douglas S. Lee, Research Fellow, Division of Clinical Epidemiology, Department of Health Policy, Management and Evaluation, University of Toronto, and post-doctoral research fellow, National Heart, Lung and Blood Institute Framingham Heart Study, Framingham, Massachusetts, discussed the epidemiology and outcomes of heart failure, as detailed in recent studies. “Heart failure continues to be of tremendous

research interest in its epidemiology and outcomes. In previous years, publications have documented the high rates of morbidity and mortality in heart failure patients. Recent studies have continued to expand on these lines of inquiry.”

Medical treatment strategies are widely employed for the treatment of established heart failure and are typical therapies for patients, he said. “For many of them, drug therapy is the only form of therapy that they will receive.”

As always, the aim of therapy for heart failure as for other diseases is to improve outcomes as well as quality of life.

### **Different Province, Different Usage**

There are also variations in heart failure drug use across Canada, Dr. Lee told delegates. Citing Cox et al. (*Can J Cardiol* 2005;21:337-43) on the trends and rates of use of heart failure drug therapies in Nova Scotia, Quebec, Ontario, Alberta and British Columbia, there was considerable variation in the rate of drug use according to the province.

In general, trends in usage are consistent with the weight of evidence-based research and published guidelines and the changes have probably contributed to the beneficial outcomes that have occurred, Dr. Lee concluded.

In a study by Roger et al. (*JAMA* 2004;292:344-56), heart failure outcomes for both men and women showed a steady increase in survival between 1979 and 2000, which may be due to better drug therapy. Dr. Lee and his team also observed survival rates for heart failure patients, but over a shorter period of time, from 1992 to 2000 (Lee et al. *Am J Med* 2004; 116:581-9). Like Dr. Roger and co-investigators, they also showed mortality improvements for heart failure patients.

“The first thing we found when we did this analysis was that hospitalized heart failure patients are getting older and they are getting sicker, and have a lot more comorbidities than years ago,” he reported.

However, after accounting for changes in age and comorbidity status, Dr. Lee found that adjusted mortality rates decreased from 1992 to 2000 in Ontario in all patients, even among those who survived hospitalization. However, he cautioned, “Although there has been an improvement, the mortality rates are still high, at around 30%.”

We can do better, Dr. Lee told delegates. “We must change our thinking about heart failure drugs to improve outcomes in this population,” he emphasized.

The first step to take is to minimize the inappropriate use of heart failure medication. Another important way to improve outcomes is to treat higher-risk patients

appropriately. In another analysis carried out by Dr. Lee and colleagues (*JAMA* 2005;294:1240-7), heart failure patients in Ontario were categorized according to their one-year mortality risk scores and then analyzed for ACE inhibitor, ARB and beta blocker prescriptions. They found that patients who were at the highest risk were least likely to receive an ACE inhibitor, ARB or beta blocker; whereas patients who were at the lowest risk were most likely to receive these drugs.

“We termed this ‘the risk treatment mismatch’ in that treatment rates were not really in accordance with the risk of mortality. The mortality risks were quite substantial: in the low-risk group, the mortality was 14%; there was a doubling of risk, 28% mortality, in the average-risk group; and in the high-risk group, only about 50% survived at one year,” according to Dr. Lee.

No matter how diligently physicians prescribe the right agents, outcomes in heart failure will not be improved unless patients become more adherent with their medication regimens, Dr. Lee stressed.

He concluded by emphasizing the importance of increasing treatment rates in patients at high risk of death, decreasing potentially inappropriate therapy, improving adherence, particularly in the post-hospitalization period, and decreasing the complexity of patients’ medical regimens.

### **Angiotensin II Suppression**

Prominent on the agenda of the 9th Annual International Heart Failure Summit were talks on the optimal use of pharmacotherapy. Dr. Michel White, Director, Heart Failure Research Program, Montreal Heart Institute, and Associate Professor of Medicine, *Université de Montréal*, Quebec, reviewed the effects of angiotensin II and modulation in heart failure patients and also presented the most recent clinical evidence about the use of dual angiotensin II suppression in this population.

“It is estimated that nearly 1.5% of the North American population suffers from congestive heart failure. While the number of deaths from ischemic heart disease and myocardial infarction are projected to continue their downward trend, the number of deaths caused by heart failure is projected to increase for both men and women,” he told the audience.

“The increasing rates of diabetes and poorly controlled hypertension are only going to make the situation worse, and so it is imperative that we begin to examine our pharmacologic armamentarium for ways to combat this emerging epidemic,” Dr. White stated.

---

Experts' understanding of heart failure has evolved in recent years. Heart failure used to be considered a hemodynamic syndrome but now it is believed to be a neuroendocrine disease. "Over the last year, it has become evident that subclinical inflammation and oxidative stress are increased in heart failure," Dr. White noted.

Angiotensin II plays an important role in the pathophysiology of this disease. Sustained elevations of angiotensin II contribute to increased afterload, sodium retention and, more importantly for heart failure, cell growth and apoptosis. Angiotensin II, therefore, plays a major role in adverse cardiac remodelling, Dr. White indicated.

### Inflammation and Oxidative Stress

Recent studies have shown that angiotensin II increases oxidative stress and inflammation in patients with coronary artery disease and heart failure. Fortunately, there are two different classes of drugs that are able to counteract these adverse effects: ACE inhibitors and ARBs, Dr. White confirmed.

"The use of ACE inhibitors has provided significant improvement in symptoms and a decrease in mortality in patients with congestive heart failure. More recently, the use of angiotensin receptor blockade has provided similar beneficial effects on morbidity and mortality in patients with symptomatic heart failure," Dr. White noted.

The combination of the two agents has also improved symptoms and exercise capacity as well as left ventricular remodelling, he added.

### Studies That Shaped the CCS Heart Failure Guidelines

Several landmark studies have had an important impact on shaping the CCS heart failure recommendations. The major trials are listed in the following paragraphs.

In the Heart Outcomes Prevention Evaluation (HOPE) trial headed by Dr. Salim Yusuf, Professor of Medicine, McMaster University, Hamilton, Ontario, the ACE inhibitor ramipril reduced the rates of death, heart attack and stroke in a broad range of patients aged 55 and older who were at high risk of cardiovascular events.

In the Valsartan Heart Failure Trial (Val-HeFT), investigators led by Dr. Jay N. Cohn, Director, Rasmussen Center for Cardiovascular Disease Prevention, and Professor of Medicine, University of Minnesota, Minneapolis, evaluated the clinical benefit of the addition of the angiotensin receptor blocker (ARB) valsartan to the conventional regimen of an ACE inhibitor, beta blocker

and diuretic. Of the 5010 patients in the study, 2511 were randomized to receive valsartan 160 mg b.i.d. and 2499 were given placebo. At the time of randomization, 93% of patients were being treated with an ACE inhibitor, 35% were receiving a beta blocker and 5% were on spironolactone. In patients with depressed left ventricular ejection fraction (LVEF), the addition of the ARB reduced mortality and nonfatal morbid events, which were predominantly hospitalizations for heart failure, by 13%. However, it did not result in improved overall mortality.

The Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity (CHARM) trial has four components.

- CHARM-Alternative specifically addresses the concept of ARB use alone in ACE-intolerant patients.
- CHARM-Added addresses the add-on hypothesis, in which 2548 patients treated with an ACE inhibitor were randomized to candesartan in addition to ACE inhibitor and other therapies.
- CHARM-Preserved evaluated the use of candesartan in an important population of heart failure patients: those who had signs and symptoms of heart failure, a history of hospitalization for a cardiovascular event, and a measured LVEF >40%.
- CHARM-Overall gave a collective assessment of these studies.

In CHARM, candesartan titrated to 32 mg/day demonstrated reduced mortality and morbidity both in patients who were on ACE inhibitors as well as those intolerant to ACE inhibitors. Benefit was also seen in adding the ARB to the combination of ACE inhibitors and beta blockers. In patients with low ejection fraction, the ARB resulted in highly significant reductions in cardiovascular death and heart-failure hospitalization as well as all-cause mortality. In patients with low ejection fraction, it improved survival, regardless of other concomitant therapy.

The Angiotensin II Antagonist Losartan Optimal Trial in Myocardial Infarction (OPTIMAAL) and the Evaluation of Losartan in the Elderly-II (ELITE-II) are direct comparisons of the ARB losartan with the ACE inhibitor captopril. Their aim is to demonstrate whether one of these therapies is superior or whether they are comparable in terms of improving survival in high-risk, post-myocardial infarction patients.

The Valsartan in Acute Myocardial Infarction Trial (VALIANT) assessed whether the ARB valsartan could be considered superior to or equal to the ACE inhibitor captopril in high-risk myocardial infarction patients. □

### Knowledge Translation Through Regular Workshops

It was widely acknowledged at the Heart Failure Summit that research is making great strides in enhancing pharmacotherapy and non-pharmacological means of managing heart failure. However, John Parker, CCS Director of Knowledge Translation, emphasized the importance of conveying this new knowledge to practitioners, and of getting it from the bench to the bedside where it can be put into practice.

The best way to do this, he revealed, is by holding conferences, such as The Toronto International Heart Failure Summit, as well as continuing workshops on heart failure guidelines. “We want to find the very best ways possible to integrate into clinical care the new knowledge that is being generated through research almost on a daily basis. Conferences such as this one help us do this,” he confirmed.

The CCS is committed to identifying best practices in heart failure and making clinicians aware of them, he noted. However, it is a time-consuming process which requires the involvement of many different people from all walks of health care life in Canada. “This includes patients and their families, and those who, on a day-to-day basis, deliver care—the nurses and pharmacists, the general practitioners, internists, community cardiologists and cardiology specialists. They all need to come together as a team to try to do the very best they can for heart failure patients across Canada.”

Keeping pace with the wealth of knowledge that is generated over the course of a given year will be a challenge, he conceded, but one that dedicated health professionals will work hard to meet. “There is a tremendous amount of research that is emerging every year. Coming to not only understand that knowledge, but also understand its implications for their day-to-day practice, will require dedication and vigilance. We are finding that this is a very significant challenge for health care professionals across Canada. So this project is aimed at identifying ways whereby we can make that easier for health care professionals in our country,” Parker remarked.

“This project” refers to the series of heart failure workshops the CCS plans to hold throughout Canada on a regular basis. The workshops will feature the current 2006 “CCS Consensus Conference Recommendations on Heart Failure: Diagnosis and Treatment” (Arnold et al. *Can J Cardiol* 2006;22(1): 23-45, also known as the CCS Heart Failure Guidelines), and will offer attendees the opportunity to explore and discuss the different options for treating their heart failure patients, in accordance with the latest evidence-based research.

“Part of the challenge, at least in Canada, is the fact that people are so geographically dispersed. Part of the effort of knowledge translation is to eliminate these kinds of barriers that exist between sharing that new knowledge of best practices across the entire cardiovascular community in Canada. The workshop we are delivering here at the International Heart Failure Summit is part of a series of regional workshops that we have planned for 2006.”

He asked that physicians should feel free to contact the CCS about any problems, suggestions or any other issues, stressing that such two-way contact and flow of information is essential to optimizing heart failure care in Canada.

“We would like to hear from you. Perhaps there are things you think you could do in your community that the CCS could help you with. Perhaps there are things you can help us test. We would love to have your input. We want to be doing things that are relevant to people in practice. So if you would like to help us in these regards, please contact John Parker at [parker@ccs.ca](mailto:parker@ccs.ca). We would love to hear from you because we’d love to have the guidelines get better each year.”

---



© 2006 Medical Frontiers International Inc. All rights reserved. Medical Frontiers™ is an independent medical news reporting service providing educational updates reflecting peer opinion from scientific and clinical meetings worldwide. Views expressed are those of the participants and do not necessarily reflect those of the publisher or sponsor. Support for distribution of this report was provided by AstraZeneca Canada Inc. through an unrestricted grant and under written agreement that ensures independence. Any therapies mentioned in this report should be used in accordance with the recognized prescribing information in Canada. No claims or endorsements are made for any products, uses or doses presently under investigation. No part of this newsletter may be reproduced in any form or distributed without written consent of the publisher. Information provided herein is not intended to serve as the sole basis for individual care. Our objective is to facilitate physicians' and allied health care providers' understanding of current trends in medicine. Your comments are encouraged.

Medical Frontiers International Inc.

Montreal

132 chemin de l'Anse, Suite 100, Vaudreuil, Quebec J7V 8P3

Toronto

2550 Argenta Road, Suite 119, Mississauga, Ontario L5N 5R1

---



## 2006 Heart Failure Guidelines



This tool is produced in conjunction with the Canadian Cardiovascular Society Consensus Conference recommendations on Heart Failure 2006: Diagnosis and Management.

# Is it heart failure and what should I do?



**Canadian Cardiovascular Society**

*Leadership. Knowledge. Community.*

To learn more of this important initiative please visit the  
CCS Heart Failure Consensus Conference Program  
<http://hfcc.ccs.ca>

or

contact

John Parker, Director Knowledge Translation,  
Canadian Cardiovascular Society (parker@ccs.ca).

---

This Medical Frontiers International report from the  
**9th Annual Toronto International Heart Failure Summit**  
is supported by an unrestricted education grant from

***AstraZeneca Canada Inc.***

