

MEASUREMENT OF COGNITIVE OUTCOME AND QUALITY OF LIFE IN CONGENITAL HEART DISEASE

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Since the 1970s, the improvement of diagnostic tools and the success of cardiac surgery have dramatically changed the natural history of complex congenital heart diseases. The number of newborns who have survived through infancy, reaching adolescence and adult age, and becoming socially integrated has increased.^{1,2} Consequently, nowadays determinants of late surgical results are evaluated by not only using survival as a measure, which was of major importance for surgeons and cardiologists up until the 1980s, but also by freedom from negative clinical events together with improvements in quality of life. Various guidelines,³ based on long post-surgical follow-up and knowledge of sequelae and complications, codify clinical evaluation of adult patients with a congenital heart defect. It is more difficult to codify the assessment of cognitive performance and quality of life.

This article reviews the mechanisms of cerebral damage in patients with congenital heart disease, the definition and measurement of quality of life, assessment of the psychological profile, and definition of cognitive functions and their measurement.

▲ AETIOPATHOGENETIC FACTORS OF POTENTIAL CEREBRAL INJURY

The aetiological factors that modify the integrity of the brain can be related to the following: congenital heart defect, duration of haemodynamic and haematologic effects of the disease, hypoxic–ischaemic insult secondary to hypothermic cardiopulmonary bypass, and cardiac arrest during surgery.⁴

In patients with chromosomal abnormalities, particularly trisomy 21 and deletion on chromosome 22q11 (Di George syndrome), the neurodevelopmental outcome seems to be related more to genetic influence than to the associated cardiac defect.

Congenital heart disease characterised by hypoxaemia and cyanosis with polycythemia and microcytosis are at risk of cerebral accident, particularly during blue spells (cyanosis) or when blood viscosity is increased. Severe metabolic acidosis secondary to hypoxaemia strengthens the negative effects of ischaemia on glial and cerebral vascular cells due to the action of free radicals on membrane lipids and proteins.

Early surgery during the neonatal period or in the first trimester of life prevents cerebral complications, particularly in patients with transposition of the great arteries, avoiding hypoxia and persistent metabolic acidosis and forestalling blue spells in patients with tetralogy of Fallot. No unusual risk of cerebral injury is present in acyanotic congenital heart disease in the absence of severe cardiac dysfunction.

Surgical correction of the majority of congenital heart disease involves those methods which protect cerebral structures, such as cardiopulmonary bypass and deep hypothermia. Both these methods may have cerebral side effects caused by the risk of microembolism during bypass, an uncertain optimal temperature to obtain a safe cardiac arrest period, and the activation of a variety of inflammatory pathways.^{5,6} Risk factors for poor cerebral outcome after hypothermic cardiac arrest include: prolonged cardiac arrest, particularly in younger patients (more than 45–50 minutes), rapid cooling (< 20 minutes), severe hypothermia, hyperglycaemia before arrest and during reperfusion, alpha-stat during cardiopulmonary bypass, severe cyanosis and blood hyperviscosity before surgery, low cardiac output in the early postoperative period, and alteration of cerebral blood flow secondary to deficiency of the autoregulatory process. Perioperative clinical and electroencephalographic (EEG) seizure and increased time to first EEG activity were associated with an increased risk of impaired cognitive functions.⁷

QUALITY OF LIFE AND HEALTH RELATED QUALITY OF LIFE

The concept of quality of life is broad and multidimensional. The temporal dimension of its assessment is very important because quality of life is not a stable and defined condition but one that changes. Because health is an important determinant of quality of life, a specific expression has been introduced—health related quality of life—which is suitable for applying to patients

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with congenital heart disease, for whom surgical correction prolongs survival but does not provide normality. Many of these patients need a programmed clinical follow-up.⁸

In 1994 the World Health Organization revised the definition of quality of life in terms of “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”. According to this definition subjective parameters were introduced with limitation of their assessment because of peculiarity, no comparability, unpredictability, and individuality. Finally, no less important are the symbolic and cultural aspects. All cultures have allegoric representations of the heart with innumerable metaphors. It is well known that the influence of congenital heart disease on the parental relationship, with negative overprotective behaviour, is not related to the severity of the cardiac defect. In the past, attention was particularly paid to the family, level of education, employment and financial circumstances, and the quality of medical care received. More recently concepts of self-perception and interaction between the disease and individual values and expectations, according to symbolic and cultural aspects of the environment (where the patient lives day to day and is confronted with the realities of life), were introduced.

The quality of life measurement has to follow the following criteria:

- ▶ good validity and psychometric fidelity
- ▶ reliable rules of manual correction, scoring, and interpretation selection
- ▶ good comprehension of all components of the quality of life, clinical functioning, and the specific needs of the patient and his or her family.

The short form 36 (SF-36)⁹ satisfies these criteria; it has an acceptable internal consistency and re-test reliability. SF-36 was worded to evaluate some prominent conceptions about health quality of life independently of age, pathology, and treatment. SF-36 includes one multi-item scale that assesses eight health concepts: physical activity, status and physical health, physical pain, general health, vitality, social activities, role and emotional status, mental health and health condition changes.

PSYCHOLOGICAL ASSESSMENT

Clinical experience and the literature both show how the psychological history of these patients is intensely conditioned not by the severity of their cardiac disease but by the type of medical care received in infancy (multiple operations, repeated hospital admissions).¹⁰ More important is how parents and relatives integrate the medical care and education with the psychological needs of their children.

The history of the patient, psychological problems, and their quality of life characterise some critical moments (table 1) that may have important negative consequences for the psychological evolution of the patient and his or her quality of life. Furthermore, during these “critical moments” patients can experience problems (for example, difficulties obeying their parents, taking their medication, or attending periodical follow-ups) which are not medical problems related to their disease.

Infancy

Is the relationship between a mother and her infant with congenital heart disease at risk because of early hospitalisation

Table 1 Description of critical moments in the four steps of life

▶ Infancy	Cardiac surgery/frequent hospital admission can cause interruption and/or modification of the relationship between child and parents Onset of preschool, physical activity limitations
▶ Childhood	Onset of school, learning deficits
▶ Adolescence	Adolescence crisis Corporeal image and sexuality
▶ Adult age	Pregnancy Employment

and cardiac surgery? Is the quality of the mother–infant relationship related to the severity of the cardiac defect?

Clinical data have shown that fetal diagnosis of congenital heart disease and the post-natal experience can negatively influence the type of attachment between the mother and her infant.¹¹ The severity of the illness does not have a direct effect on the quality of the infant–mother relationship, but a “securely attached infant” showed more subsequent improvement in health than “insecurely attached” peers showed.

This is the reason why it is important during the period of hospitalisation to limit the time the infant is separated from the parents to the surgical event only; to protect the infant from pain during all phases of care; and if necessary to give psychological support to the parents. During the psychological assessment of the parents, attention has to be paid to their mental health, and to their intellectual, relation, and social capacities. Furthermore, it is important to analyse their understanding of the disease, its prognosis, and the possibility of treatment.

In newborns, psychological development can be evaluated by specific scales which measure delays in development and attachment.

In babies psychological development can be evaluated by specific psychodiagnostic instruments that measure intellectual, emotional, social, and relational capacities. Moreover, the psychologist can assess the presence of psychological abnormalities according to the *International classification of diseases*, 10th revision (ICD-10) or the *Diagnostic and statistical manual*, 4th revision (DSM-IV) and/or the CFTM (Clasificación Française des Troubles Mentaux de l’Enfant e de l’Adolescent).

Childhood

It is interesting to observe through evidence provided by clinical experience and from the literature that most psychological problems emerge during childhood and adolescence, while they seem to attenuate or disappear once adulthood is reached. The major problems emerge during the period of schooling. The child may show difficulties because of repeated absences resulting from frequent hospitalisations and because he or she has some limitations in sharing physical activities with classmates. It becomes necessary to give clear indications about the physical activities of the child. If there are contraindications to certain sporting activities it might be useful to consider the experience of some specialised centres that propose alternative experiences, with the instruction of corporeal techniques that facilitate psychosomatic integration of the child.¹²

If a child shows learning problems it is important to evaluate him or her using an appropriate cognitive assessment test.

Adolescence

During adolescence, requests for medical counselling usually increase. Parents have difficulty controlling the relationship with their children, who often consider the parents responsible for their handicap. The onset of sexual maturity and the difficulty accepting the physical aspects of their condition, in particular the scarring on the chest caused by the cardiac operations, exacerbate the discomfort. Moreover, these patients do not accept the limitations related to their physical status.¹³

Psychotherapeutic support, preceding the psychological clinical interview, must be focused on individual sessions with the patient and, when necessary, with the family nucleus.

Adulthood

Patients may experience difficulties finding a satisfying job, first because of a low educational level, and also because an employer may be wary of giving a job to a person with potential physical disabilities. In these situations social workers play an important role in assisting patients and advising them of their legal position.

In women, pregnancy continues to be a risk following surgical correction of complex congenital heart disease. There is the risk that the patient's own clinical status will deteriorate, and also the risk that the cardiac defect will occur in their offspring. So genetic counselling is recommended, and also fetal echocardiography. Psycho-prophylactic support can be useful, particularly in the last trimester of pregnancy, to attenuate anxiety over the possibility the patient might die during the delivery; this can be achieved by means of autogenic training and by preparing for the birth with breathing exercises.

A series of instruments can be used for the psychological assessment: clinical interview with the parents of the infant with congenital heart disease; observation of the infant; observation of the child; clinical interview with the adolescent with congenital heart disease; psycho-diagnostic tests for infant age, childhood age, adolescence, and adult age.

Psychological assessment is based on a 45 minute semi-structured interview and administration of the Minnesota multiphasic personality inventory (MMPI-2). During the interview, psychological, social and economic areas are investigated through questions about family status, educational level, and work.

The MMPI-2^{14 15} is an effective and reliable test constructed in order to evaluate the most significant structural characteristics of personality. It comprises a self-administered questionnaire to which the subject must respond "true" or "false" to a series of 567 statements about his or her personal experiences, physical conditions, habits, and attitude. It suggests an exhaustive clinical picture of the patient by means of a series of numerical variables. It has a high discriminative power to discern between normal and pathological traits of personality. It is one of the most diffuse and validated tests of personality, and its high degree of accuracy is widely accepted.

The subject must be at least 18 years of age. The administration time for the test is about 90 minutes. The test is composed of three scales of validity (L-lie,

F-infrequency, K-correction), 10 base clinical scales (Hs-hypochondriasis, D-depression, Hy-hysteria, Pd-psychopathic deviate, Mf-masculinity-femininity, Pa-paranoia, Pt-psychasthenia, Sc-schizophrenia, Ma-hypomania, Si-social introversion), and 15 clinical content scales (ANX-anxiety, FRS-fears, OBS-obsessiveness, DEP-depression, HEA-health concerns, BIZ-bizarre mentation, ANG-anger, CYN-cynicism, ASP-antisocial practices, TPA-type A, LSE-low self-esteem, SOD-social discomfort, FAM-family problems, WRK-work interference, TRT-negative treatment indicators). For psychological diagnostic purposes the entire profile is determined from both the 10 base scales and the 15 subject scales in order to achieve maximum discriminating power. The scales of the test are standardised according to a normal distribution (T scores); scores above the 65th centile are considered clinically significant.

NEUROPSYCHOLOGICAL ASSESSMENT

What is neuropsychological assessment?

Neuropsychological assessment originated in the late 19th and early 20th centuries to evaluate the mental capacities of patients with brain disease (particularly aphasics). The primary purpose of neuropsychological assessment is to draw inferences about the structural and functional characteristics of a person's brain by evaluating an individual's cognitive functions. Cognitive functions are detected by studying behaviour in defined stimulus-response situations. Neuropsychological assessment is based on tests—namely, elicitation of a specific behavioural response to specific stimuli under controlled conditions. The use of a standard test battery allows the study of behavioural characteristics that are not accessible to clinical observation; however, it is important to stress that a cognitive evaluation is more than merely administration of a test list. A comprehensive neuropsychological assessment is an evaluation of cognition, mood, personality, and behaviour. Such an evaluation usually includes a formal interview, review of medical and/or educational/vocational records, interview of significant others (as necessary), and standardised neuropsychological testing. A comprehensive assessment covers a range of cognitive domains including intelligence, learning, memory, attention, receptive and expressive language, visuospatial ability, sensory processing, motor ability, reasoning, and higher order executive functions.¹⁶

Sometimes the psychologist personally gives the test, but other times a technician who has been thoroughly trained in administration of the measures may do it. In either case, the psychologist is responsible for interpreting the data obtained.

Why should cognitive functions be evaluated in the congenital heart disease patient?

The scope of neuropsychological assessment has expanded enormously in recent decades to encompass areas beyond clinical neurology. It plays an indispensable role in detecting cerebral dysfunction in clinical situations in which there is no clear anatomical evidence of alterations to the brain. For example, such situations include evaluating the effects of environmental and industrial toxins, the cognitive changes associated with alcoholism, chronic obstructive pulmonary diseases, the behavioural sequelae of carotid endarterectomy and cardiac surgery, as well as monitoring the outcome of pharmacological treatments.

Until now, the neuropsychological consequences of various dimensions of cardiovascular diseases have generally been

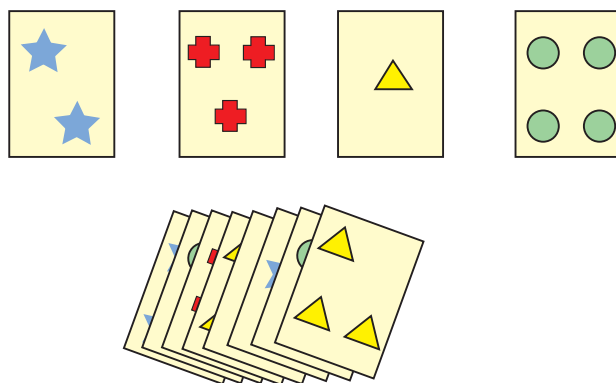


Figure 1 The Wisconsin card sorting test. "Please sort the 60 cards under the four samples. I won't tell you the rule, but I will announce every mistake. The rule will change after 10 correct placements".

examined in isolation. Furthermore, studies have shown that although the vast majority of children with congenital heart disease have normal outcomes, as a group they generally show high rates of neurodevelopmental problems.¹⁷ These problems include mild deficits in cognition, attention, and neuromotor functions. The aetiology of cognitive deficits in congenital heart disease patients is probably multifactorial and includes preoperative, operative, and postoperative factors. The preoperative factors include congenital brain abnormalities, genetic syndromes, hypoperfusion, acidosis, and cyanotic episodes; operative factors consist of circulatory arrest and cardiopulmonary bypass; postoperative factors take into account low cardiac output and embolic events.

Which are the most frequent cognitive deficits observed in patients with congenital heart disease?

Most of the studies on the cognitive development of children with cardiopathy have distinguished between cyanotic and non-cyanotic conditions. Many studies report cognitive deficits in children with congenital heart disease and a positive correlation between the level of cognitive ability and the cardiopathic clinical severity. Children younger than 3 years of age with cyanotic cardiopathy showed deficits in gross motor, adaptive, social, and fine motor areas (Gesell developmental schedules), with the lowest score reported for gross motor abilities.¹⁸ A delay in motor development has been found, despite a normal language development.

Children older than three years reported normal values of intellectual parameters, measured by the IQ index, with mildly reduced scores only in the cyanotic population. The IQ of the cyanotic patients was significantly lower than that of acyanotic patients for both the Stanford-Binet and the Wechsler adult intelligence scale, the two IQ tests used most often. The IQ measures are not sufficient to investigate the cognitive domain. In a previous study¹⁹ a more exhaustive neuropsychological investigation revealed an impairment of cognitive abilities such as executive functions and calculation. The term "executive function" is a complex construct that can be broadly defined as higher order cognitive abilities that allow for strategic planning, cognitive flexibility, self regulation, and goal directed behaviour requiring the coordination of several sub-processes. Executive functions are those involved in complex cognitions, such as solving novel problems, modifying behaviour in the light of new information,

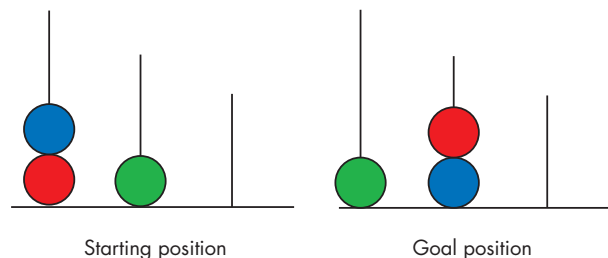


Figure 2 The Tower of London test. "Please rearrange the balls on the pegs, so that each peg has one ball only. Use as few movements as possible".

generating strategies, or sequencing complex actions. Neuropsychological evidence suggests that executive processes are intimately connected with the intact function of the frontal and pre-frontal cortices.²⁰ Usually, patients with damage to the prefrontal cortex can show impaired judgment, organisation, planning and decision making, as well as behavioural disinhibition and impaired intellectual abilities. In a neuropsychological evaluation setting, patients are impaired on tests such as set shifting (for example, the Wisconsin card sorting test (fig 1)), planning (for example, the Tower of London test (fig 2)), and various fluency tasks (for example, the verbal fluency test). The Wisconsin card sorting test²¹⁻²² was devised to measure abilities to identify abstract categories and to shift cognitive set. The test requires the subject to sort a series of cards according to selected dimensions, which are changed from time to time during the course of examination. The subject must formulate a hypothesis about the correct sorting principle and be capable of changing the hypothesis when the feedback from the examiner indicates that it is incorrect. The Tower of London test²³ is a specific task to investigate executive functions and planning ability. This test is a problem solving task which requires subjects to rearrange three coloured rings (in accordance with some very simple rules) from their initial position on three upright sticks to a new set of predetermined positions. Subjects are instructed to try to achieve the goal arrangement in as few moves as possible. In the Phonemic verbal fluency test subjects are required to say words beginning with a particular letter of the alphabet for a specific time (usually one minute for each letter). Although it is a test to measure the lexical access, phonemic fluency places higher demands on frontally mediated strategic search processes.

Frontal lobe impairments all point to a breakdown of coordination processes. Patients are relatively unimpaired in a test focusing on a particular function, but when a number of different functions must be coordinated in the evaluation setting or in real life, deficits are observed. The calculation deficits found in patients with congenital heart disease might be caused by a deficit in prefrontal and frontal lobe functioning. A recent brain imaging study²⁴ showed that in approximate calculation tasks, bilateral intraparietal, precentral, dorsolateral, and superior prefrontal regions were involved, while the left inferior prefrontal cortex and the bilateral angular regions were more activated during exact calculation tasks.

Executive dysfunctions and calculation deficits might be directly related to academic performance. These patients may have difficulty in setting a goal (that is, understanding what

Measurement of cognitive outcome and QoL in congenital heart disease: key points

- ▶ Improvement of diagnostic tools and success of cardiac surgery has increased dramatically the survival of patients with congenital heart disease
- ▶ Potential cerebral injury from hypoxaemia, cyanosis, hypothermic cardiac bypass, and cardiac arrest can occur during surgery
- ▶ Quality of life is a multidimensional concept in whom health is an important determinant
- ▶ Quality of life can be obtained by well validated instruments that can be easily administered (short form 36)
- ▶ Psychological history seems not to be influenced by the severity of the cardiac defect but by the duration of hospitalisation and by the quality of the attachment with the mother during infancy
- ▶ Limitation of physical activity and difficulty in accepting the physical aspects of their condition, particularly during adolescence, and difficulty in finding a satisfactory job, are other psychological stressors for patients with congenital heart disease
- ▶ IQ is an insufficient index of cognitive assessment, which needs a complete investigation of all cognitive domains such as language, learning, memory, psychomotor speed, attention, concentration, calculation, and executive function
- ▶ Deficits of cognitive functions can be related to cerebral injury secondary to the cardiac defect and surgery
- ▶ Measurements of quality of life and cognitive outcome need to be repeated during follow-up, with particular attention to the critical moments of life

the assignment or question one is being asked to achieve), planning a course to achieve it, (that is, remembering the procedure appropriate to the task), holding the plan in working memory while executing it, sequencing the steps in the plan, initiating taking those steps and shifting between them, monitoring progress for both pace and quality, regulating attention and emotional responses to challenges that arise, making flexible changes in the plan as needed, and evaluating the outcome for use of the plan in a subsequent similar activity.

FINAL CONSIDERATIONS

A patient with a congenital heart disease usually has an unusual development, as a result of physical, psychological, and cognitive findings characteristic of the cardiac defect, and the impact that the disease has on the family setting, particularly the parents. In the last 20 years interest in patients with congenital heart disease has progressively increased, because of improvements in diagnostic and therapeutic standards resulting in the prolonging of life. But survival is not always synonymous with improved quality of life; despite positive medical results, physical, psychological and cognitive problems are present in this population and can be a limitation to therapeutic success. It is desirable that evaluation of these parameters by means of validated instruments performed by specialised operators is included in the programmed clinical follow-up of these patients. The value of a unique assessment is relative; over time patients may adapt to their physical status and denial is a common behaviour to normalise functioning. However, during the

“crisis periods” in adolescence and adult life, when the challenges of everyday life (sexuality, job, pregnancy) are being encountered, many psychological problems can emerge which affect the quality of life. The cognitive assessment cannot be limited to the IQ index, which in the majority of cases is normal; a complete evaluation of all the domains, such as learning, memory, psychomotor speed, attention, concentration, reasoning, calculation and executive function, is required. The deficit of some cognitive functions would support the presence of an organic pathological substrate secondary to the cardiac defect and/or surgery, which can be made worse by psychosocial conditions. Knowledge of these aspects is important in order to implement adequate prevention and support measures, particularly during the “crisis periods”, with consequent improvement in the quality of life of these patients.

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