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REVIEW ARTICLE/BRIEF REVIEW

Perioperative care of adults with Down syndrome: a narrative review

Soins périopératoires des adultes atteints du syndrome de Down: un compte rendu narratif

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Abstract *Because of enhanced life expectancy due to medical and surgical therapeutic advances, it is estimated that there are more adults than children living with Down syndrome (DS), or trisomy 21, in the United States. Therefore, DS can no longer be considered a syndrome limited to the pediatric population. These patients are presenting for surgery and anesthesia in adult care settings, where anesthesiologists will encounter these patients more frequently. As these patients age, their commonly associated co-morbidities not only progress, but they also develop other cardiac, respiratory, gastrointestinal, and neurologic conditions. The manifestations and consequences of chronic disease can present new challenges for the anesthesiologist and require expertise and judgement to minimize patient risk. The purpose of this narrative review is to describe the common pediatric co-morbidities associated with DS and discuss the age-acquired manifestations. Additionally, considerations for anesthetic care of the adult with DS will be presented, including the preoperative assessment, intraoperative management, and postoperative care.*

Résumé *En raison de l'augmentation de l'espérance de vie grâce aux progrès thérapeutiques médicaux et chirurgicaux, on estime qu'il y a plus d'adultes que d'enfants vivant avec le syndrome de Down, ou trisomie 21, aux États-Unis. Pour cette raison, le syndrome de Down ne peut plus être considéré comme une affection qui se limite à la population pédiatrique. Ces patients se présentent pour des chirurgies et donc de l'anesthésie dans des contextes de soins adultes, où les anesthésiologistes rencontreront ces patients plus fréquemment. Au fur et à mesure que ces patients vieillissent, non seulement les co-morbidités qui leur sont communément associées progressent, mais ils développent également d'autres problèmes cardiaques, respiratoires, gastro-intestinaux et neurologiques. Les manifestations et les conséquences de la maladie chronique peuvent présenter de nouveaux défis pour l'anesthésiologiste et nécessitent expertise et jugement afin de minimiser les risques pour le patient. Le but de ce compte rendu narratif est de décrire les co-morbidités pédiatriques fréquemment liées au syndrome de Down et de discuter des manifestations acquises avec l'âge. En outre, des considérations concernant les soins anesthésiques de l'adulte atteint du syndrome de Down seront présentées, y compris l'évaluation préopératoire, la prise en charge peropératoire, et les soins postopératoires.*

Keywords Down syndrome · trisomy 21 · perioperative management · adults with pediatric disease · transition of care · pediatric anesthesiology

Approximately 750,000 pediatric patients with chronic diseases become adults each year in the United States.[1] The process for the transition from the pediatric to adult healthcare system and age at which this transition takes place has not been standardized. Therefore, these patients, often with long medical histories, will present for surgery and anesthesia in adult care settings. As the life expectancy of patients with pediatric chronic diseases increases, the manifestations and consequences of these conditions can present new challenges for the "adult" anesthesiologist who has little exposure to a pediatric population.

Down syndrome (DS), or trisomy 21, is no longer a syndrome limited to the pediatric population. The overall

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prevalence of DS is increasing, but solely in the age groups above 19 yr old.[2,3] The pediatric prevalence has remained stable since the 1960s, and 80% of people with DS are surviving into adulthood.[4] This is due to improved surgical techniques and better management of congenital heart diseases (CHD) since the 1970s. The median age of death at that time was under ten years old, which increased to 35 yr old in the 1980s, and today reaches almost 60 yr old.[4–6] It is now estimated that there are more adults living with DS than children.[2,3] Reflecting this longevity, dementia is now the third leading cause of death in DS patients, following cardiac and respiratory causes.[4,7]

Guidance for the medical management and health screening of DS patients were written for pediatricians in 1994 and revised in 2011, but do not specifically address preoperative evaluation.[8] Few clinical trials have involved adults with DS and therefore consensus on screening recommendations or treatment of chronic conditions for adult DS patients does not exist.[9] A recent systematic review of a growing literature of clinical experience with this population in internal medicine and family practice specialties defined the most frequent chronic conditions reported in adults with DS and suggested a path for future guidelines.[3,10] For now, comprehensive guidelines for the perioperative care and anesthetic management of the adult with DS are lacking. This narrative review will highlight the common pediatric co-morbidities associated with DS and review how these conditions progress with age. Adult-acquired co-morbidities and manifestations in this population will also be discussed. Finally, considerations for perioperative and anesthetic management of the adult with DS will be presented.

Pediatric co-morbidities of DS that progress with age

Down syndrome is associated with a wide variety of systemic co-morbidities, and most of these conditions not only persist into adulthood but also worsen as the patient ages. Table 1 provides a system-wise summary of these common pediatric co-morbidities in DS. Down syndrome patients are prone to conductive hearing loss and vision issues, which continue to worsen with age.[11,12] Age-related sensorineural hearing impairment is reported in up to 73% of DS adults at a time period of 30–40 years earlier than the general population.[5] It has also been reported that 100% experience hearing loss by 60 yr old.[3] Autism has been reported to be almost ten times more common in children with DS than in the general population.[4]

The characteristic facial features of DS patients, which include mid-face hypoplasia, macroglossia, micrognathia, high-arched palate, poor dentition, and small upper airway,[13–15] predispose these patients to obstructive sleep apnea (OSA); there is an 85% prevalence of OSA among DS adults, with a mean apnea-hypopnea index of 25.[3] Additionally, airway management can be difficult and these patients may have laryngotracheal or subglottic stenosis.[16,17] While subglottic stenosis is commonly associated with children with DS, its frequency in adults is unclear. Dental lesions are frequently encountered in DS children, as well as respiratory infections. Down syndrome patients are prone to infection as a result of their lower cellular and humoral immunity, anatomical defects of the respiratory tract, and high rates of gastroesophageal reflux (GERD), dysphagia, and OSA.[5,18] Increased adjusted relative risk (RR) ratios of pneumonia (RR, 6.60; 95% confidence interval [CI], 4.44 to 9.80), bronchitis (RR, 6.79; 95% CI, 4.51 to 9.95), and respiratory failure (RR, 4.20; 95% CI, 2.24 to 7.87) have been reported in DS adults compared with controls.[19] Influenza and pneumonia account for 25% of hospital admissions in these adult patients and pneumonia is the cause of death in 25–50% of DS adults, with infection-related mortality increasing with age.[4,5,7,20] This is an important consideration for the postoperative period, as these patients may be more prone to developing infectious complications, including pneumonia, aspiration pneumonitis, and urinary tract infections, leading to longer hospital stays and increased infection-related mortality with age.[5,21]

Cardiac diseases are the leading cause of death for adults with DS, accounting for 25–40% of mortality.[4] Approximately half of all DS patients have CHD, most commonly involving endocardial cushion defects such as atrioventricular septal defects (AVSD), atrial septum defects (ASD), ventricular septum defects (VSD), and Tetralogy of Fallot (Table 2).[4] Complete or partial AVSD is the most frequent CHD in DS patients, with a 30–60% incidence.[22] Surgical correction usually occurs before the individual is six months old, before heart failure and pulmonary circulation overload occurs as a result of gradually falling pulmonary vascular resistance (PVR) after birth and bidirectional shunting. Surgical repair of endocardial cushion defects is challenging and usually associated with some degree of regurgitation across newly constructed tricuspid and mitral valves, which may worsen as age advances. Repair also can produce atrioventricular conduction tract fibrosis, progressing to symptomatic bradycardia or complete AV block in 25% of adults with DS, necessitating pacemaker placement.[22–24] In addition, residual VSD and left ventricular outflow tract obstruction or subaortic stenosis may be encountered.[22,23,25] For ASDs and VSDs, the degree of left-to-right shunting, pulmonary hypertension, and volume overload causing dilation and hypertrophy determines the timing of repair. Large ASDs or VSDs may require surgical or device closure by six months old, while small ASDs or VSDs may become

TABLE 1 Common pediatric co-morbidities associated with Down syndrome that progress with age

System	Co-morbidity	% in DS	% in general population*
Central nervous system	Hearing loss	12–100[4,5,44]	15
	Vision loss	60–70[4]	2–3[72]
Psychiatric	Autism spectrum disorder	7.4–18.2[73]	2
HEENT	Obstructive sleep apnea	85[3]	17–22[75]
	Tracheal stenosis	6[74]	0.63[74]
	Dental lesions	94[4]	17–32
	Respiratory infections	20–40[20]	0.5
Cardiovascular	Congenital heart disease	40–50[4]	1
	Atrioventricular septal defect	30–60[22]	3[25,26]
	Atrial septal defect	16–21[22]	6–10[25]
	Ventricular septal defect	14–22[22]	30[25]
	Tetralogy of Fallot	2–11[22]	10[25]
	Pulmonary hypertension	5–34[36]	0.1[36]
Musculoskeletal	Atlantoaxial instability from ligamentous laxity	14[4,5,44]	rare
Gastrointestinal	Hirschsprung's disease	2–15[5]	0.15[5]
	GERD/dysphasia	50[4,5]	20[76]
Endocrine	Thyroid dysfunction	7–50[4,5,44]	12[77]
	Type 1 diabetes	4[5]	1
Immune	Leukemia	2.7[4]	<0.1

*Unless otherwise specified, all information for the general population is sourced from the Center for Disease Control

DS = Down syndrome; GERD = gastroesophageal reflux disease; HEENT = head, ear, eye, nose, throat

clinically significant later in life.[25,26] Additionally, if PVR increases above systemic vascular resistance (SVR), a right-to-left shunt may result in hypoxia, risk of paradoxic embolus, and Eisenmenger syndrome.[25] While rare, Eisenmenger syndrome is most commonly linked with the DS population.[13,27]

Tetralogy of Fallot is the most common cyanotic CHD and may be associated with AVSD in DS. Surgical repair is typically undertaken between six and 12 months. Long-term sequelae of repair include pulmonary regurgitation or residual pulmonary stenosis requiring valve replacement, arrhythmias necessitating a pacemaker or defibrillator, residual shunt lesions, and right ventricular dilation and failure.[25,28]

Single ventricle pathology, such as tricuspid atresia, hypoplastic left heart, and double outlet right ventricle, is rare in DS but represents a high-risk patient population.[29,30] Early single ventricle palliation, which is still seen in some adults, involves an anastomosis connecting the right atrium directly to the pulmonary artery. Later complications of this repair include atrial dilation, atrial thrombosis, atrial tachyarrhythmia, and pulmonary vein stenosis.[31] Modern palliation is the total cavopulmonary connection (TCPC), which is performed in staged surgeries (Glenn and Fontan procedures), in which systemic venous return is passively directed to a common pulmonary venous atrium via either an intra-arterial (lateral tunnel) or extra-cardiac conduit "baffle," and then flows to the single ventricle, which pumps oxygenated blood to the systemic circulation.[31,32] Fenestrations, or small holes between the common atrium and baffle, may be performed with either approach to serve as a "pop-off" valve to temporarily support cardiac output at the cost of systemic desaturation in the case of pulmonary hypertensive crisis. As the TCPC patient ages, Fontan failure and complications may involve arrhythmias requiring pacemaker or defibrillator placement (atrial fibrillation, atrial flutter, intra-atrial reentrant tachycardia, or ventricular tachycardia); heart failure; chronic hypoxia and elevated PVR from increasing right-to-left shunt (persistent fenestration, baffle leak) or low pulmonary venous saturation (pulmonary effusions, plastic bronchitis); protein-losing enteropathy; liver and renal failure from low cardiac output and systemic venous hypertension; and embolic events secondary to fenestration.[31,32] Additionally, DS Fontan patients with OSA or recurrent respiratory complications are at elevated risk for pulmonary hypertension.[33]

Overall, pulmonary hypertension has a higher incidence in children with DS.[34] Shunting can increase blood flow to the pulmonary vasculature, inducing endothelial dysfunction, intimal fibrosis, and vascular remodelling. Other intrinsic physiology to DS patients, including

TABLE 2 Anesthetic management of common congenital heart disease in Down syndrome

Lesion	Corrected			Uncorrected	
	Surgical repair	Hemodynamic concerns	Management goals	Hemodynamic concerns	Management goals
AVSD	Atrial patch Ventricular patch	Mitral or tricuspid regurgitation Atrioventricular block Bradycardia Residual VSD Subaortic stenosis/ left ventricular obstruction	Maintain or decrease SVR Maintain sinus rhythm and avoid bradycardia Avoid air bubbles	Bidirectional shunting: • Right heart failure • Pulmonary hypertension • Left heart failure	Maintain or decrease PVR Maintain SVR Avoid air bubbles Avoid additional preload Maintain contractility
ASD	Atrial patch	Atrioventricular block Bradycardia	Maintain sinus rhythm and avoid bradycardia	Left-to-right shunt: • Right heart dilation, hypertrophy, and failure • Arrhythmias, including atrial fibrillation • Pulmonary hypertension Shunt reversal: • Hypoxia • Embolus • Eisenmenger syndrome	Maintain or decrease PVR Maintain SVR Avoid air bubbles
VSD	Ventricular patch	Atrioventricular block Residual shunt	Maintain sinus rhythm and avoid bradycardia Avoid air bubbles	Left-to-right shunt or bidirectional shunting: • Right heart dilation, hypertrophy, and failure • Pulmonary hypertension • Left heart dilation, hypertrophy, and failure • Arrhythmias Shunt reversal: • Hypoxia • Embolus • Eisenmenger syndrome	Maintain or decrease PVR Maintain SVR Maintain sinus rhythm Avoid air bubbles Avoid additional preload Maintain contractility
TOF	Resection of RVOT VSD closure Pulmonary valvotomy Transannular patch	Pulmonary regurgitation or stenosis Right heart dilation and failure Residual shunt Atrioventricular block Arrhythmias Sudden cardiac death	Decrease PVR Avoid air bubbles Maintain sinus rhythm and avoid bradycardia Maintain contractility	Right-to-left shunt • Hypoxia • Cyanosis Right ventricular hypertrophy and dysfunction from outflow tract obstruction	Decrease PVR Increase SVR Increase preload Decrease heart rate Maintain contractility

TABLE 2 continued

Lesion	Corrected			Uncorrected	
	Surgical repair	Hemodynamic concerns	Management goals	Hemodynamic concerns	Management goals
Single ventricle pathology	Total cavopulmonary connection (Glenn and Fontan)	Arrhythmias Hypoxia Pulmonary hypertension Heart failure Protein-losing enteropathy Liver failure Renal failure Embolic events (if fenestrated)	Augment preload Decrease PVR Avoid increased SVR Maintain contractility and sinus rhythm Avoid air bubbles	Varies by specific lesion/pathology	Varies by specific lesion/pathology

ASD = atrial septal defect; AVSD = atrioventricular septal defect; PVR = pulmonary vascular resistance; RVOT = right ventricular outflow tract; SVR = systemic vascular resistance; TOF = Tetralogy of Fallot; VSD = ventricular septal defect

pulmonary hypoplasia from alveolar development abnormalities and excess antiangiogenic factors, impairment of nitric oxide production, upregulation of pro-inflammatory genes contributing to endothelial dysfunction, and chronic hypoxia from OSA, respiratory tract infections, and chronic aspiration, can increase PVR.[23,24,34–36]

In approximately 15% of children with DS, ligamentous laxity leads to occipitoatlantoaxial instability evident on radiographs, although only 1–2% of patients report symptoms.[5] Because atlantoaxial instability may cause spinal cord compression, careful attention should be paid to head and neck positioning during intubation and surgery.[37,38] As adults, ligamentous laxity leads to acquired hip dislocation and other common orthopedic problems, including scoliosis, osteoarthritis, and degenerative joint disease.[18,21]

Visceral anomalies seen in the pediatric DS patient include GERD, duodenal atresia, imperforate anus, and Hirschsprung's disease. Gastroesophageal reflux and dysphasia commonly progress as patient's age with 50% showing risk factors for aspiration,[4] and the manifestations from surgical management of these anomalies can require care as an adult patient.

Hypothyroidism is common in both adults and children with DS, occurring in approximately one-third of the DS population. The likelihood of autoimmune thyroiditis increases with age and the prevalence of all thyroid disorders, including hyperthyroidism, is higher in DS than in the general population.[3,4] Screening for thyroid disorders should be done throughout life, as clinical diagnosis is unreliable in DS patients because of overlap with features commonly seen in the syndrome, such as dry skin, thin hair, and constipation.[39] The rate of type 1 diabetes mellitus is four times higher in DS patients. Last, there is a 10- to 20-fold increase in the risk of leukemia in these children; fortunately, this is one of the few pediatric conditions that is not seen commonly in the adult population.[4]

Age-acquired manifestations

Table 3 summarizes the age-acquired manifestations of DS by system. Dementia, including Alzheimer's, is a common age-acquired condition in DS. Genetic mutations in the amyloid precursor protein (APP) or enzymes involved in APP cleavage to amyloid beta peptide have been shown to cause early-onset Alzheimer's disease.[40] Because APP is encoded by a gene located on chromosome 21 and DS patients have three copies of this chromosome, the onset of dementia is usually earlier in DS patients compared with the general population. Mild cognitive impairment is seen in the fifth decade of life, with the majority of patients older than 60 yr having full dementia.[41] This is a challenging diagnosis to make in these patients, as it typically presents with personality and behavioural changes as the first symptoms, unlike the short-term memory and language deficits seen in the general population.[4,18] Most mini-mental status examinations do not take into account intellectual disability and are therefore unreliable.[4,18] There are validated instruments

TABLE 3 Age-acquired manifestations of Down syndrome

System	Co-morbidity	% in DS	% in general population*
Central nervous system	Dementia/Alzheimer's	50–75 [5,44]	9.7–13.9[78]
	Seizures	12–46 [5]	1.2
Psychiatric	Psychiatric disorders	11–30,[4,5,44]	5–11
Cardiovascular	Valvular disease	8–57 [4,5,44]	2.5
Musculoskeletal	Cervical spine degeneration	64–70[4]	25–60[79]
Gastrointestinal	Celiac disease	7–1[4]	0.3–0.5[4]
Endocrine	Obesity or overweight	65–95[3–5]	70
	Osteoporosis	25–50 [4]	5.1–24.5
Immune	Ovarian/testicular tumours	0.5[80]	0.09[80]

Unless otherwise specified, all information for the general population is sourced from the Center for Disease Control. DS = Down syndrome

with high sensitivity and specificity, including the Dementia Scale for Down syndrome and Cambridge Examination for Mental Disorders of Older People with Down syndrome for this population, which require administration and interpretation by a psychologist.[18] Both instruments involve structured interviews with at least two caregivers and focus on the patient's best level of functioning, cognitive and functional decline, and current physical health. They can differentiate the stage of dementia, as well as rule out other differential diagnoses, like depression.[42] Depression, anxiety, obsessive-compulsive disorder, and other psychiatric disorders are also seen frequently in adults with DS. Seizures occur in a trimodal distribution in DS: 40% occur before one year of age, 40% between 20 and 30 yr of age, and the third peak correlates with the onset of Alzheimer dementia later in life.[18]

In adults with DS, cardiovascular and respiratory issues account for the majority of the morbidity and mortality. Those born without CHD may independently develop valvular disease, most commonly mitral valve prolapse and regurgitant lesions, and should be monitored for developing atrial fibrillation and left heart failure.[36,43] While these lesions are typically asymptomatic or benign, the high incidence of periodontal disease in DS may increase the risk of infective endocarditis.[5,44,45] The incidence of coronary artery disease and hypertension is decreased in DS patients compared with the general population, but there is increased mortality from peripheral vascular disease and cerebral vascular disease despite a lack of risk factors.[4,18,46] Occasionally, DS adults may be considered for heart transplantation for dilated cardiomyopathy from corrective surgery or chemotherapy, or irreversible pulmonary vascular disease complicated by uncorrected heart lesions.[47,48] Successful heart transplantation in DS patients has been reported with short-term and long-term outcomes similar to those of non-DS recipients.[49,50] Nevertheless, the number of DS heart transplant recipients is low, as their immunological abnormalities may place them at higher risk for infection, malignancy, or autoimmune disease.[23]

Degenerative disease of the cervical spine occurs in over 60% of adults and can cause severe cord compression.[4,37] There is also a high prevalence of obesity from lower metabolic rates and lower activity levels, with 65–95% of DS adults classified as overweight or obese compared with 70% of the general population.[3,4,51] Many of the co-morbidities associated with DS may be worsened by obesity, including OSA, GERD, pulmonary hypertension, and osteoarthritis.[24] Typically, DS adults demonstrate low functional status due to a sedentary lifestyle, which can place the patient at higher risk for complications like deep vein thrombosis in the perioperative period.[4,18,52] The prevalence of type 2 diabetes mellitus appears to be lower than what would be predicted based on the rates of moderate to severe obesity in DS adults.[10,24,44] DS is an independent risk factor for osteoporosis, with 50% of patients over age 50 yr developing long bone fractures as adults and 30% obtaining vertebral body fractures.[4] DS adults are at lower risk for solid tumours, such as cervical, breast, lung, or prostate cancers, but are at higher risk for ovarian and testicular tumours, potentially requiring surgical care.[4,53]

Perioperative care of adults with DS

The adult with DS can present for cardiac interventions and cardiac surgeries as well as non-cardiac surgeries.[54] Common non-cardiac surgeries include orthopedic, ophthalmologic, otolaryngologic, endocrine, and dental procedures. Additionally, the development of dementia, psychiatric disorders, or other behavioural disorders may necessitate examinations under anesthesia. While men with

DS are sterile, DS women can present for gynecologic or obstetric procedures. These women do have decreased fertility compared with the general population but have a 50% likelihood of having a child with DS.

The rate of perioperative, medical, and surgical complications, including cardiac arrest and syncope, is more common in adults with DS than in the general population.[10,24] Adverse outcomes in DS adults have been associated with the Eisenmenger syndrome, older age, OSA, and pulmonary hypertension.[13,24,27] Therefore, a detailed history and physical based on the parameters discussed previously and in Tables 1 and 3 should be taken, as summarized in Table 4.

Preoperative assessment

Down syndrome adults with corrected CHD, uncorrected CHD, or acquired cardiac disease may present for surgery. It essential that each patient must be evaluated based on their individual course of cardiac disease, as preoperative assessment, and ultimately anesthetic management, depends on the lesion, the type of repair, the long-term complications and progression of corrected or uncorrected defects, other co-morbidities, and the type of surgical procedure (Table 2). Objective laboratory tests, imaging, diagnostic criteria, and physical examinations are relied upon in the DS patient population as subjective cardiac evaluation can be challenging because of developmental delay and underlying CHD. It can be difficult to estimate physical status and exercise tolerance as these patients often have sedentary lifestyles or may be unable to complete an exercise stress test. Considering the risk of heart failure, valvular lesions, conduction defects, and pulmonary hypertension, if the patient has not had an echocardiogram since childhood, one should be ordered, and a brain natriuretic peptide level may be obtained.[4,5,44] Down syndrome patients' chronotropic incompetence makes them prone to bradycardia, but other arrhythmias may go undetected because the patient may not be able to describe palpitations or distinguish these from other symptoms.[24] An electrocardiogram and Holter monitoring may be obtained. Nevertheless, the patient may not tolerate Holter monitoring, so implantable loop recorders, which require sedation or general anesthesia, may be necessary for full evaluation (at a time separate from the preoperative assessment).[55] Ultimately, any test abnormality, new murmur, or signs of heart failure or pulmonary hypertension, such as dyspnea, orthopnea, raised jugular venous pressure, rales, fatigue, syncope, chest pain, or lower extremity edema should trigger a referral to a cardiologist for full evaluation. Many patients with known arrhythmia receive antiplatelet therapy or anticoagulants. Interestingly, despite a lack of risk factors like hypertension, there is some evidence that spontaneous hemorrhagic strokes are more common in DS adults.[24] Therefore, perioperative management of anticoagulated patients should be carefully evaluated by a multidisciplinary team. Patients with fenestrated TCPC are at risk for emboli, so anticoagulation therapies should be continued or bridging therapy prescribed in the perioperative period and pneumatic compression boots can be used for prophylaxis.[31,32]

A pulmonary evaluation should focus on any recent respiratory illnesses and degree of OSA. Uncooperative patients suspected to have OSA may not be able to tolerate a sleep study, so the STOP-Bang criteria and caregiver reports may yield a high suspicion for this diagnosis.[56] Adults with DS have anatomical features that predispose them to difficult airways, so it is important to elicit an airway history, gather prior intubation records, and perform a detailed airway exam. If there is any suspicion for cervical spine degenerative disease, a low threshold for flexion and extension x-rays and a neurologic evaluation is advisable. Early warning signs and symptoms, such as neck pain, abnormal head posture, torticollis, reduced neck movements, frequent falls, deterioration of fine motor skills, hyperreflexia, clonus, and ataxia are often attributed to dementia, Alzheimer's disease, or behavioural issues instead of cervical stenosis. Routine cervical imaging for asymptomatic individuals is not recommended, but cervical spine positioning precautions with in-line stabilization may be performed during intubation for all patients.[8]

Because these patients are prone to early-onset dementia, referral to a psychologist for psychometric testing for dementia might be necessary. Many DS patients with dementia may be taking centrally acting acetylcholinesterase inhibitors, like donepezil, galantamine, or rivastigmine, which decrease peripheral cholinesterase activity and can interact with neuromuscular blockade and cause reversal (which will be discussed in the Intraoperative Management section). There are some recommendations to discontinue donepezil two weeks, rivastigmine three to four days, and galantamine one to two days prior to surgery.[57] Nevertheless, discontinuing acetylcholinesterase inhibitors before surgery could worsen cognition and place the patient at high risk of postoperative delirium or cognitive dysfunction.[40] A risk-benefit assessment regarding medication discontinuation should be performed.

Hearing impairment, vision loss, and mental status may decrease the ability of the patient to communicate or give informed consent. A caregiver, power of attorney, or guardian may need to provide the majority of the history in the preoperative assessment. To examine the patient, ask the caregiver for the suggestions on how to best approach the patient. These patients usually have a long history of

TABLE 4 Summary of perioperative management of adults with Down syndrome

Preoperative assessment	Ask about these symptoms:	Neurologic: neck pain, head posture, torticollis, recent falls, decline of fine motor skills
		Cardiac: orthopnea, dyspnea, fatigue, syncope, chest pain
		Respiratory: dyspnea, fever, snoring, STOP-BANG
		Other: dysphagia, reflux
	Note on physical exam:	Neurologic: cervical spine range of motion, hyperreflexia, clonus, ataxia
		Cardiac: increased jugular venous pressure, murmur, arrhythmia, lower extremity edema
		Respiratory: rales, wheezing
		Other: Airway exam, dental lesions
	Consider tests and imaging:	Neurologic: cervical spine imaging (if symptomatic), hearing and vision tests, dementia testing
		Cardiac: echocardiography, brain natriuretic peptide, ECG/Holter
		Respiratory: chest imaging, sleep study
		Other: thyroid function tests
	Note these medications:	Neurologic: anticholinesterase inhibitors, memantidine
		Cardiac: antiplatelets and anticoagulants
	Other considerations:	History and consent may need to be given by power of attorney or caregiver.
		Child-Life specialists may be of assistance.
		Consider referrals to cardiology, neurology, or psychiatry/psychology.
		Obtain prior anesthetic and intubation records.
Anesthetic plan	Preoperative management:	Consider use of anxiolytic premedication and aspiration precautions.
	Type of anesthesia:	Consider use of regional anesthesia if tolerated and no contraindications. Blocks can be placed asleep or awake.
		Induction of anesthesia can be inhalational, intravenous, or rapid sequence depending on patient history.
	Airway management	Expect a difficult airway and have equipment available.
		Use cervical spine precautions and a smaller endotracheal tube.
	Intraoperative management:	Careful positioning given ligamentous laxity.
		Use strict aseptic technique given infectious risk.
		If indicated, give antibiotic prophylaxis for spontaneous bacterial endocarditis.
		Judicious use of medications that decrease heart rate or prolong the QT interval as patients are prone to bradycardia.
		Careful fluid management and hemodynamic monitoring, particularly if congenital heart disease is present.
	Considerations for dementia and delirium:	Total intravenous anesthesia with propofol may be preferred over volatile agents.
		If the patient is on anticholinesterase inhibitors, consider avoiding succinylcholine and neostigmine. Non-depolarizing blockade may be prolonged and can be reversed with suggamadex.
		If the patient is on memantidine, consider avoiding ketamine.
		Careful use of anticholinergics as patients are more sensitive.
	Postoperative management:	Use multimodal pain control and alternative pain scales.
		Watch for worsening of dementia or postoperative cognitive dysfunction.
		Consider if intensive care monitoring is needed, given congenital heart disease or other pathology.

ECG = electrocardiogram

interaction with the healthcare system, in particular the pediatric system and its nuances, and Child-Life specialists can also be of great assistance. Dolls or toys can be used to demonstrate procedures and create trust. Nevertheless, diagnostic imaging such as echocardiograms, cardiac catheterizations, or cervical radiology studies may need to be performed under sedation or even general anesthesia. The anesthesiologist may need to spend more time with the patient and caregivers addressing their previous experience with anesthesia, explaining the anesthetic plan in simple language, and answering questions. Additionally, the anesthesiologist should remain creative and flexible in

determining an anesthetic plan for the patient to allow for safety and comfort, as these patients may be accustomed to pre-medications, inhalational inductions, and parental presence on induction.

On the day of surgery in the preoperative area, it may be necessary to administer an anxiolytic, such as midazolam, ketamine, or dexmedetomidine. It is helpful to know if there has been a paradoxical reaction to an anxiolytic, which route it should be administered (oral, nasal, intramuscular, intravenous), and the timing (prior to or after intravenous catheter placement). Elderly patients are more sensitive to benzodiazepines, so consider avoiding this class of medication in patients over 60 or with dementia. Because of the high rate of swallowing difficulties and chronic silent aspiration, aspiration precautions, including administration of sodium bicitrate, metoclopramide, and famotidine, may be beneficial. Vascular access can be challenging as a result of a history of multiple surgeries and high rates of obesity. The patient may also be needle-phobic, so a topical local anesthetic, cold spray, or other distraction techniques can be used to facilitate intravenous induction.

Intraoperative management

A decision between providing sedation, a regional anesthetic, or a general anesthetic will depend on the patient's mental capacity, history of dementia, and the airway history and assessment.[58–60] For DS patients with CHD, there are no studies favouring one anesthetic technique over another for non-cardiac surgery.[61] While regional or epidural anesthesia may offer good hemodynamic stability and pain control in patients with CHD, anticoagulation may contraindicate its use. Additionally, if required, it should be planned meticulously in DS patients with corrected CHD. Post spinal hemodynamic consequences may be precipitous in patients with Fontan physiology, left ventricular outflow obstruction, or Eisenmenger syndrome, depending on the rapidity of onset and level of spinal block achieved.[61] Regional techniques may also be considered for patients with known dementia with a goal of reducing the exposure to general anesthetic agents and the contribution of pain to delirium.[40] Asleep blocks are an option in adults with DS, as they are commonly placed in pediatric patients with no adverse outcomes.[62] If a general anesthetic is required, the potential for and history of a difficult ventilation and/or intubation may necessitate an awake intubation. Nevertheless, this may not be possible if the patient has dementia or other mental impairment. Asleep inductions, maintaining spontaneous ventilation, can be performed through the inhalational route if there is a difficult airway, if vascular access is too challenging, or if the patient is accustomed to inhalational inductions; however, the risk of aspiration or degree of GERD might dictate a rapid sequence induction. The high rates of cervical spine degeneration and atlantoaxial instability may necessitate the use of cervical spine in-line stabilization or fibreoptic intubation. Last, consider using a smaller endotracheal tube. Often there is no clear or best option for the induction, so the anesthesiologist's knowledge and judgement is required to determine the safest route that minimizes risk to the patient. After induction, positioning and padding of the patient can be challenging because of obesity, ligamentous laxity, and osteoporosis.

Volatile agents may promote beta amyloid development to a greater degree than propofol; therefore, a propofol total intravenous anesthetic may be beneficial for DS patients with dementia.[40] In patients taking acetylcholinesterase inhibitors, it might be best to avoid the depolarizing neuromuscular blocker succinylcholine because of the risk of developing a phase 2 block and prolonged paralysis.[57,63,64] Additionally, non-depolarizing agents may require increased doses and acetylcholinesterase inhibitor reversal agents, like neostigmine, may be unpredictable or may lead to cholinergic crisis.[57,64] Consider using a short-acting non-depolarizing neuromuscular blocking agent, like rocuronium or vecuronium, if paralysis is needed, and reversing with sugammadex or allowing the blockade to reverse spontaneously.[40] Because the cardiovascular effects of acetylcholinesterase inhibitors include bradycardia from parasympathetic stimulation, carefully monitor the patient when using other medications that lower heart rate (beta-blockers, calcium-channel blockers, amiodarone) or prolong the QT interval (haloperidol, ondansetron).[57] Memantidine, another medication used to treat Alzheimer's disease, acts at the NMDA receptor, and concurrent administration of ketamine may lead to pharmacotoxic psychosis.[57,65] Patients at risk for dementia or with dementia may also be more sensitive to anticholinergic drugs, from the loss of cholinergic neurons in the nucleus basalis of Meynert.[26,40] Consider careful dosing of atropine, scopolamine, and diphenhydramine because of exaggerated response and possible increased risk of anticholinergic syndrome, with delirium, agitation, and hallucinations.[40,57]

Hemodynamics and fluids should be carefully monitored, and in the presence of cardiac co-morbidities, management goals should depend on the particular lesion, corrected or palliated status, and the physiology (Table 2). Many anesthetic agents may depress myocardial function and reduce SVR, which can result in shunt reversal, hypoperfusion, cyanosis, acidosis, and right and left heart dyfunction.[27,66,67] For any CHD patients with ventricular dysfunction, aim to preserve contractility and SVR while

preventing volume overload and increased PVR. If acute PVR elevation occurs, it may present as hypoxia (residual shunt or fenestrated Fontan) or rapid hemodynamic deterioration (pulmonary hypertension or non-fenestrated Fontan). To quickly lower PVR, increase inspired oxygen, hyperventilate and decrease mean airway pressures, minimize positive end-expiratory pressure to avoid compression of pulmonary vasculature, assure adequate anesthesia and analgesia, treat metabolic acidosis, consider Trendelenburg position to augment venous return, and administer pharmacologic agents such as nitric oxide, inodilators (milrinone, dobutamine), or vasodilators (isoproterenol, magnesium).[31,32] Drug effects on SVR can be ameliorated with vasopressin, which increases SVR without a concomitant increase in PVR, or epinephrine and norepinephrine, which enhance pulmonary blood flow by improving ventricular performance.

If the patient is at risk for infective endocarditis, antibiotic prophylaxis should be used. For DS patients with severely progressed cardiac disease, transesophageal echocardiography, arterial blood pressure monitoring, and central venous pressure monitoring are options for monitoring ventricular function, preload, and shunting, depending on the nature of the surgical procedure and anesthetic plan.[13] In Fontan circulation patients, a central venous catheter placed in the superior vena cava will reflect venous return to the lungs, rather than atrial pressure, but is an excellent guide for fluid management. Emergency transvenous pacing should be immediately available, recognizing that this is not an option in those with Fontan circulation, as the central veins are not in continuity with the atria. Transcutaneous pacing should be available for this population. All adults with DS have a degree of autonomic system dysfunction and low catecholamine levels that may be responsible for their sensitivity to volatile agents, resulting in rapid bradycardia, hypotension, and decreased minimum alveolar concentration.[26,68,69]

While full discussion of management of the palliated single ventricle DS patient is beyond the scope of this narrative, several important points can be highlighted. Because the venous return is passive in TCPC, the driving force for maintaining pulmonary blood flow and cardiac output is the transpulmonary gradient or the pressure difference between the central venous pressure (ideally 10–15 mmHg) and common atrial pressure (ideally 5–10 mmHg).[31] Pulmonary blood flow is optimal when PVR is low, preload is augmented, and systemic venous return is unobstructed.[31,32] Cardiac output is dependent on the systolic function and diastolic compliance of the ventricle, atrial-ventricular valve function, ventricular filing, afterload, and atrial contraction.[32] Intraoperative management should focus on maintaining cardiac output and actively reducing PVR. Patients may require significant preload, but excessive volume may increase afterload and decrease cardiac output because of the systemic and pulmonary circulation systems being in series. Medications that decrease preload (nitroglycerin, nitroprusside), lower SVR (alpha-adrenergic agonists), produce negative inotropy (beta-adrenergic antagonists, calcium channel blockers), and/or affect atrioventricular conduction (adenosine) should be used with caution or avoided.[32] Because fenestrations predispose to emboli, intravenous lines should be meticulously de-aired.

Down syndrome patients are at high infection risk, which can result in postoperative complications and longer hospital stays. The use of aseptic techniques is paramount, and lung-protective ventilation techniques should be considered. Remove any invasive cannulas, such as arterial lines, as soon as possible in the postoperative period.

Postoperative considerations

In the postoperative setting, close monitoring may be required if the patient's OSA is severe. Additionally, postoperative monitoring in the intensive care unit might be appropriate for adult DS patients with CHD. Pain control may be challenging. The high rates of OSA may dictate judicious use of opioids, so a number of techniques can be used, including patient-controlled analgesia, scheduled medications, or regional techniques. The choice often depends on the patient's mental status and severity of OSA. If the patient has dementia or diminished mental capacity, he or she may not be able to self-report with numeric rating scales and may require use of alternative pain assessment tools, such as the Wong-Baker Faces[70] or modified Face, Legs, Activity, Cry, Consolability (FLACC) score.[71] Considering the early onset of dementia, these patients are likely at risk for postoperative cognitive dysfunction, as the largest studies indicate a positive association between anesthesia and surgery exposure with the development or worsening of dementia, postoperative delirium, and postoperative cognitive dysfunction.[40]

Conclusion

Life expectancy for DS patients has been enhanced by improved healthcare. As they age, these patients not only have progression of their pediatric associated co-morbidities but also can develop other cardiac, respiratory, gastrointestinal, and neurologic conditions with which the anesthesiologist should be familiar. There are challenges associated with this patient population that

require the anesthesiologist's expertise and judgement to minimize patient risk. Based on the current literature that reports the age-associated manifestations of the adult with DS, we have described the considerations in anesthetic care of this population. Certainly, as more adults with DS undergo surgery and we learn more about proper screening and medical management, we will be able to develop best practices for their anesthetic care.

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