

Canadian Cardiovascular Congress



Co-hosted by the Canadian Cardiovascular Society and the Heart and Stroke Foundation of Canada



PLEASE PLAN TO ATTEND

SATURDAY, October 20

"State-of-the-Art Management of Acute Coronary Syndromes: Integrating New Evidence with Antithrombotic Therapies into Practice—A Case-Based Approach to Optimize Antithrombotic Therapy in RCS"

Saturday, October 20, 13:00-16:00, Room 200A, Level 2

"Maximizing the Benefits of Prevention Strategies in Cardiovascular Disease"

Saturday, October 20, 18:00-21:00, Room 200C, Level 2

SUNDAY, October 21

"The CV Show: Expert Insights into the Management of Cardiovascular Risk in the Vulnerable Patient"

Sunday, October 21, 7:00-10:00, Room 200B, Level 2

"Managing Cardiometabolic Complexities: Will New Treatment Strategies Improve Health Outcomes?"

Sunday, October 21, 10:00-12:00, Room 200A, Level 2

MONDAY, October 22

"The 3rd Annual Medical Debate in Lipid Management: Meeting the Challenge of Evolving Evidence"

Monday, October 22, 7:00-9:00, Room 200A, Level 2

"Straight from the Heart: Managing the Cardiovascular Risk Continuum"

Monday, October 22, 7:00-9:00, Room 200C, Level 2

"Expert Opinions: Advances in Cardiology"

Monday, October 22, 12:00-14:00, Room 200B, Level 2

"Managing Heart Failure in Complex Clinical Scenarios—A Case-Based Application of the 2007 CCS Heart Failure Guidelines" WORKSHOP

Monday, October 22, 14:00-15:30, Room 2000A-B, Level 2

TUESDAY, October 23

"Harnessing the Endocannabinoid System to Reduce Cardiometabolic Risk"

Tuesday, October 23, 7:00-9:00, Room 200B, Level 2

"Heart Failure and BNP" ORAL SESSION

Tuesday, October 23, 9:00-10:30, Room 302A-B, Level 3

WEDNESDAY, October 24

"Expert Opinions: Current Issues in Cardiology"

Wednesday, October 24, 7:00-9:00, Room 200B, Level 2

"The Clinical Roadmap to Acute Heart Failure: ASCENDING to New Heights"

Wednesday, October 24, 7:00-9:00, Room 200A, Level 2



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INFO CARDIO

REGISTRATION ISSUE

Saturday / Sunday Edition

12th Anniversary of the Official Newspaper of the Annual Canadian Cardiovascular Congress
October 20-24, 2007 / Quebec City, Quebec



Welcome to Quebec!

Abdominal obesity, one of the CVD risk factor heavyweights

Abdominal obesity should be numbered among the true heavyweights in the traditional risk-factor line-up for cardiovascular disease (CVD) as it confers as much risk for CVD as smoking and hypertension, and is independent of body mass index (BMI).

Such will be the thrust of The Heart and Stroke Foundation of Canada lecture this year, given by renowned obesity expert, Dr. Jean-Pierre Després, Director of Cardiology Research, *Centre de recherche de l'Hôpital Laval*, and Professor of Medicine, *Université Laval*, Quebec City, who will be speaking at the opening ceremonies on Sunday afternoon. Having spent the last 25 years of his professional life exploring the deleterious effects of abdominal fat, Dr. Després has a vast store of evidence to support his argument that abdominal obesity should be considered the "new cholesterol" of the 21st century. "Abdominal fat is a big endocrine organ and it makes a lot of toxic substances," he notes, among them a cascade of inflammatory cytokines that wreak havoc on the arterial walls throughout the vascular system. Over time, this sets the stage for CVD as well as type 2 diabetes, a CVD surrogate from which the majority of patients with type 2 diabetes die.



Dr. Jean-Pierre Després

L'obésité abdominale, l'un des poids lourds du risque de MCV

L'obésité abdominale – qui doit figurer parmi les poids lourds avérés des facteurs de risque traditionnels de la maladie cardiovasculaire (MCV), car elle pèse aussi lourd dans la balance que le tabac et l'hypertension – est indépendante de l'indice de masse corporelle (IMC).

Telle sera l'idée maîtresse de la conférence de la Fondation des maladies du cœur du Canada, qui sera donnée cette

année par un grand expert de l'obésité, le Dr Jean-Pierre Després, directeur de la recherche en cardiologie, Centre de recherche de l'Hôpital Laval, et professeur titulaire de médecine, Université Laval, Québec, lors de la cérémonie d'ouverture dimanche après-midi. Ayant consacré les 25 dernières années de sa vie professionnelle à l'étude des effets délétères de la graisse abdominale, le Dr Després a plus d'une corde à son arc pour étoffer sa théorie, à savoir que l'obésité abdominale est « le nouveau cholestérol » du XXI^e siècle. « La graisse abdominale est un gros organe endocrine qui génère plein de substances toxiques », entre autres une cascade de cytokines inflammatoires qui ravagent les parois artérielles d'un bout à l'autre du système vasculaire. Avec le temps, le terrain devient propice à la MCV et au diabète de type 2, substitut de la MCV dont meurent la majorité des patients atteints d'un diabète de type 2.

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As Dr. Després emphasizes, it's not how fat an individual is but where that fat is located. "For a long time, we've gauged CVD risk by BMI," he states. However, as results from the INTERHEART study showed, a larger waist than hip circumference was highly and significantly associated with the risk of myocardial infarction (MI) whereas BMI was only modestly associated with MI risk and not at all associated with MI risk in certain ethnic groups. Data to be presented by Dr. Després from the International Day for the Evaluation of Abdominal Obesity (IDEA) study are expected to confirm that waist circumference is a better predictor of both CVD risk and the risk for type 2 diabetes at any BMI value.

Even among Asian populations in IDEA, where the average waist circumference and BMI indices are lower than they are in most of the rest of the world, a larger waist circumference was associated with a disproportionate increase in coronary artery disease (CAD) across this patient group. Previous studies by Dr. Després and his colleagues had already shown that waist circumference was a good predictor of intra-abdominal adiposity, which in turn is a strong predictor of increased cardiometabolic risk.

"Abdominal obesity increases your risk of CVD irrespective of whether you are hypertensive or if you smoke," Dr. Després confirms, "but the other route by which to get CVD is through type 2 diabetes because we know type 2 diabetes is a powerful risk factor for CVD."

If healthcare professionals are now conscious of the health risks conferred by excess abdominal fat, getting patients to normalize body weight may not be the answer for CVD risk reduction.

Rather, as Dr. Després will demonstrate, results from the CIHR-funded Synergie lifestyle modification program conducted at the Quebec Heart Institute showed that patients could sometimes lose significant amounts of abdominal obesity without losing a lot of weight. As he emphasizes, "We have to stop promoting the magnitude of weight loss as the target of therapy because it may not always appropriately assess therapeutic success."

Dr. Després will direct healthcare professionals to the new Web site—www.cardiometabolic-risk.org—developed by the Université Laval-based International Chair on Cardiometabolic Risk, where they will find a wealth of information on abdominal obesity and cardiometabolic risk, all free of charge, and which they can download and incorporate into their own professional endeavours to educate other healthcare professionals about the toxic nature of abdominal obesity.

The opening ceremonies take place on Sunday, October 21, starting at 14:00 in Room 2000A-B on the second level of the convention centre. □

La question n'est pas de savoir dans quelle mesure le patient est gras, mais bien où se trouve sa graisse, insiste le Dr Després. « Pendant longtemps, nous nous sommes fiés à l'IMC pour évaluer le risque de MCV », enchaîne-t-il. Cependant, comme l'a montré l'étude INTERHEART, le lien entre un tour de taille supérieur au tour de hanches et le risque d'infarctus du myocarde (IM) était fort et significatif alors que le lien entre l'IMC et le risque d'IM était modeste, voire nul dans certains groupes ethniques. On s'attend à ce que les résultats de l'étude IDEA (*International Day for the Evaluation of Abdominal Obesity*) – que le Dr Després présentera – confirment que le tour de taille est un meilleur facteur prédictif du risque de MCV et du risque de diabète de type 2, quel que soit l'IMC.

Même chez les sujets asiatiques de l'étude IDEA, dont le tour de taille et l'IMC moyens sont plus faibles que presque partout ailleurs dans le monde, un tour de taille plus élevé était associé à une augmentation démesurée de l'incidence de la maladie coronarienne dans ce groupe. Des études antérieures réalisées par le Dr Després et ses collaborateurs avaient déjà montré que le tour de taille est un bon facteur prédictif de l'adiposité intra-abdominale, qui est à son tour un important facteur prédictif de l'augmentation du risque cardiometabolique.

« L'obésité abdominale augmente votre risque de MCV, que vous souffriez d'hypertension ou non et que vous fumiez ou non, confirme le Dr Després. L'autre façon d'arriver assurément à la MCV est le diabète de type 2, parce que le diabète de type 2 est reconnu comme étant un puissant facteur de risque de la MCV. »

Si les professionnels de la santé sont maintenant conscients des risques pour la santé que confère un excès de graisse abdominale, ce n'est pas nécessairement en demandant à leurs patients de normaliser leur poids corporel qu'ils réussiront à réduire le risque de MCV. En effet, les résultats du programme de modification des habitudes de vie Synergie – qui a été financé par les Instituts de recherche en santé du Canada (IRSC) et qui s'est déroulé à l'Institut de cardiologie de Québec – ont montré qu'un patient peut perdre une importante quantité de graisse abdominale sans pour autant perdre beaucoup de poids. « Nous devons cesser de préconiser une importante perte de poids comme étant l'objectif du traitement, parce que ce n'est pas forcément un bon étalon de la réussite thérapeutique. »

Le Dr Després invitera les professionnels de la santé à visiter le nouveau site Web – www.cardiometabolic-risk.org – créé par la chaire internationale du risque cardiometabolique dont le siège est à l'Université Laval. Ils y trouveront beaucoup d'information sur l'obésité abdominale et le risque cardiometabolique, qu'ils pourront télécharger sans frais et intégrer aux efforts qu'ils déploient pour convaincre d'autres professionnels de la santé de la nature toxique de l'obésité abdominale.

La cérémonie d'ouverture aura lieu le dimanche 21 octobre à 14 h dans la salle 2000A-B, au deuxième étage du Centre des congrès. □

Alberta-based scientist captures prestigious CCS Research Achievement Award

This year, the prestigious CCS Research Achievement Award goes to the University of Alberta's Gary Lopaschuk, PhD, for his world-class research in cardiac metabolism.

Dr. Lopaschuk, Director of the university's Cardiovascular Research Group and Professor in the Departments of Pediatrics and Pharmacology, has long devoted his time to research of the metabolic regulation of the myocardium and its implications in health and disease. One of his seminal works was the identification of the role of fatty acid oxidation in the heart, including the molecular mechanisms responsible for the maturation of this process in the heart immediately following birth. He also identified high rates of fatty acid oxidation in diabetic hearts, and how excess use of fatty acids by the heart contributes to ischemic heart disease.



Dr. Gary Lopaschuk

At the same time, Dr. Lopaschuk fully characterized a number of key enzymes in this pathway, including the precise role of cardiac malonyl CoA in fatty acid oxidation and its implications for heart function.

The Alberta-based researcher also collaborated with cardiovascular surgeons and together tested promising metabolic modulators in children recovering from cardiovascular surgery. In 1997, this work led him to create Metabolic Modulators Research Limited, a University of Alberta spin-off company and research facility that fosters the development of new compounds in the clinical management of CV diseases.

Dr. Lopaschuk was recently appointed Scientific Director of the new Mazankowski Alberta Heart Institute and will continue his ongoing work with the CIHR-funded cardiovascular training program at the University of Alberta. □

CCS 60th anniversary: your passport to prizes!



Ann Ferguson

The 60th anniversary of the Canadian Cardiovascular Society (CCS) has a few treats in store for delegates this year, including a "passport" that they can enter into a draw for a chance at one of three big prizes.

"It's just a fun thing to do," remarks CCS CEO Ann Ferguson. All delegates need is to pick up the passport when they register at the on-site registration desk and then have their passport stamped at any 15 exhibitors of their choice. Once completed, they need to drop the passport off at the CCS booth where it will be entered into a draw. The first prize is an all-expenses-paid (accommodation and registration fees) trip to next year's CCS meeting in Toronto, while the second prize is a laptop computer. Third prize is a PDA loaded with CARDIOMATH.

In addition to the "passport to prizes" feature, the exhibit hall itself has been renamed the "community forum" to more

accurately reflect its true purpose. "We changed the name because we wanted to highlight the area more as a meeting place for delegates, not just a place for exhibitors," Ferguson explains. Indeed, delegates will find a new session theatre for interactive workshops. "We also have a clinical trials board, where people looking for participants for clinical trials can put their notices up," she adds. There are also two additional moderated poster theatres where presenters of selected posters can better explain their research to attendees.

"And of course," she adds, "it's where we have lunches and coffee breaks, so it really is what the meeting is all about—it's a meeting place where everyone who is part of the cardiovascular health community can come together and share common interests." □



CCS: a growing Canadian family with unique concerns

Membership continues to expand as the CCS reaches out to community members with a package that is uniquely Canadian.

In the past year, membership in the CCS has grown by 113 new regular members—“the single largest growth year ever in the CCS history,” CCS President Dr. Lyall Higginson informs *INFO-Cardio*, “so it’s been a very successful, very productive year.” He attributes much of that growth to a concentrated effort by the Society to seek out community cardiologists, a group that members of the Society believed has been underrepresented in the past and to whom special efforts have been directed in order to make the Society, and the uniquely Canadian CCC, appeal to their needs more specifically.

At the same time, “our trainees are also extremely important to us as a Society,” Dr. Higginson stresses, and the sixth annual Cardiovascular Trainee Day is testament to the Society’s innate concern for their needs as well. The fact that all but one of the trainees attended a separate trainee day held by the CCS is a sure indicator that these days are a success, and the CCS efforts will likely be extended to cardiac surgery residents in the near future.

Access-to-care continues to dominate CCS policy concerns. “What we wanted was for the Society to set benchmarks for access to CV care from initial consultation through to tertiary care services, which they have done,” Dr. Higginson explains, “and now we need to monitor how many [institutions] are following these benchmarks and get wait times down to within acceptable levels.”

Another top priority for the Society is to set up a certification program for post-graduate training. As Dr. Higginson notes, the Royal College of Physicians and Surgeons of Canada (RCPSC) already trains, gives exams to and certifies cardiologists and cardiac surgeons, and they will continue to fulfill this essential role in the future.



Dr. Lyall Higginson

Nevertheless, he adds, “all of our trainees go beyond certification from the RCPSC yet there is no process to certify that further training.” Because the Society can’t expect the RCPSC to respond to the needs of smaller CV subspecialties, the CCS knows they must step in and fill the void, which they hope to do in the near future.

Of course, knowledge translation remains a policy cornerstone for the CCS, and every effort is being made to extend the Congress experience beyond the physical meeting itself through strategies such as the CCS Web site.

Another initiative being tested as a pilot program this year (although not at the actual Congress) is to bring expert speakers together who can discuss findings presented at sister cardiology meetings. This way, members can stay abreast of the latest research even if they were unable to attend the meeting itself.

The Society is also concentrating on “closing the gap” between knowledge as embodied in practice guidelines and translation of that knowledge into day-to-day clinical practice. For the first time this year, consensus guidelines have not been developed by expert panel members but rather the emphasis from now on will be on the applicability of those guidelines and how to make physicians aware of their content and confident they can implement recommendations into clinical practice.

“With all of the other societies participating in the Congress, working together has been tremendously beneficial for all of us and we’re looking forward to another tremendous year in attendance and another tremendous program,” Dr. Higginson enthuses, extending a personal welcome to one and all to the CCC 2007.

We invite all delegates to enjoy the national treasure that is la *Vieille Capitale*, a UNESCO World Heritage Centre since 1985, as well as the opportunity to take part in a unique learning and sharing experience in a French setting. *Bienvenue!* □

Fifty years of excellence celebrated at *Canadian Journal of Cardiology* symposium

Fifty years of excellence in research, education and health care under the stewardship of the Quebec Heart Institute will be celebrated during the fourth annual *Canadian Journal of Cardiology* symposium, held in collaboration with the Quebec Heart Institute, on Sunday, October 21, between noon and 14:00 in the Porte du Palais/Porte Kent, on the first floor of the Hilton Hotel.

Abdominal obesity will be front and centre as researchers from Quebec City and other centres of excellence discuss the cardiovascular disease (CVD) risk associated with metabolically active visceral fat. “Abdominal obesity is increasingly being recognized as a major risk factor for atherosclerosis and coronary artery disease,” confirms symposium chair and Order of Canada recipient Dr. Eldon Smith, “and there is an increasing frequency of abdominal obesity among Canadian men, women and children—so much so that some have described it as the ‘obesity epidemic.’”

In addition to speaker Dr. Jean-Pierre Després, co-chair of the symposium and a recognized pioneer in the field of abdominal obesity, cardiovascular surgeon Dr. Patrick Mathieu, *Université Laval*, will deliver a surgeon’s perspective on the management of abdominal obesity, while CACR chair Dr. Paul Poirier, Director, Cardiac Rehabilitation Program, *Hôpital Laval*, will seek to determine whether cardiologists can effectively reduce CVD-related risk if they target abdominal obesity.

Dr. Robert Ross, Research Chair, School of Kinesiology and Health Studies, Queen’s University, Kingston, will also address the controversial issue of whether weight loss in and of itself is a relevant target for CVD risk reduction, especially in light of the landmark INTERHEART study, in which principal investigator Dr. Salim Yusuf, Director, Population Health Research Institute and Professor of Medicine, Division of Cardiology, McMaster University, Hamilton, and multicentre colleagues clearly found

that the waist:hip ratio was highly and significantly associated with the risk of myocardial infarction (MI) in all ethnic groups. Indeed, an increased waist:hip ratio correlated with a threefold increase in the population-attributable risk of MI compared with BMI.

In contrast, a relatively weak association was seen between the traditional BMI measurement (ratio of body weight divided by height, mathematically squared) and MI across all ethnic groups, and no significant relationship was seen between BMI and MI risk in South Asians, Arabs or mixed-race Africans. In short, INTERHEART showed that the use of BMI as a measure of obesity underestimates the magnitude of obesity-attributable MI risk regardless of age, gender, ethnicity or concomitant medical history.

The clinical implications of these findings boil down to a single message: If practitioners wish to assess patients’ future CVD risk, waist circumference is a critical risk marker in each and every patient, regardless of their baseline BMI. □

Quebec Night a potpourri of music, food for every taste



A feast of music and food awaits at least 1000 delegates expected to attend the Quebec Night at the grande dame Fairmont Château Frontenac starting at 19:30 pm on Monday night.

Delegates will have a chance to discover three different kinds of cuisine—Québécois, French and Aboriginal—in one of three rooms set aside for each of them; a fourth room is designated solely for dessert.

“For entertainment, we have a different music style in each of the rooms as well as in the ballroom,” reveal local arrangement co-chairs Dr. Franck Molin, cardiology researcher, *Centre de recherche de l’Hôpital Laval*, and Dr. Bernard Cantin, Medical Director, Cardiac Transplant Program, *Institut de cardiologie de Québec, Hôpital Laval*.

First, there’s to be the Moondance Orchestra, a small big band-era troupe playing crooner music after the likes of Frank Sinatra, Dean Martin and Michael Bublé. Next up is a Quebec-based group known as the Karma Kameleons who will pay tribute to big hits of the 1980s from stars like Michael Jackson and Duran Duran. The Marginal Donors, backed by lead singer/cardiac transplant surgeon Dr. Heather Ross, University of Toronto, favour music from the 1960s and 1970s, and a jazz trio and DJ lounge music will round out the evening’s full musical repertoire.

“I think anybody who wants to will have an opportunity to be at the Château and find the music they love and are comfortable with,” Dr. Molin indicates.

A shuttle has been organized to ferry guests to the Château Frontenac from the convention centre and the major hotels in Quebec City starting at about 19:00. □

Clinical Teasers

- Three-year follow-up of C-SIRIUS *de novo* CAD patients who received a sirolimus-eluting stent showed benefits seen at one year in patients with long lesions in small vessels were sustained, with no evidence of very late stent thrombosis. Five-year data will be presented. [Schampaert et al., Oral 232. Monday, October 22, 17:15, Room 202, Level 2]
- Tranexamic acid reduced post-operative bleeding by about 50% in patients undergoing off-pump CABG and may eliminate the need for blood scavenging devices. [Bracco et al., Poster 876, Board 134. Tuesday, October 23, 12:30-15:30, Community Forum]
- High thoracic epidural anesthesia provided better myocardial and renal protection and decreased pneumonia rates, in cardiac surgery patients who underwent immediate extubation in the OR (ultra-fast track cardiac anesthesia). [Bracco et al., Poster 880, Board 138. Tuesday, October 23, 12:30-15:30, Community Forum]
- Reduce My Risk—a brief intervention program in which surgical patients who smoked were routinely advised to stop smoking and given help to do so—found that over half seriously tried to quit after they were discharged from hospital and 15% had not taken up smoking again two months after discharge. [Finegan et al., Poster 855, Board 101. Tuesday, October 23, 12:30-15:30, Community Forum]
- High-dose statin therapy reduces the incidence of any cancer by 25% while low-dose statin therapy reduces any cancer risk by 12% compared with non-statin users. [Karp et al., Poster 447, Board 048. Monday, October 22, 12:30-16:30, Community Forum]
- Patients who had their cardiac surgery carried out by supervised residents were not more likely to die in hospital or experience adverse events associated with the surgery than those whose surgery was performed by staff surgeons. Post-operative mortality rates at one, three and five years were almost identical as well. [Martin et al., Oral 983. Tuesday, October 23, 16:30, Room 203, Level 2]
- Sleep deprivation did not affect post-operative outcomes in a large group of cardiac surgery patients whose procedures were undertaken by surgeons who had less than six hours of sleep at night compared with those whose surgeries were carried out by surgeons who got six or more hours of sleep at night. [Chu et al., Oral 550. Monday, October 22, 15:15, Room 203, Level 2]
- Chronic job stress significantly increased the risk of patients having a recurrent CAD event over a follow-up of 5.9 years once they returned to work after their first MI. [Brisson et al., Oral 539. Monday, October 22, 14:30, Room 205A-B, Level 2]
- Old historical pathological specimens have been successfully scanned using MRI techniques. The three-dimensional datasets generated from the scan can now be used towards greater understanding of the congenitally malformed heart without needing to refer to the fragile specimens themselves. [Jutras LC, Poster 668, Board 043. Tuesday, October 23, 10:00-12:30, Community Forum]
- The APPROACH registry database from Alberta indicates that almost half of all patients who underwent non-emergency PCI required re-admission to hospital or attended the ER within six months of the index PCI. [Wold et al. Poster 111, Board 063. Sunday, October 21, 11:30-17:00, Community Forum]

How to curb CVD burden among Canadians: Suggestions welcome at the CHHS-AP workshop

Attendees will be welcome to table their suggestions on how to curb the growing cardiovascular disease (CVD) burden among Canadians during a special workshop on the Canadian Heart Health Strategy-Action Plan (CHHS-AP). The CHHS-AP was announced by federal health minister Tony Clement last October in an effort to improve the future CVD health of all Canadians. The minister promised an initial investment of \$3.2 million to develop a heart health framework and support efforts to address hypertension and CVD surveillance. In 2009-2010, an additional \$5.2 million will be invested each year for all CVD activities. Importantly, the CCS was singled out by the federal government to spearhead the entire initiative, but other partners include the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research. The Public Health Agency of Canada is funding the initiative. Earlier efforts to improve CV health in Canada included the Canadian Heart Health Initiative that focused on prevention and promotion of heart health. The Canadian Stroke Strategy is also focusing on improving access to services for the prevention and treatment of stroke, as well as rehabilitation and reintegration of stroke patients into the community.

Nation-wide Effort

However, to date, a pan-Canadian strategy to improve the CV health of Canadians does not truly exist, nor does any clear collaborative leadership or coordinating mechanisms to guide such a strategy.

Thus, the CHHS-AP, as developed by many members of the CVD community in Canada, represents the first real nation-wide effort to advance CV health care for all Canadians. “Many people at the Congress are participants in the program,” confirms CCS CEO Ann Ferguson, “and there is a real mix of people who have contributed to the process already, including patients and their caregivers.” Chaired by Order of Canada recipient Dr. Eldon Smith, the CHHS-AP is drawing on a wide spectrum of members from the CVD community for their insights into how to improve CV care for all Canadians.

A team of 29 members comprises the CHHS-AP steering committee chaired by Dr. Smith, and it is primarily they who are charged with the development of the action plan by November 2008, one which will cover the full continuum of care from policy and environmental changes through to end-of-life care issues. It will also address disparities in the delivery of that care, suggest and discuss strategies to enhance CVD health, using evidence or best clinical practice to ensure standardization of care.

In May of this year, the CHHS-AP held a consultation meeting in Toronto, where 175 individuals including CHHS-AP steering committee members, members from the six Theme Working Groups, opinion leaders from across the country, consumers, researchers and government officials convened to begin developing a framework for the strategy. The final report to be submitted to the federal minister of health will include a strategy and action plan with recommendations based on the best available evidence.

This scheme will be accompanied by a business plan to support the implementation of their recommendations as well as a plan for a CVD surveillance system. “We are very pleased to be in a position to provide an update on our progress at the CCC,” Dr. Smith observed, “and we hope that attendees will join us to provide input into this potentially important means by which the care system can be made more effective.” The workshop will be held on Monday, October 22, between 14:00 and 15:30, in the Session Theatre at the Community Forum in the convention centre. Delegates can pick up more information at any time at the CHHS-AP booth.

For more information, visit the CHHS-AP Web site at www.chhs-scsc.ca.

DID YOU KNOW...

- A 10-mm Hg decrease in usual systolic BP and a 5-mm Hg decrease in usual diastolic BP is associated with a 15% to 20% reduction in CAD risk.
- A 0.6-mmol/L drop in cholesterol is associated with an 11% to 30% reduction in ischemic heart disease (IHD).
- Diabetes increases the relative risk of fatal CAD by 100% to 200% over non-diabetics.
- Each 1 kg/m² decrease in BMI is associated with a 5% to 10% reduction in IHD risk.
- Sedentary people have a 30% to 70% higher risk of IHD than active people while insufficiently active people have a 20% to 44% higher risk (age-attenuated).
- Current smokers have a 50% to 100% higher risk of CAD than non-smokers while former smokers have a 30% to 72% higher risk.
- Low to moderate alcohol consumption confers a 20% to 50% reduction in CAD risk but heavy drinking increases the risk.
- Higher intake of omega-3 fatty acids likely decreases CAD mortality.

[Luo et al., Poster 287, Board 080. Monday, October 22, 10:00-12:30, Community Forum]

DID YOU KNOW...

- A diet that includes over 30 g/day of fibre reduces stroke by 15%, fatal CAD events by 20%, non-fatal CAD events by 30% and all CAD events combined by 16%.
- A diet that includes five to 10 servings of fruits and vegetables a day reduces stroke by 23%, fatal CAD events by 27%, non-fatal CAD events by 20% and all CAD events combined by 20%.
- Consuming less than three servings of red meat a week reduces fatal CAD events in men, non-fatal CAD events in women as well as all CAD events.

[Dobbins et al., Oral 541. Monday, October 22, 15:00, Room 208A-B, Level 2]





Canadian Cardiovascular Congress 2007

Quebec City, Quebec / October 20-24, 2007

Progress in Assessing Cardiovascular Risk: Refining Atherosclerotic Measurement

Quebec City - The science of estimating cardiovascular (CV) risk is evolving rapidly with major implications for more precise CV risk management. At the Sunday morning symposium, a panel of experts will assess the options for risk assessment, an essential tool for determining how aggressively to manage CV risk factors such as hyperlipidemia. Much of the interest in more accurate risk assessment is being driven by the intensive lipid-lowering trials that are showing consistent risk reductions with greater lipid lowering. In a series of trials using intravascular ultrasound, aggressive lipid lowering has halted progression of atherosclerosis. Use of a potent statin in the ASTEROID trial produced a regression in atherosclerotic plaque burden. The Sunday symposium will provide guidance about when the most effective treatments should be used.

Québec - *L'estimation du risque cardiovasculaire (CV) est une science qui évolue rapidement et dont les retombées – une prise en charge mieux adaptée au risque CV – sont énormes. Au symposium de dimanche matin, un groupe d'experts se penchera sur les options qui s'offrent à nous pour évaluer le risque et qui nous permettent de jauger l'intensité du traitement de facteurs de risque CV comme l'hyperlipidémie. L'intérêt que suscite l'exactitude de l'évaluation du risque découle en grande partie des essais sur le traitement hypolipidémiant intensif ayant prouvé qu'une baisse toujours plus marquée des taux lipidiques se traduit par une réduction systématique du risque. Dans une série d'essais où l'on a eu recours à l'échographie endovasculaire, le traitement hypolipidémiant intensif a réussi à stopper la progression de l'athérosclérose. L'utilisation d'une statine puissante lors de l'essai ASTEROID a donné lieu à une régression de la masse athéromateuse. Le symposium de dimanche aidera les participants à déterminer dans quelles circonstances ils doivent prescrire les agents les plus efficaces.*

By: Ted Bosworth

Efforts to improve risk stratification are critical for directing aggressive therapies to patients who need them most. At Sunday morning's symposium, a panel of experts will discuss how to improve the precision with which high-risk patients are identified. This is a field that has been evolving rapidly on the basis of evidence that vulnerability to plaque rupture may be more important than atherosclerotic burden. It is also clear that patients treated to goal for traditional modifiable risk factors such as hyperlipidemia and hypertension still have residual risk. In the intensive statin trials such as TNT (Treating to New Targets), the rate of cardiovascular (CV) events was still 8.7% in those randomized to the aggressive lipid-lowering arm. Although this was a 22% reduction ($P < 0.001$) in risk relative to less aggressive therapy, it demonstrates room for improvement.

"In my presentation, I will describe current traditional CV risk stratification strategies and critically assess their shortcomings for identifying vulnerable atherosclerotic patients who are candidates for aggressive treatment," reveals Dr. Khurram Nasir, Instructor in Radiology, Massachusetts General Hospital, Harvard Medical School, Boston. "There has been substantial progress in non-invasive imaging technologies for detecting subclinical coronary heart disease, which is helping us understand the clinical risks associated with increasing burden of subclinical atherosclerosis."

Defining the High-risk Patient

Increasingly, "high risk" is understood to be determined by the relative vulnerability of atherosclerotic plaques to rupture, which initiates the cascade of events leading to myocardial infarction and stroke. Risk stratifications which emerged from

the Framingham study or other epidemiologic data are useful, but appear to be incomplete. Additional risk factors, such as levels of C-reactive protein (CRP), may increase the sensitivity of scoring systems to risk of an event, but imaging may provide the most precise picture of plaque vulnerability.

"Although the Framingham risk score remains a reasonable starting point for CV risk stratification, this strategy may underestimate risk in certain populations. The availability of non-invasive imaging techniques to directly visualize atherosclerosis has created considerable excitement about the role of imaging in screening large populations," observes Dr. Milan Gupta, Chief of Cardiology, William Osler Health Centre, Brampton, and Assistant Clinical Professor of Medicine, McMaster University, Hamilton, who is also presenting during the Sunday symposium. Although Dr. Gupta cautions that it "remains to be determined" whether newer strategies incorporating imaging will be cost-effective, he indicates that better risk stratification could lead to improved outcomes. As reflected in the title of the symposium, the goal is to find the vulnerable patient.

Pathophysiology

The concept of the vulnerable patient is built on the concept of the vulnerable plaque. While the size of stenotic lesions was once believed to be an important sign of CV risk, it is now well appreciated that large plaques with thick caps are often less vulnerable to rupture than smaller, more recently formed plaques. Plaque rupture is believed to be the precipitating event in most thrombotic events. Upregulation of the inflammatory system, identified by elevated CRP and other markers, is

believed to contribute to plaque instability and thrombi formation in the event of rupture. A series of recent studies have demonstrated that sufficient reductions in LDL cannot only halt plaque growth but reverse atherosclerosis. In some studies, these reductions have been associated with a reduction in inflammatory markers, such as CRP.

“Dr. Jean-Claude Tardif, Director, Clinical Research, Montreal Heart Institute Research Centre and Professor of Medicine, *Université de Montréal*, will be speaking about intravascular ultrasound (IVUS) in measuring atherosclerosis. Although IVUS is not going to be a practical approach to measuring risk outside of expensive clinical trials, the concept of imaging is a very hot area in cardiovascular risk prediction,” confirms symposium moderator Dr. Jacques Genest, Jr., Director, Division of Cardiology, MUHC-Royal Victoria Hospital, Montreal. “The Holy Grail is imaging that can reveal plaque composition in order to predict risk of rupture, but we are not there yet.”

As a tool for measuring CV disease, IVUS, which is capable of reproducibly measuring the thickness of atherosclerotic plaques, captured attention in a series of lipid-lowering studies. In REVERSAL (Reversal of Atherosclerosis with Aggressive Lipid-Lowering), patients were measured with IVUS after being randomized to pravastatin 40 mg, which reduced average LDL levels to approximately 2.5 mmol/L, or atorvastatin 80 mg, which reduced average LDL levels to approximately 1.6 mmol/L. After 18 months, progression of atherosclerosis as measured with IVUS continued to be observed in those receiving the less aggressive LDL-lowering therapy but not in those receiving the more aggressive cohort. In ASTEROID (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden), the concept was taken a step further by the same team of investigators. In this open-label study, all patients received rosuvastatin 40 mg which reduced average LDL levels to nearly 1.5 mmol/L. For the first time, regression of atherosclerosis was observed.

The results of this study appear to explain why each incremental reduction in LDL in clinical trials has been associated with an additional reduction in risk of thrombotic events. Current Canadian guidelines now suggest that the

treatment goal in all high-risk patients is ≤ 2.0 mmol/L, but clinical trials have yet to show a level of LDL below which no further protection from clinical events is observed. While aggressive lipid-lowering in high-risk patients is well demonstrated, the problem is that many such patients are not achieving treatment goals. One issue may be insufficient uptitration of statin therapies when goals are not achieved. Importantly, statins differ markedly in potency, requiring very high doses of some agents to reach goals.

These relative differences in potency of statins is reflected in a study at this year’s CCC in which the cost-effectiveness of commonly used statins is being compared (Costa-Scharplatz et al., Abstract 859). In that study, the annual cost of reaching treatment goals was calculated using efficacy data from a trial of 2431 patients who had a baseline LDL between 4.0 and 6.5 mmol/L. In the study, the most potent statin, rosuvastatin, was found to be the most cost-effective from a Canadian system perspective. The reason was that lower doses of the more potent agent were more effective in reaching goal. According to the authors, “To achieve the same cost per per cent of LDL reduction as that of 10 mg rosuvastatin, the cost of generic simvastatin 10 mg, 20 mg, 40 mg, and 80 mg needed to be reduced by 26.07%, 26.6%, 18.23%, and 3.55%, respectively.”

With better risk assessment, it is hoped that clinicians will develop a greater sense of urgency for aggressive treatment in those who can be more reliably identified as high-risk. With current categories, many patients at high risk survive event-free while many patients at moderate to low risk experience events. This may discourage the rigorous adherence to treatment guidelines that might be expected to yield improvements in overall survival.

“The problem we have is that risk estimates based on epidemiologic data are very accurate for the general population but less accurate in the individual,” Dr. Genest remarks. Although he cautioned that imaging introduces other issues, particularly those of access and cost, progress in this area has “exciting potential for more precisely identifying the vulnerable patient” and, therefore, the patient most in need of aggressive treatment. □

Please plan to attend:

“The CV Show: Expert Insights into the Management of Cardiovascular Risk in the Vulnerable Patient,”
Sunday, October 21, 7:00-10:00, Room 200B, Level 2.

AND

CCC #859. Costa-Scharplatz M, Beamer B, Frial T, Gandhi SK. Cost-effectiveness of commonly used statins in the management of dyslipidemia: A Canadian system perspective. Tuesday, October 23, 12:30-15:30, Community Forum.

These symposia are accredited and co-developed as an Accredited Group Learning Activity under Section 1 of the framework of Continuing Professional Development options as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada (RCPSC).

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Canadian Cardiovascular Congress 2007

Quebec City, Quebec / October 20-24, 2007

The Evolving Science of Acute Coronary Syndromes Management

Quebec City - The management of acute coronary syndromes has been an area of evolution. Recent studies have emphasized the benefits of antithrombotic therapies but some have also revealed high rates and risks from treatment-associated bleeding complications. At this interactive, case-based session, congress participants will have the opportunity to enhance their knowledge of evidence-based optimal practices for risk stratification and application of early and long-term therapy; efficacy and safety data on newer antithrombotic agents used in the emergency room and at cardiac catheterization; and measures that may help prevent bleeding, the need for transfusion, and associated morbidity and mortality.

Québec - Le traitement des syndromes coronariens aigus est en plein essor. Des études récentes ont souligné les bienfaits des antithrombotiques, mais certaines ont aussi mis en lumière les taux élevés et les risques de complications hémorragiques de ces traitements. Lors de cette séance interactive axée sur des études de cas, les congressistes auront l'occasion d'enrichir leurs connaissances sur les pratiques optimales éprouvées en matière de stratification du risque et de traitement à court et à long terme, sur l'efficacité et l'innocuité des nouveaux antithrombotiques utilisés aux urgences et dans la salle de cathétérismes ainsi que sur les mesures qui pourraient contribuer à prévenir les saignements, la nécessité d'une transfusion et la morbi-mortalité qui en découle.

By: Carol Duthie

The management of acute coronary syndromes (ACS) has been an area of ongoing evolution. Given the volume of data on new strategies, as well as the heterogeneity of clinical presentation and the wide spectrum of risk and prognosis, it can also be an area of uncertainty—especially when a patient's risk of further ischemic events is not clearly high or low. The range of treatments recommended in evidence-based guidelines may also lead to difficulties for emergency room physicians attempting to determine the correct approach for an individual patient. A practical, case-based session on October 20 offers congress participants the opportunity to discuss current findings and recommendations related to several crucial aspects of optimal patient care in ACS.

“There are knowledge gaps and sometimes there is confusion about what is the best treatment, what is the best timing, what is the best dose of medication, [and about the gravity of bleeding as a result of medical treatment]. There's a need to share our understanding of the current evidence. For example, those attending will understand the benefits of new antithrombin agents that have a unique combination of efficacy and safety [and] may be a way in which we can reduce complications,” observes Dr. Jean-François Tanguay, Associate Professor of Medicine, *Université de Montréal*, who will co-chair the meeting with Dr. Salim Yusuf, Professor and Heart and Stroke Foundation Chair in Cardiology, and Director, Population Research Institute, McMaster University, Hamilton.

Risk Stratification

For all patients with ACS, it is essential to undertake an assessment of the risk of subsequent cardiovascular events to ensure appropriate clinical decisions are taken and timing

considerations respected. Inadequate attention to this step may lead to ineffective and inappropriate care and raise the risk of recurrent ischemic events and adverse outcomes. Dr. Jafna Cox, Professor of Medicine and Director of Research (Division of Cardiology), Dalhousie University, Halifax, will examine the importance of risk stratification in estimating prognosis and in influencing decisions on the site of care and early and late therapeutic approaches.

According to newly issued American College of Cardiology/American Heart Association guidelines on unstable angina and non-ST-segment elevation myocardial infarction, early risk stratification should include a medical history, history of angina symptoms, assessment of physical and electrocardiographic (ECG) findings and measurement of troponin (*Circulation* 2007;116(7):803-77). Multivariate tools such as the Thrombolysis in Myocardial Infarction (TIMI) or Global Registry of Acute Coronary Events (GRACE) risk scoring systems can assist in initial and ongoing risk stratification and decisions on treatment options.

Simplified Algorithm

A multidisciplinary group in Ontario recently developed a simplified algorithm that clarifies risk stratification and treatment approaches for patients with non-ST-segment elevation (NSTEMI) ACS (*Can J Cardiol* 2006;22(8):663-77). The algorithm, which promotes both expedited initial management and consistent long-term vascular protection, will be presented by Dr. David Fitchett, Associate Professor of Medicine, University of Toronto and cardiologist, Terence Donnelly Heart Centre, St. Michael's Hospital. To date, the

feedback from Canadian physicians on this practical, guidelines-based tool has been very positive, he adds. "We've simplified risk stratification so that patients are either high-risk or are indeterminate-risk, [the latter] because they haven't been observed long enough to determine whether they are in fact high-risk. It has been an attractive approach because it encourages active management for the high-risk patient and doesn't minimize the risk of the patient without high-risk features – he is at lower risk, but not at 'no risk.'"

Dr. Fitchett will also consider the possible impact on the algorithm of recently updated US and European guidelines for NSTEMI ACS. He notes that a likely point for debate is a statement in the new ACC/AHA document that patients with elevated troponins do not require early catheterization but can be treated conservatively. In addition, he remarked, more information has become available about the role of fondaparinux in the management of patients with ACS. The ACC/AHA guidelines indicate that when a conservative approach is chosen, enoxaparin and fondaparinux are preferred over unfractionated heparin. In patients requiring an invasive strategy, any of the three or bivalirudin are acceptable options. The Canadian experts' algorithm recommends that institutions choose an antithrombin strategy for the majority of patients and use it consistently. Fondaparinux is considered the preferred agent due to its safety profile. Bivalirudin is an option for patients undergoing early angiography.

Focus on Prevention of Bleeding

The benefits of modern antithrombotic therapies have widely been considered to outweigh any increased risk of bleeding. Recently, recognition of the high incidence of bleeding and blood transfusion during index hospitalization and the associated hazards for the patient has meant a re-evaluation of this notion. According to Dr. Christopher Granger, Associate Professor of Medicine and Co-director of Clinical Trials, Duke University Clinical Research Institute, Durham, North Carolina, bleeding and transfusion are each associated with a three- to eightfold increased risk of death for patients with ACS. Dr. Granger will discuss possible biological and clinical explanations for this relationship. He will also recommend strategies for prevention of bleeding, which includes careful selection and dosing of anticoagulants. Radial access for catheterization may also be beneficial.

Data on Newer Antithrombins

Dr. Shamir Mehta, Director of Interventional Cardiology, Hamilton Health Sciences and Associate Professor of Medicine, McMaster University, will review the preferred options for antithrombotic therapy in ACS. An appropriate decision requires consideration not only of efficacy but of the benefit:risk ratio for a given patient.

In recent studies, newer antithrombin agents have demonstrated efficacy comparable to or better than those of older medications but substantially lower rates of bleeding. For example, in the OASIS-5 (Fifth Organization to Assess Strategies for Ischaemic Syndromes. *New Engl J Med* 2006;354:1464-76) study of patients with NSTEMI ACS, the factor Xa inhibitor fondaparinux was noninferior to enoxaparin in reducing death/MI/recurrent ischemia, death/MI and mortality at nine days, and was significantly more effective at reducing all-cause mortality at 30 days and death and ischemic outcomes at six months. Moreover, fondaparinux-treated patients (even those also receiving unfractionated heparin during cardiac catheterization) were about half as likely to experience major bleeding over nine days of therapy, with differences apparent as early as the first day of treatment. Similarly, studies have documented reductions in bleeding with the factor IIa inhibitor bivalirudin vs. glycoprotein (GP) IIb/IIIa inhibitors in patients undergoing catheterization.

One of the benefits of employing fondaparinux as a component of early ACS therapy is a smooth shift from the emergency room to catheterization, as Dr. Mehta will explain. The low risk of bleeding means there is no need to delay the procedure. In the laboratory, unfractionated heparin, bivalirudin or GP IIb/IIIa inhibitors may also be employed as usual. After the procedure, the sheath may be removed immediately if a closure device or radial approach was employed. A delay of six hours is recommended if no closure device was used.

Practical Strategies

Employing cases for illustration and discussion, this three-hour session will focus on practical management in ACS. As Dr. Tanguay emphasizes, "We seek a better understanding of all these important issues. I expect to have people participate and ask questions. It's really a meeting to fulfill the needs of the audience." □

Please plan to attend:

"State of the Art Management of Acute Coronary Syndromes: Integrating New Evidence with Antithrombotic Therapies into Practice," Saturday, October 20, 13:00-16:00, Room 200A, Level 2.

This symposium is accredited and co-developed as an Accredited Group Learning Activity under Section 1 of the framework of Continuing Professional Development options as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada (RCPSC).

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Clinical Supplement



Canadian Cardiovascular Congress 2007

Quebec City, Quebec / October 20-24, 2007

Measuring the Value of Biomarkers in Heart Failure Diagnosis and Management

Quebec City - Canadian Cardiovascular Society (CCS) guidelines indicate that B-type or brain natriuretic peptide (BNP) and the amino-terminal fragment NT-proBNP are a valuable adjunct to clinical evaluation in the diagnosis of heart failure and may be useful in risk stratification and ongoing management. The recent IMPROVE-CHF study determined that physicians' knowledge of NT-proBNP in patients with dyspnea produced time and resource savings in the two months following the patient's first visit. Further analysis of the study data, to be presented here, reveals that patients whose care was guided by NT-proBNP assessment had shorter initial and subsequent hospital stays. Anemia, which is closely associated with elevated NT-proBNP, strongly predicted 60-day rehospitalization in IMPROVE-CHF patients with acute heart failure.

Québec – Selon les lignes directrices de la Société canadienne de cardiologie, le dosage du peptide natriurétique de type B (BNP) et celui du fragment aminé terminal, le NT-proBNP, sont des aides utiles à l'évaluation clinique dans le diagnostic de l'insuffisance cardiaque et pourraient servir à la stratification du risque et à la prise en charge continue. Il est ressorti de l'étude récente IMPROVE-CHF que le médecin qui connaît le taux de NT-proBNP de son patient dyspnéique économise temps et ressources au cours des deux mois suivant la première visite. Une analyse plus approfondie des données de l'étude – qui sera présentée au congrès – a révélé que le séjour initial à l'hôpital et les séjours subséquents étaient plus courts chez les patients dont le plan de traitement avait été guidé par le dosage du NT-proBNP. Lors de l'étude IMPROVE-CHF, l'anémie – qui est étroitement liée à une élévation du taux de NT-proBNP – était un facteur de risque important d'une nouvelle hospitalisation à 60 jours chez les patients souffrant d'insuffisance cardiaque aiguë.

By: Carol Duthie

Heart failure diagnosis is typically based on clinical evaluation, including history, physical examination, chest X-ray, and sometimes a left ventricular function assessment. However, various symptoms of heart failure, such as dyspnea, edema and fatigue, may mimic those of other illnesses. Greater speed and accuracy of heart failure diagnosis in primary and emergency care settings has the potential to expedite and improve both early and longer-term management of the condition.

Several studies have now determined that measurement of B-type or brain natriuretic peptide (BNP) and/or the amino-terminal fragment NT-proBNP are complementary to clinical evaluation in the diagnosis and management of heart failure. Released when cardiac myocytes are stretched excessively, these peptides reach elevated levels in the blood in the setting of heart failure and other conditions in which cardiac ventricles are under strain. Their release leads to decreases in cardiac output and blood volume.

Biomarker Measurement Recommended in Guidelines

In its current guidelines on heart failure (Arnold et al. *Can J Cardiol* 2006;22(1):23-45 and 2007;23(1):21-45), the CCS recommends that one of the two biomarkers should be measured “to help confirm or rule out...heart failure... in patients in whom the clinical diagnosis is in doubt.” Their measurement may also help establish prognosis in patients with confirmed heart failure (for example, the concentration of NT-proBNP in the blood has been shown to be significantly related to New York Heart Association heart failure class) and help guide therapeutic decisions, although the evidence for these

applications is considered less robust, comments Dr. Gordon Moe, Associate Professor of Medicine, University of Toronto, and Director, Heart Failure Program and Biomarker Laboratory, St. Michael's Hospital, Toronto. “For diagnostic purposes...the data are strong. For someone in whom the diagnosis is obvious, I don't think it's helpful. That said, if the patient already has a history of heart failure, it's a good prognostic marker, but the problem is we're not sure how to deal with that information: we know the patients with higher measurements do not do well, but what to do about it? That's still a dilemma. A third indication is following patients in terms of therapy. The data are not very clear-cut yet – that's why we don't give it a very strong recommendation – but that's something to be considered, as well,” Dr. Moe suggests.

Clinicians measuring BNP or NT-proBNP as an adjunct to diagnosis can be guided by the cutpoints in the CCS guidelines, which emanate from the recent PRIDE study (Januzzi et al. *Am J Cardiol* 2005;95:948-54) and take into account the effect of age on NT-proBNP, Dr. Moe adds. For example, in patients aged between 50 and 75 years, heart failure is considered very likely if the patient's NT-proBNP is >900 pg/mL, while the cutpoint is >1800 pg/mL in more elderly individuals.

IMPROVE-CHF Findings

Findings from the IMPROVE-CHF study (Improved Management of Congestive Heart Failure) (*Circulation* 2007;115(24):3103-10) have contributed to the CCS recommendations on the use of BNP or NT-proBNP, notes Dr. Moe. In this study, investigators evaluated the clinical and

economic value of adding NT-proBNP measurement to clinical assessment of patients presenting to emergency rooms with dyspnea of suspected cardiac origin. Five hundred patients (mean age approximately 70 years) were included in the analysis; about 35% had or reported a prior history of heart failure or left ventricular dysfunction. They were randomly allocated to NT-proBNP-guided care (n=246) or usual care (n=254). Physicians caring for the first group were given the NT-proBNP findings and information on their interpretation. “We also did a second NT-proBNP assay on patients who were admitted to hospital and those results were also given to the doctor [to guide management post-discharge],” Dr. Moe specified.

The IMPROVE-CHF results confirmed that NT-proBNP levels have strong predictive value in patients with dyspnea: they are significantly higher in patients with heart failure than in those without (median 3697 vs. 212 pg/mL, $P<0.00001$). The study’s key findings were that management guided by NT-proBNP measurement leads to time and resource savings in the first 60 days after the patient’s presentation. Notably, individuals whose biomarker levels were known spent 21% less time in the emergency room (5.6 vs. 6.3 hours, $P=0.031$) and underwent fewer tests for investigation of dyspnea. In the 60 days following their entry into the study, direct inpatient and outpatient medical costs for patients whose NT-proBNP levels were measured were 15% lower (US\$5180 vs. \$6129, $P=0.0232$). Over the same period, the number of patients who required rehospitalization for heart failure was 35% lower in the NT-proBNP group than in the usual care group. According to Dr. Moe, there are several possible reasons for this finding, including more targeted use of heart failure therapies in patients with a definitive diagnosis.

More Analysis on Outcomes

Dr. Moe and colleagues will present additional analysis from the IMPROVE-CHF study during the scientific sessions on Tuesday, October 23. In one paper (abstract 628), they

indicate that the individuals whose therapy was guided by NT-proBNP had shorter length of both initial hospital stay (4.6 vs. 6.1 days, $P=0.014$) and subsequent hospital stays (1.3 vs. 2.5 days, $P<0.004$). They also had about 50% fewer readmissions (24 vs. 50, $P=0.029$). Dr. Moe comments, “Interestingly enough, NT-proBNP did not predict rehospitalization, which is in contrast to our previous studies. But then, our follow-up was only out to 60 days following randomization, so that may be too soon [to see an effect].” In this analysis, older age was the principal predictor of rehospitalization or death. Body mass index greater than 25-30 kg/m² was predictive of fewer events, Dr. Moe adds.

In a separate presentation, Dr. Moe will describe the finding that anemia strongly predicted 60-day rehospitalization in the IMPROVE-CHF study. “This is observed consistently with the patient with chronic heart failure, but in acute heart failure it has not been reported before,” he remarks. There is a strong relationship between anemia and NT-proBNP, he states. “The higher the NT-proBNP, the lower the hemoglobin.”

Wider Role for Biomarkers?

Current evidence on BNP and NT-proBNP confirms their utility in differentiating heart failure from other conditions causing dyspnea and to some degree in guiding therapy. If the results of IMPROVE-CHF can be extrapolated to national health care, the use of NT-proBNP would mean savings of approximately \$210 to 345 million annually. Unfortunately, Canadian hospitals and physicians have been slow to employ these biomarkers on a routine basis, remarks Dr. Moe. He adds that while the IMPROVE-CHF study focused on emergency room presentation, many elderly patients with dyspnea present to general or family physicians’ offices and that the test might prove highly useful in such primary care settings. “General practitioners see a lot of patients who have shortness of breath and in whom a diagnosis is unclear. This test could be extremely helpful.” □

Please plan to attend:

Oral Sessions: “Heart Failure and BNP.” Tuesday, October 23, 2007, 9:00-10:30, Room 302A-B, Level 3.

9:30 – #628. Provision of knowledge of NT-proB-type natriuretic peptide results improves hospitalization outcomes in patients with suspected acute heart failure. Moe G, Mariano Z, Camacho F.

9:45 – #629. Relationship between anemia and natriuretic peptide level in patients with suspected acute heart failure. Moe G, Mariano Z, Camacho F.

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Canadian Cardiovascular Congress 2007

Quebec City, Quebec / October 20-24, 2007

High Heart Rate and Mortality Risk: A New Cardiovascular Risk Factor?

Quebec City - Evidence indicates that individuals with a persistently high heart rate die sooner than those who do not and this is true of all species, from hummingbirds to whales—the higher the heart rate, the shorter the life span. The mechanism behind this link to longevity is not clear but since the sympathetic nervous system, and adrenalin in particular, activates the heart rate, any activity or state that keeps adrenalin in overdrive is deleterious to the system over the long term. Beta blockers have long been used to slow heart rate, especially in patients with coronary artery disease (CAD) and a prior acute myocardial infarction, but not everyone can tolerate them and there are relative contraindications to their use. With increasing recognition that slowing the heart rate in patients with various manifestations of CAD improves prognosis, new therapies that lower the heart rate specifically, but which are better tolerated than beta blockers, would be a welcome addition to the cardiovascular armamentarium.

Québec – Il a été démontré que les personnes dont la fréquence cardiaque est chroniquement élevée meurent plus jeunes que les autres. Ce phénomène s'applique à toutes les espèces, depuis l'oiseau-mouche jusqu'à la baleine : plus la fréquence cardiaque est élevée, plus la survie est de courte durée. Le mécanisme qui sous-tend ce lien avec la longévité n'a pas été élucidé, mais comme le système nerveux sympathique, l'adrénaline en particulier, accélère la fréquence cardiaque, toute activité ou tout état qui entraîne une hypersécrétion d'adrénaline est délétère à long terme. Les bêta-bloquants sont utilisés depuis longtemps pour ralentir la fréquence cardiaque, surtout chez les patients coronariens ayant des antécédents d'infarctus du myocarde aigu, mais ils ne sont pas toujours bien tolérés et il y a des contre-indications relatives à leur usage. Comme on reconnaît de plus en plus que le ralentissement de la fréquence cardiaque améliore le pronostic chez les patients qui présentent diverses manifestations de la maladie coronarienne, tout nouveau traitement qui ralentirait la fréquence cardiaque, mais qui serait mieux toléré qu'un bêta-bloquant, aurait assurément sa place dans l'arsenal de produits cardiovasculaires.

By: Pam Harrison

Among mammals, the higher the heart rate, the shorter the lifespan. Hummingbirds, for example, with a heart rate of approximately 600 bpm, have dramatically shorter lives than whales, whose heart rate is closer to 20 bpm. In humans, a high resting heart rate is strongly associated with an increased mortality risk in both the general population and in those with various manifestations of coronary artery disease (CAD), including hypertension, acute myocardial infarction (AMI), left ventricular dysfunction and heart failure.

For example, at a median follow-up of 14.7 years, all-cause and cardiovascular (CV) mortality were directly related to resting heart rate at study entry among almost 25,000 men and women with suspected or proven CAD enrolled in the CASS (Coronary Artery Surgery Study) (Diaz et al. *Eur Heart J* 2005;26(10):967-74). In CASS, the hazard ratio (HR) for total mortality was 1.16 for patients with a resting heart rate of between 77 and 82 bpm vs. those with a resting heart rate of ≤ 62 bpm. The HR for total mortality was even higher at 1.32 in CASS patients with a resting heart rate of ≥ 83 bpm. CASS also demonstrated that a resting heart rate of ≥ 83 bpm was a strong predictor of CV mortality as well, at an HR of 1.31, again relative to those with a heart rate of ≤ 62 bpm.

The relationship between heart rate and mortality was also independent of other CV risk factors, including hypertension, diabetes and smoking. As Dr. Paul Dorian, Director, Cardiac Electrophysiology Program, St. Michael's Hospital, and Professor of Medicine, University of Toronto, explained in an

interview, it is not clear why a persistently high heart rate is associated with increased all-cause and CV mortality but his belief is that it may reflect the effect the autonomic nervous system has on the heart, the most important component of which is the sympathetic nervous system, and adrenalin in particular. "The more adrenalin you make, the more activated the system and the more your heart rate goes up," he explains. Conversely, vagal activity counteracts the sympathetic nervous system, slowing heart rate down. Of course, the most important determinant of how much oxygen the myocardium needs is determined by the heart rate, "so the faster the heart beats, the higher the oxygen demand," Dr. Dorian adds.

The fact that most episodes of ambulatory or exercise-induced myocardial ischemia in patients with stable CAD are preceded by an increase in heart rate is testimony to this intimate relationship (Fox et al. *J Am Coll Cardiol* 2007; 50(9):823-30). Indeed, patients with a heart rate >80 bpm experience ischemia almost twice as often as those with a heart rate of <70 bpm, according to the same study. Researchers also found that as heart rate increased, patients experienced a linear and significant increase in episodes of ST-segment depression (Kop et al. *J Am Coll Cardiol* 2001;38(3):742-9, while another group reported that for every five bpm increase in heart rate, there was an 1.14 increase in the incidence of coronary events at 48 months follow-up in a cohort of older CAD patients (Aronow et al. *Am J Cardiol* 1996;78(10):1175-6).

Moreover, heart rate at discharge following an AMI seems to predict mortality outcomes six months later. In the GISSI-3 study, for example, only 1.9% of AMI patients with a heart rate of <60 BPM on hospital discharge had died at six months compared with 9.3% of those with a heart rate of between 81 and 100 BPM and 20.2% of those with a heart rate >100 bpm.

These and other findings support the concept that a high resting heart rate is an independent CV risk factor that carries considerable prognostic weight.

Strategies for Heart Rate and Angina Management

In an effort to reduce mortality risk, beta blockers to lower heart rate have long been used in patients with CAD and heart failure with considerable success. In one review of early randomized trials where beta blockers were given within six hours of AMI symptom onset, it was determined that the mean reduction in infarct size was directly related to the mean reduction in heart rate (Kjekshus JK. *Am J Cardiol* 1986;57(12):43F-49F). In the same article, a review of long-term trials of beta blockers following AMI confirmed a reduction in heart rate was associated with a significant reduction in mortality.

In the Norwegian Timolol Multicenter Study, treatment with timolol was associated with a 41.6% reduction in mortality (Gundersen et al. *Am J Cardiol* 1986; 58(1):20-4). The authors attributed the entire effect of timolol on mortality to its effect on heart rate.

Conversely, beta blockers also reduce myocardial contractility and they can cause paradoxical vasoconstriction of the large epicardial arteries (Borer et al. *Circulation* 2003; 107(6):817-23). Not all patients can safely take beta blockers and they may be contraindicated in patients with peripheral vascular disease, hypotension or obstructive airway disease. Beta blockers and calcium channel blockers, both used to decrease ischemic attacks in CAD patients, do not always provide adequate anti-anginal control either. For example, in one study of patients with stable angina, participants reported a median of

two anginal attacks per week, even though two-thirds of them were taking more than one CV agent (Pepine et al. *Am J Cardiol* 1994;74(3):226-31). The side effects of the beta blockers are also well known, as Dr. Dorian has observed, and include fatigue, sexual dysfunction, cold extremities and provocation of asthma.

Thus, despite having several different drug classes to prevent and treat angina, medical therapies that slow heart rate and diminish myocardial oxygen demand are far from ideal and there is a need for improved or at least additional medical strategies to improve anti-anginal control. To this end, a novel, selective heart rate-lowering agent is being explored that acts specifically on the sinoatrial node. As described by researchers, this new selective heart rate-lowering molecule selectively inhibits the pacemaker I_f in a dose-dependent manner (Tardif et al. *Eur Heart J* 2005; 26(23):2529-36). In a comparison of the molecule with atenolol, the new agent proved to be non-inferior to atenolol, a standard in chronic stable angina. Safety data revealed the agent was well tolerated. The most frequent adverse events were increases in brightness in limited areas of the visual field, which were transient and reversible, leading to treatment discontinuation in fewer than 1% of patients.

Summary

The optimal heart rate for patients with CV disease has not yet been identified but recommendations from both the American Heart Association and the American College of Cardiology indicate that the dosage of beta blockers used should be adjusted to reduce resting heart rate to between 55 and 60 bpm in stable angina patients. In those with more severe angina, heart rate can be reduced to <50 bpm provided patients do not develop symptomatic bradycardia or heart block. Given that physicians routinely measure heart rate in the clinic, this simple parameter should prove useful in the selection of treatment options to lower heart rate now and in the future. □

Please plan to attend:

“The Heart Rate Debate,” Monday, October 22, 13:25, during the symposium “Expert Opinions: Advances in Cardiology,” 12:00-14:00, Room 200B, Level 2. *Presenters:* Dr. Jean-Claude Tardif—“Resting Heart Rate Is a Predictor and Target for Coronary Atherosclerosis Outcomes”/Dr. Beth Abramson—“Heart Rate is a Poor Predictor of Coronary Atherosclerosis Outcomes.”

This symposium is accredited and co-developed as an Accredited Group Learning Activity under Section 1 of the framework of Continuing Professional Development options as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada (RCPSC).

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