SPECIAL ARTICLE

Canadian Cardiovascular Society 2009 Consensus Conference on the management of adults with congenital heart disease: Introduction

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With advances in pediatric cardiology and cardiac surgery, the population of adults with congenital heart disease (CHD) has increased. In the current era, there are more adults with CHD than children. This population has many unique issues and needs. Since the 2001 Canadian Cardiovascular Society consensus conference report on the management of adults with CHD, there have been significant advances in the field of adult CHD. Therefore, new clinical guidelines have been written by Canadian adult CHD physicians in collaboration with an international panel of experts in the field. The present introductory section is a summary of the epidemiology and scope of adult CHD in Canada, the structure of the Canadian health care system and adult congenital cardiac health services in Canada. The recommendations for antibiotic prophylaxis and genetic evaluation in this population are included. The complete document consists of four manuscripts, which are published online in the present issue of *The Canadian Journal of Cardiology*, including sections on genetics, outcomes, diagnostic workups, surgical and interventional options, treatment of arrhythmias, assessment of pregnancy and contraception risks, and follow-up recommendations. The complete document and references can also be found at www.ccs.ca or www.cachnet.org.

Key Words: *Adult congenital heart disease; Congenital heart disease; Endocarditis; Epidemiology; Genetics; Health services*

La conférence consensuelle 2009 de la Société canadienne de cardiologie sur la prise en charge des adultes ayant une cardiopathie congénitale : Introduction

Étant donné les progrès de la cardiologie pédiatrique et de la chirurgie cardiaque, la population d'adultes ayant une cardiopathie congénitale (CPC) a augmenté. Il y a maintenant plus d'adultes que d'enfants ayant une CPC. Cette population a de nombreux problèmes et besoins uniques. Depuis le rapport de la conférence consensuelle 2001 de la Société canadienne de cardiologie sur la prise en charge des adultes ayant une CPC, on constate d'importantes avancées dans le domaine des CPC chez les adultes. Par conséquent, de nouvelles lignes directrices cliniques ont été rédigées par des médecins canadiens s'occupant des CPC chez les adultes, en collaboration avec un groupe d'experts internationaux dans le domaine. La présente introduction résume l'épidémiologie et l'étendue de la CPC chez les adultes au Canada, la structure du système de santé canadien et les services de santé en CPC pour les adultes au Canada. Les recommandations quant à la prophylaxie antibiotique et à l'évaluation génétique de cette population sont incluses. Le document complet se compose de quatre manuscrits publiés par voie électronique dans le présent numéro du *Journal canadien de cardiologie*, y compris des rubriques sur la génétique, les issues, les bilans diagnostiques, les possibilités chirurgicales et d'intervention, le traitement des arythmies, l'évaluation des risques de la grossesse et de la contraception et les recommandations de suivi. Le document complet et les références figurent également aux adresses www.ccs.ca et www.cachnet.org.

EPIDEMIOLOGY AND SCOPE OF THE PROBLEM

Anomalies of the heart and circulation constitute one of the most common forms of congenital birth defects (1). The Canadian Congenital Anomalies Surveillance System measured congenital heart disease (CHD) birth rates, which varied from eight per 1000 live births to 10 per 1000 live births between 1989 and 1999 (1). Although infant mortality rates due to congenital anomalies decreased by 70% between 1960 and 1999 (2), 1.9 deaths per 1000 were still attributed to congenital defects in Canada (1). For congenital cardiac defects, a 39% decline in mortality was documented between 1979 and 1997 in the United States (US), with a rate of 1.5 deaths per 100,000 documented in 2001 (3).

Advances in pediatric cardiology and cardiac surgery have therefore resulted in an increasing number of adult CHD (ACHD) patients and a change in the epidemiology of CHD (4-7). Although the overall prevalence of CHD has increased over time, population trends indicate proportionally different changes in children and adults. The prevalence of severe CHD increased by 85% in adults compared with 22% in children, consistent with the notion that the greatest survival benefit has occurred in those with more severe forms of CHD (7). Over the past two decades, the overall CHD population has aged, most notably in those with severe forms of CHD, where the mean age increased from 11 years in 1985 to 17 years in 2000 (7). In 2000, the median age of the entire adult CHD population was 40 years, while in the subset of adults with severe CHD, the median age was 29 years (7).

Accurate determination of the number of ACHD patients, whether estimated or measured, is difficult (4,7). In a Quebec population-based study, the prevalence of CHD in the year 2000 was four per 1000 adults and 12 per 1000 children. Extrapolated to a Canadian population of 24 million adults (8) and a US population of 209 million adults (9), 96,000 adult patients in Canada and

856,000 adults in the US were expected to have CHD in 2000. In the US and Canada, there is one child for every three adults in the population (8,9). Therefore, although prevalence rates of CHD in children are higher than those in adults, the overall number of adults with CHD exceeds the number of children with CHD (7); and the number of adults and children with severe CHD was nearly equal by the year 2000 (7). In the year 2000, one in 84 persons had CHD diagnosed in childhood and one in 245 adults had CHD (7), corresponding to 181,000 Canadians with CHD. Because the greatest increase in prevalence has been observed in those 13 to 25 years of age between 1985 and 2000 (7), it can be expected that the ACHD population has continued to grow rapidly since the year 2000.

STRUCTURE OF THE CANADIAN HEALTH CARE SYSTEM

The Canadian health care system evolved from the advent of the first public health insurance program in Saskatchewan in 1947, to the Canada Health Act in 1984 (10). This Act resulted in Canada's federal insurance legislation, which defines the principles of comprehensiveness, universality, portability and accessibility to reasonable health care for all Canadians (10). The decades between 1947 and 1984 coincide with a period of accelerated progress in the diagnosis and treatment of CHD with the serial introduction of the most important 'reparative' CHD procedures (11-14). It may be expected that where geographic accessibility was optimal, a majority of Canadians with CHD benefitted from this progress, the result of which is reflected in the changing epidemiology of CHD in Canada. At the current time, patients with CHD in Canada should not be exposed to the same limitations in insurability experienced by those in the US, where ACHD patients are at risk for having no health insurance (15).

The financial burden of general progress in medical and surgical care is considerable. In the 1990s, a 138% increase in per capita health expenditures was observed (10). It is now critical to maintain the continued health of the increasing ACHD population whose disease burden is high (16,17). For most, if not all, diseases, allocation of health care resources has known a pediatric and adult divide for at least the past 50 years, with a bimodal distribution of expenditures; individuals zero to 24 years of age and those older than 65 years of age account for nearly 60% of Canada's total health costs (10). Although predominantly publicly funded, Canada's health care system is partially privately financed. In 2000/2001, the ratio of public and private share of total health care expenditures was 71% to 29%, with a decreasing share of private financing with age from 40% in those zero to 14 years of age, to 21% in those older than 65 years of age (10). From 1980 to 2000, the public share of total health expenditures decreased in all age groups, except in the 25- to 34-year-old population (10), suggesting that in Canada, individuals in their third and fourth decades of life are not seeking additional health insurance.

Per capita health expenditure varies widely with age from $1,437 for those zero to 14 years of age, to $10,834 for those 65 years of age and older (10). This is relevant to the care of the ACHD population, who have a median age between the bimodal pattern of expenditures. These patients may inadvertently escape the public's attention in terms of health advocacy and are, therefore, at risk for inadequate allocation of funds commensurate with their growing needs. The cost of lifelong conditions such as CHD are unknown. Because shifts in the age distribution of diseased populations are expected to change the allotment of health expenditures, we are compelled to address whether disease-specific rather than age-specific models should govern health care budget allocation. Data are needed to determine whether such a change in health care policy could be supported.

ACHD HEALTH SERVICES IN CANADA

In 2000/2001, overall hospital-based expenses in Canada represented 53% of total health expenditures (10). Data on use of inpatient services revealed that over a five-year period, 50% of ACHD individuals in Canada were hospitalized; 16% of these required critical care (17).

Among six large Canadian regional ACHD centres, an average of 10% of patients were hospitalized each year (18). At one large centre in the United Kingdom, the fastest growing segment of hospitalized patients was ACHD patients older than 30 years of age (4).

After leaving pediatric care, a proportion of patients with CHD are not successful in achieving specialized and uninterrupted cardiovascular care in adulthood, and are underserved by the health care system. Examination of the use of health services during the transition years showed that 68% of Canadian ACHD patients visited the emergency department at least once during the five-year period (17). Gurvitz et al (19) examined hospitalization patterns during late adolescence and early adulthood, and found that, although overall hospitalization rates decreased in young adults, a higher proportion of admissions occurred via the emergency department, consistent with a dispersion of care during the transition years. In a pan-Canadian study (20), only 47% of young adults with complex ACHD were successfully transferred to an ACHD centre.

Care for ACHD patients should be integrated from the primary care level to highly specialized subspecialty care in ACHD regional centres (15,21,22). Adult patients with CHD of great complexity should be followed in regional ACHD centres (4,15). Analysis of surgical trends in ACHD patients from 1990 to 2000 revealed that the fastest growing segment of patients requiring interventions were those with disease of moderate complexity (23). The majority of new ACHD patients should be seen at least once by an ACHD specialist to determine the most appropriate venue of care (4,15,22).

The Canadian Adult Congenital Heart Network, founded in 1991 by health care professionals (24), lists 15 self-identified ACHD care facilities of any kind, with varying sizes and services offered, a subset of which are regional ACHD centres (21). This corresponds to one centre per 2.1 million indexed to a Canadian population of 31 million (8). Specialized adult CHD centres in Canada have experienced significant increases in their volume of activities. At the Toronto ACHD regional centre in Ontario, the workload in outpatient visits increased by 268% from 1987 to 1997 (25). In self-reported published data by six well-established regional ACHD centres worldwide, a median of 2850 active registered patients were documented in 2004 (18). An analysis of Quebec data from 1985 to 2000 (7) revealed that the yearly growth of the ACHD population corresponds to 1500 new patients annually, indexed to the Canadian population of the same year.

The proceedings from the 2001 Bethesda Conference recommended that regional centres target an approximate 50% of the ACHD population expected to be at high enough risk to require at least yearly follow-up in a regional ACHD centre, and that low-risk patients should generally be followed in the community (4,22). The catchment population of ACHD centres should therefore include all those with the most complex forms of CHD and most new patients for at least one initial assessment (4). Of the 15 self-reported ACHD Canadian facilities, the nine centres listed on the American Heart Association (AHA) Web site reportedly follow a total of 9778 patients of the approximate minimum 96,000 ACHD patients expected to be alive in Canada. Data are needed to quantify ACHD-dedicated infrastructure, resources and clinical volumes in Canada, and to determine whether wait times for ACHD services are within recommended targets. Outcomes related to care in specialized centres need to be measured. It is likely that pediatric cardiologists will continue to play a significant role at all Canadian ACHD clinics until a higher proportion of ACHD caregivers receives formal training.

The recommended ratio of regional or national ACHD centres to the population is wide: 1:2 million to 1:10 million (22,21). In Canada, where there is one ACHD facility of any kind per 2.0 to 2.5 million population, a minority of ACHD patients are receiving specialized ACHD care. Hospital-linked health service use rates are high, and the demands of transition from the pediatric to adult health care delivery system are not being met, despite a publicly funded health care system. Optimization of transition and services in at least one ACHD centre for a population of 2.0 million adults appears to be

closer to what would be required for improving access to specialized care for ACHD patients in Canada (6). Unique issues specific to ACHD patients include long-term and multisystemic effects of single-ventricle physiology, cyanosis, systemic right ventricles, complex intracardiac baffles and failing subpulmonary right ventricles. Genetic counselling, birth control and high-risk pregnancy management have become integral components of care. Acquired comorbidities, such as diabetes, hypertension and coronary artery disease, may further impact the congenital substrate and potential for long-term adverse events. Complications include distinctive forms of heart failure, pulmonary hypertension, thromboemboli, complex arrhythmias and sudden death. With longer-term survival, quality-of-life issues (such as autonomy, employment, education, functional capacity and physical activities) have assumed increasing importance. To advance the care of ACHD patients, evidenced-based approaches are increasingly sought. Nationally, a critical mass of caregivers is emerging to coordinate medical and scientific advances, and to support patients with CHD as they survive to adulthood and continue to age.

ANTIBIOTIC PROPHYLAXIS

Infective endocarditis is a well-recognized complication of CHD (26). Although data on infective endocarditis in ACHD are limited, recent multi-institutional surveys suggest that morbidity and mortality rates remain elevated in this population (27,28). Recently published guidelines from the AHA have further defined the role of antibiotic prophylaxis in the prevention of infective endocarditis (29). Changes to these recommendations reflect, in part, an increased emphasis on evidence, which has translated into a more restrictive use of antibiotic prophylaxis. Revision of the guidelines was also based on the following (29):

- Endocarditis is much more likely to result from frequent exposure to random bacteremia associated with daily activities than that caused by procedures.
- Prophylaxis prevents an exceedingly small number of cases of endocarditis in individuals who undergo procedures.
- The risk of antibiotic-associated adverse events often exceeds the benefit from prophylactic antibiotic therapy.
- Maintenance of optimal oral health and hygiene is more important than prophylactic antibiotics for a dental procedure to reduce the risk of endocarditis.

The AHA guidelines also emphasize the notion that infective endocarditis in patients with certain high-risk cardiac conditions is associated with particularly poor clinical outcomes. Patients with high-risk cardiac conditions are the ones who should receive antibiotic prophylaxis (29). The list of high-risk cardiac conditions is relevant to the ACHD population and includes the following (29,30):

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair.
- Previous infective endocarditis.
- CHD, specifically:
  - Unrepaired cyanotic CHD, including palliative shunts and conduits;
  - Completely repaired CHD with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure; and
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device.
- Cardiac transplantation recipients who develop cardiac valvulopathy.

Finally, the AHA guidelines describe a more focused list of procedures, in high-risk individuals, for which antibiotic prophylaxis is indicated. They include (29) all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa; and procedures involving the respiratory tract (that involve incision or biopsy), infected skin or musculoskeletal tissue. Gastrointestinal and genitourinary procedures do not require antibiotic prophylaxis (unless there is infection). Antibiotic prophylaxis for tattooing and body piercing is still not recommended (29). Although antibiotic prophylaxis is not recommended for women with structural heart disease at the time of labour and delivery, some experts continue to administer antibiotics because they believe that the risks of bacteremia cannot be predicted in advance, the risks of adverse reactions to antibiotics is small and developing endocarditis has major health consequences.

The Canadian Cardiovascular Society has issued a statement endorsing the AHA guidelines (30,31). The members of this panel also endorse the AHA antibiotic prophylaxis recommendations and its implementation to the ACHD population.

GENETIC EVALUATION

The genetic contribution to CHD has been significantly underestimated in the past. Clinically available genetic testing has increased over the years, as has the availability of newer technology that provides higher resolution to detect subtle genetic aberrations (deletions, duplications and mutations) causing disease. For the clinician caring for a patient with CHD, identifying a genetic etiology is important for several reasons: identification of a syndromic phenotype would help guide investigations for other potential medical problems involving other organ systems; risk stratification, because some syndromes are associated with poor prognosis; genetic and reproductive counselling for recurrence risk in future pregnancies; and screening family members to identify individuals at risk for the cardiac lesion. Current genetic techniques include chromosome analysis or karyotype, and fluorescence in situ hybridization (FISH) (to identify gene deletions) including subtelomeric FISH to identify tiny deletions, duplications or translocations involving the distal ends of chromosomes (32-35). Conventional cytogenetic methods identify large changes in chromosome number or structure. Identification of single gene defects requires mutation analysis using polymerase chain reaction-based assays, denaturing high-performance liquid chromatography, single-strand conformation polymorphism, or exon sequencing (36,37). The vast majority of ACHD patients have not had genetic testing or family screening. The clinician is advised to consult the Gene Tests Web site (www.genetests.org), a publicly funded medical genetics information resource, for updates on what testing is currently available. Readers are referred to the scientific statement from the AHA Congenital Cardiac Defects Committee on the genetic basis of congenital heart defects for additional details, which is also relevant to ACHD (38). It is recommended that the evaluation of ACHD should include the following:

- Detailed family history for birth defects including CHD to identify a potential genetic contribution.
- Physical examination should include evaluation for dysmorphic facies, eye and ear abnormalities, limb defects, other skeletal defects, other organ system involvement, neurodevelopmental delay or learning disabilities.
- Family screening: While most clinically significant CHDs manifest in childhood, others, including atrial septal defects, small ventricular septal defects, bicuspid aortic valve and right aortic arch, may escape attention. Given the phenotypic heterogeneity among family members harbouring the same genetic defect, it is important to screen family members for cardiac defects through electrocardiography or echocardiography.
- Once a genetic etiology is identified in a patient, the family members can be offered genetic testing to identify those at risk of developing a disease needing cardiac evaluation versus genotype-negative individuals who do not need further cardiac evaluation.
- Cytogenetic testing should be considered in the following situations:
  - Recognizable chromosomal syndrome (eg, trisomy 21).
  - Associated dysmorphic features, growth retardation, developmental delay or mental retardation, or multiple congenital anomalies.

○ History of multiple miscarriages and/or family history of birth defects.

• Genetic consultation is recommended in the presence of associated extracardiac anomalies, a clinical suspicion of a genetic abnormality or a positive family history of birth defects. Advanced cytogenetic techniques, including FISH, subtelomeric FISH or multiplex ligation-dependent probe amplification, may be performed when chromosome analysis is normal. Multiplex ligation-dependent probe amplification is a quantitative multiplex polymerase chain reaction approach for determining the relative copy number of a genomic target sequence. It has been shown to be successful in diagnosis of 22q11.2 deletions.

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