Networks in Canadian paediatric surgery: Time to get connected

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There has been a recent trend of improved outcomes for most infants born with surgically correctable congenital malformations, despite the fact that current surgical treatment is not standardized, with wide variations in practice among institutions. Because care for these infants is multidisciplinary, it is difficult to ascertain with clarity the specific role of neonatal surgery in determining outcomes. Moreover, the lack of validated measures of illness severity for most complex congenital malformations makes risk adjustment difficult. For these reasons, the utility of randomized controlled trials in determining best surgical practice in neonatal surgery for congenital malformations is impractical, and another means of deriving medical evidence to justify 'optimal' treatment is necessary.

The Canadian Paediatric Surgical Network (CAPSNet) was developed specifically to address these issues. Patterned after the highly successful Canadian Neonatal Network, CAPSNet collects standardized data on every case of gastroschisis and congenital diaphragmatic hernia evaluated in the 16 referral perinatal centres in Canada. These centres serve as provincial referral centres for perinatal care, and, therefore, the data set created is population-based for gastroschisis and congenital diaphragmatic hernia in Canada. In addition to neonatal data fields recorded in the Canadian Neonatal Network, CAPSNet collects specific prenatal data, and details on surgical treatment and outcomes within each of the 16 participating centres. It is hoped that by using advanced analytical techniques, including outcomes modelling and multiple logistic regression analysis of risk-adjusted outcome variations by type of surgery performed, optimal treatment paradigms will be identified that will lead to further outcome improvement in babies born with complex birth defects.

Key Words: *Congenital diaphragmatic hernia; Gastroschisis; Network; Outcomes; Paediatric surgery*

Les réseaux en chirurgie pédiatrique au Canada : Il est temps de se relier

On remarque une récente tendance vers de meilleures issues pour la plupart des nourrissons nés avec des malformations congénitales pouvant être corrigées par voie chirurgicale, même si le traitement chirurgical actuel n'est pas normalisé et que la pratique varie considérablement d'un établissement à l'autre. Puisque les soins de ces nourrissons sont multidisciplinaires, il est difficile d'établir avec clarté le rôle précis de la chirurgie néonatale dans la détermination des issues. De plus, l'absence de mesures validées de la gravité de la maladie en présence des malformations congénitales les plus complexes complique le rajustement du risque. Pour ces raisons, les essais aléatoires et contrôlés ne sont pas commodes pour déterminer les meilleures pratiques chirurgicales néonatales en cas de malformations congénitales, et d'autres moyens de dériver les données médicales probantes pour justifier le traitement « optimal » s'imposent.

Le *Canadian Paediatric Surgical Network* (CAPSNet) a été mis sur pied précisément pour se pencher sur cette question. Modelé d'après le Réseau néonatal canadien qui fonctionne si bien, le CAPSNet collige des données normalisées sur tous les cas de gastroschisis et de hernie diaphragmatique dans les 16 centres périnatals de référence du Canada. Il s'agit de centres de référence provinciaux en soins périnatals, et par conséquent, l'ensemble de données créées à l'égard du gastroschisis et de la hernie diaphragmatique au Canada se fonde sur la population. Outre les champs de données néonatales du Réseau néonatal canadien, le CAPSNet collige des données prénatales précises et de l'information détaillée sur les traitements chirurgicaux et les issues dans chacun des 16 centres participants. On espère qu'en utilisant des techniques analytiques évoluées, y compris la modélisation d'issues et l'analyse de régression logistique multiple des variations d'issues rajustées selon le risque par type d'opération, les paradigmes de traitement optimal seront dépistés et permettront d'améliorer encore davantage les issues des bébés nés avec des anomalies congénitales complexes.

Over the past decade, there has been an unequivocal acknowledgement of the importance of using quality medical evidence in determining best medical and surgical practices (1). The randomized control trial (RCT) has been accepted as the gold standard in evaluating therapeutic interventions and shaping clinical practices, and in addition to the increased attention given to the conduct of RCTs by industry and funding agencies, there has been a concerted emphasis on the quality of reporting of RCTs through advocacy groups, such as the CONsolidated Standards Of Reporting Trials (CONSORT) group (2).

Paediatricians have long been champions of the practice of evidence-based medicine. Groups such as Children's Oncology Group and its predecessors, the Children's Cancer Study Group and the Pediatric Oncology Group, were among the first to recognize the importance of standardized, protocol-driven clinical trials that sought to enroll virtually every child with cancer in a study that would lead to the creation of high-quality medical evidence and enable continued improvements in paediatric cancer care.

Surgeons, including paediatric surgeons, have been less successful in producing medical evidence of high quality, and have tended to use retrospective cases series as the principle vehicle for reporting surgical outcomes. A computer-assisted English-language search for RCTs in the paediatric surgery literature identified only 134 among more than 80,000 paediatric surgical articles published over a 30-year period (3). An analysis of these 134 trials by 'quality' criteria

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(data collection, randomization and statistical analysis) revealed that the majority of reported RCTs contained a major design flaw. However, in fairness to surgeons, it is important to acknowledge that there are unique challenges inherent to the design and conduct of RCTs in which one surgical therapy is compared with another surgical therapy, a medical therapy or a placebo (4). These challenges include the following:

- the relative infrequency of disease states (this is especially true in neonatal surgery in which rare birth defects are treated), which leads to difficulties in timely accrual of an adequate sample size;
- a lack of clinical equipoise required to justify the ethical comparison of one invasive surgical treatment with another;
- issues related to rapidly evolving technology, where a technique that is likely to change or become obsolete over the predicted period of study precludes its inclusion in a therapeutic trial;
- patient preferences influencing the randomization process. A patient bias for or against surgery versus a medical therapy or placebo, or between surgical procedures, creates difficulties in patient recruitment and threatens the external validity of the study;
- nonstandardization of surgical procedures. Although a single surgeon could be expected to perform an operation in a standardized manner, different surgeons (with variable skills and experience) could not, which makes therapeutic standardization quite difficult when studies include patients accrued from multiple centres. This is in stark contrast to clinical trials involving medication, in which therapy (in the form of a 'pill') is easily standardized;
- the role of 'sham' surgery. Invasive, placebo surgical procedures pose undeniable risks to patients, and many argue against their ethical nature. Also, the surgeon performing the procedure cannot be 'blinded', and therefore must be separated from the assessment of outcome. The potential importance of placebo surgery in analyzing the efficacy of surgical procedures was shown recently in sham surgery-controlled trials for osteoarthritis of the knee (5), and this issue remains controversial.

The above-mentioned challenges represent impediments to the performance of RCTs for the purpose of evaluating surgical procedures. If paediatric surgeons wish to design studies capable of producing high-quality medical evidence, then we need to have or develop alternative strategies for data collection and analysis.

LESSONS LEARNED FROM THE CANADIAN NEONATAL NETWORK

The Canadian Neonatal Network (CNN) was established in 1995 by Shoo Lee and colleagues (6). The CNN consists of 17 neonatal centres that collectively account for 75% of the level III nursery beds in Canada. By compiling and analyzing standardized clinical data in a prospective manner, the CNN has identified several opportunities for neonatal practice improvement, including strategies for reducing the risk of intraventricular hemorrhage in premature infants (7), and improved screening standards for the detection of retinopathy of prematurity (8). However, the CNN does not attempt to influence or create care standards within the participating neonatal centres, and therefore does not rely on RCTs as the means of generating medical evidence. Somewhat simplified, the CNN method of outcomes analysis relies on the facts that neonatal disease states can be severity-stratified; data summarizing risk variables and treatment variables can be standardized; outcomes can be modelled through predictive equations derived from multiple linear or logistic regression analysis of risk variables; and variations in outcome can be at least partially explained by treatment differences in a risk-adjusted cohort.

Because the CNN database is searchable by *International Classification of Diseases*, 10th revision (9) codes, we assessed its utility for studying outcomes of neonatal surgical conditions (congenital diaphragmatic hernia [CDH], abdominal wall defects, intestinal atresias and tracheoesophageal fistula) (10). Although the database gives good information on the number of cases treated in neonatal intensive care units (NICUs) across Canada, it lacks information related to prenatal diagnosis, timing and type of surgery performed, and specific information on outcomes and complications related directly to surgical treatment. In its current form, the CNN database does not discriminate between gastroschisis and omphalocele, both abdominal wall defects but with significantly different treatments and prognoses. Perhaps most significantly, the database only captures patients admitted to the NICU; in some children's hospitals, infants with CDH, and sometimes other neonatal surgical conditions, are preferentially admitted to the paediatric intensive care unit.

CREATION OF A CANADIAN PAEDIATRIC SURGICAL NETWORK

The community of paediatric surgeons across Canada is a close-knit group, unified by its relatively small size and a supportive national society (the Canadian Association of Paediatric Surgeons) that has taken a major advocacy position in support of evidence-based medical practice. Our single-payer health care system and the centralization of paediatric surgical practice within metropolitan, tertiary paediatric centres with close functional links to prenatal diagnosis creates an ideal environment for the creation of a multidisciplinary network focussed on outcomes for prenatally diagnosed birth defects for which major surgery is required in the newborn period. These facts, and the historical success of the CNN, form the foundation for the creation of a multidisciplinary network – the CAnadian Paediatric Surgical Network (CAPSNet) – dedicated to studying outcomes in surgical neonates.

The CAPSNet hospitals include 16 perinatal centres from across Canada (Table 1) that meet the following criteria: a geographically or functionally linked fetal diagnostic unit; a level III NICU; and the availability of subspecialty-trained paediatric surgeons and anesthesiologists. Each CAPSNet hospital has at least one site investigator from a multidisciplinary clinical group that includes surgeons, neonatologists, perinatologists and medical geneticists, and each centre is responsible for its own data collection, which is performed by hired, trained data abstractors. The site investigators report to a steering committee, which has administrative oversight over the data collection, handling and reporting; knowledge dissemination; and budgetary issues.

TABLE 1
Canadian Pediatric Surgery Network centres

Hospital	ECMO
Victoria General Hospital, Victoria, British Columbia	No
BC's Children's Hospital, Vancouver, British Columbia	Yes
Alberta Children's Hospital, Calgary, Alberta	No
Royal Alexandra Hospital, Edmonton, Alberta	Yes
Royal University Hospital, Saskatoon, Saskatchewan	No
Health Sciences Centre, Winnipeg, Manitoba	No
The Hospital for Sick Children, Toronto, Ontario	Yes
McMaster Children's Hospital, Hamilton, Ontario	No
St Joseph's Health Centre, London, Ontario	No
Children's Hospital of Eastern Ontario, Ottawa, Ontario	No
Kingston General Hospital, Kingston, Ontario	No
Montreal Children's Hospital, Montreal, Quebec	Yes
Hôpital Sainte-Justine, Montreal, Quebec	No
Centre Hospitalier de l'Université Laval, Sainte-Foy, Quebec	No
IWK Health Centre, Halifax, Nova Scotia	No
Janeway Children's Health and Rehabilitation Centre, St John's, Newfoundland	No

ECMO Extracorporeal membrane oxygenation

CAPSNet DATA COLLECTION

In choosing pilot diagnoses for CAPSNet data collection, we wanted to select neonatal conditions that occur frequently, are easily diagnosed prenatally, and for which there is considerable uncertainty regarding optimal perinatal care. Two diagnoses that easily meet these criteria are CDH and gastroschisis. CDH is a condition with a highly variable outcome (11,12) and several areas of therapeutic controversy, including modality and intensity of ventilatory support (13,14), role of extracorporeal life support (15), and timing and type of surgery (16,17) performed to correct the diaphragmatic defect. Gastroschisis is a common birth defect with an expected survival of greater than 90% (18). There are areas of controversy regarding the timing and type of delivery (19-21), and the surgical technique used to close the abdominal defect (22-24). Both diagnoses yield babies that have long hospital stays and consume considerable resources; thus, identification of treatment strategies that improve outcome will increase the efficiency of resource use and benefit our health care system as well.

Patient information will be abstracted regularly by trained data abstractors and will include prenatal diagnostic information specific to the antenatal diagnosis, as well as daily postnatal treatment and outcomes data during the entire postnatal hospitalization, regardless of hospital unit. Deidentified data will be transmitted electronically to the Centre for Healthcare Innovation and Improvement in Vancouver, British Columbia, where the data is cleaned, stored and managed thereafter by a geographically representative multidisciplinary steering committee comprised of epidemiologists, informatics experts, surgeons, neonatologists and perinatologists.

PATIENT INFORMATION

Each patient's data file will be opened at either prenatal diagnosis or birth (if no prenatal diagnosis is made). Prenatal information includes parental demographic data; detailed antenatal history, including perinatal diagnostic data, which is specific to both diagnoses; timing and mode of delivery; and maternal outcomes. It will also include information on all pregnancy outcomes, including spontaneous and therapeutic abortion and stillbirths. Infant characteristics will include sex, size, associated anomalies, Apgar scores, illness severity profiles (Score for Neonatal Acute Physiology, version II [SNAP-II] [25]) and therapeutic intensity profiles (Neonatal Therapeutic Intensity Scoring System [26]). Treatment fields will include information on the timing of surgery, surgical and anesthetic techniques, perioperative monitoring and postoperative care. Among many outcome variables reported, those most relevant to CDH and gastroschisis patients are survival to discharge, survival with major morbidity (ie, chronic lung disease for CDH and short gut syndrome for gastroschisis), length of hospital stay, surgical complications, and data on technology and resource use, including information on vascular access (umbilical, central and peripherally inserted central catheters), respiratory support (nature and duration of support, and respiratory adjuncts, including surfactant, nitric oxide and extracorporeal life support), nutritional support and use of blood products.

SPECIFIC OBJECTIVES OF CAPSNet

Because prenatal diagnosis and perinatal treatment of birth defects is perinatal centre-based, and because the CAPSNet hospitals provide essentially all of the perinatal care in Canada, it would be reasonable to assume that our data set will be population-based. We hope, therefore, that by tracking all outcomes (including prenatal outcomes of termination, spontaneous loss or stillbirths), we will be able to derive a true Canadian incidence for CDH and gastroschisis. Another important objective is to develop and validate an illness severity measure for both conditions. Using data from the CNN on a cohort of patients with CDH, we have derived a predictive equation for survival, in which a combination of gestational age and NICU admission day SNAP-II score predicts, with good calibration and discrimination, the

likelihood of survival to NICU discharge (27). To derive a similar equation for gastroschisis, we will need to consider risk factors that have been purported to be predictive of outcome in retrospective literature (eg, severity of bowel injury, gestational age at delivery, route of delivery and fetal growth profile) and model these against a variety of outcomes (eg, survival, length of hospital stay and time to full enteral nutrition). Finally, we will use the methodology of the CNN to study outcome variations and to determine what role treatment paradigms play in determining outcome.

CURRENT STATUS AND FUTURE OF CAPSNet

In June 2004, we received a four-year award from the Canadian Institutes of Health Research to proceed with the CAPSNet project. The database was created, data abstractors were hired and trained, and data collection commenced in May 2005. To date, all CAPSNet centres have enrolled at least one patient. The future of databases such as CAPSNet includes expansion to other neonatal surgical conditions, and transfer of responsibility for database maintenance from external funding agencies to hospitals and provincial health jurisdictions. Eventually, we hope that it will be possible to establish data links to centres outside Canada through the development of international neonatal networks that seek to share standardized data on large patient populations for the purposes of improving child and maternal outcomes worldwide.

REFERENCES

1. Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA 1992;268:2420-5.
2. Begg C, Cho M, Eastwood S, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA 1996;276:637-9.
3. Moss RL, Henry MC, Dimmitt RA, Rangel S, Geraghty N, Skarsgard ED. The role of prospective randomized clinical trials in pediatric surgery: State of the art? J Pediatr Surg 2001;36:1182-6.
4. Solomon MJ, McLeod RS. Should we be performing more randomized controlled trials evaluating surgical operations? Surgery 1995;118:459-67.
5. Moseley JB, O'Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2002;347:81-8.
6. Lee SK, McMillan DD, Ohlsson A, et al. Variations in practice and outcomes in the Canadian NICU network: 1996-1997. Pediatrics 2000;106:1070-9.
7. Synnes AR, Chien LY, Peliowski A, Baboolal R, Lee SK; Canadian NICU Network. Variations in intraventricular hemorrhage incidence rates among Canadian neonatal intensive care units. J Pediatr 2001;138:525-31.
8. Lee SK, Normand C, McMillan D, Ohlsson A, Vincer M, Lyons C; Canadian Neonatal Network. Evidence for changing guidelines for routine screening for retinopathy of prematurity. Arch Pediatr Adolesc Med 2001;155:387-95.
9. World Health Organization. International Classification of Diseases, 10th Revision. Geneva: World Health Organization, 1992.
10. Skarsgard ED, Blair GK, Lee SK. Toward evidence-based best practices in neonatal surgical care-I: The Canadian NICU Network. J Pediatr Surg 2003;38:672-7.
11. Reickert CA, Hirschl RB, Atkinson JB, et al. Congenital diaphragmatic hernia survival and use of extracorporeal life support at selected level III nurseries with multimodality support. Surgery 1998;123:305-10.
12. Boloker J, Bateman DA, Wung JT, Stolar CJ. Congenital diaphragmatic hernia in 120 infants treated consecutively with permissive hypercapnea/spontaneous respiration/elective repair. J Pediatr Surg 2002;37:357-66.
13. Cacciari A, Ruggeri G, Mordenti M, et al. High-frequency oscillatory ventilation versus conventional mechanical ventilation in congenital diaphragmatic hernia. Eur J Pediatr Surg 2001;11:3-7.
14. Somaschini M, Locatelli G, Salvoni L, Bellan C, Colombo A. Impact of new treatments for respiratory failure on outcome of infants with congenital diaphragmatic hernia. Eur J Pediatr 1999;158:780-4.
15. Frenckner B, Ehren H, Granholm T, Linden V, Palmer K. Improved results in patients who have congenital diaphragmatic hernia using preoperative stabilization, extracorporeal membrane oxygenation, and delayed surgery. J Pediatr Surg 1997;32:1185-9.
16. Langer JC, Filler RM, Bohn DJ, et al. Timing of surgery for congenital diaphragmatic hernia: Is emergency operation necessary? J Pediatr Surg 1988;23:731-4.
17. Moyer V, Moya F, Tibboel R, Losty P, Nagaya M, Lally KP. Late versus early surgical correction for congenital diaphragmatic hernia in newborn infants. Cochrane Database Syst Rev 2002;(3):CD001695.
18. Baerg J, Kaban G, Tonita J, Pahwa P, Reid D. Gastroschisis: A sixteen-year review. J Pediatr Surg 2003;38:771-4.
19. How HY, Harris BJ, Pietrantoni M, et al. Is vaginal delivery preferable to elective cesarean delivery in fetuses with a known ventral wall defect? Am J Obstet Gynecol 2000;182:1527-34.
20. Adra AM, Landy HJ, Nahmias J, Gomez-Marin O. The fetus with gastroschisis: Impact of route of delivery and prenatal ultrasonography. Am J Obstet Gynecol 1996;174:540-6.
21. Sipes SL, Weiner CP, Sipes DR II, Grant SS, Williamson RA. Gastroschisis and omphalocele: Does either antenatal diagnosis or route of delivery make a difference in perinatal outcome? Obstet Gynecol 1990;76:195-9.
22. Coughlin JP, Drucker DE, Jewell MR, Evans MJ, Klein MD. Delivery room repair of gastroschisis. Surgery 1993;114:822-7.
23. Schlatter M, Norris K, Uitvlugt N, DeCou J, Connors R. Improved outcomes in the treatment of gastroschisis using a preformed silo and delayed repair approach. J Pediatr Surg 2003;38:459-64.
24. Kidd JN Jr, Jackson RJ, Smith SD, Wagner CW. Evolution of staged versus primary closure of gastroschisis. Ann Surg 2003;237:759-64.
25. Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II: Simplified newborn illness severity and mortality risk scores. J Pediatr 2001;138:92-100.
26. Gray JE, Richardson DK, McCormick MC, Workman-Daniels K, Goldmann DA. Neonatal therapeutic intervention scoring system: A therapy-based severity-of-illness index. Pediatrics 1992;90:561-7.
27. Skarsgard ED, MacNab YC, Qiu Z, Little R, Lee SK; Canadian Neonatal Network. SNAP-II predicts mortality among infants with congenital diaphragmatic hernia. J Perinatol 2005;25:315-9.