International Journal of Cardiology 279 (2019) 57–61

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Advanced care planning in adult congenital heart disease: Transitioning from repair to palliation and end-of-life care

Els Troost [a,b], Leen Roggen [a,c], Eva Goossens [c,d], Philip Moons [c,e,f], Pieter De Meester [a,b], Alexander Van De Bruaene [a,b], Werner Budts [a,b,*]

[a] Congenital and Structural Cardiology, University Hospitals Leuven, Leuven, Belgium
[b] Department of Cardiovascular Sciences, KU Leuven - University of Leuven, Leuven, Belgium
[c] Department of Public Health and Primary Care, KU Leuven - University of Leuven, Leuven, Belgium
[d] Research Foundation Flanders (FWO), Brussels, Belgium
[e] Institute of Health and Care Science, University of Gothenburg, Gothenburg, Sweden
[f] Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa

ARTICLE INFO

Article history:
Received 20 June 2018
Received in revised form 7 September 2018
Accepted 24 October 2018
Available online 26 October 2018

ABSTRACT

As a result of advances in pediatric care, the majority of patients born with congenital heart disease (CHD) survive into adulthood [1]. Effective transfer and transition programs assure that patients with CHD remain in follow-up and receive continuous holistic care. Unfortunately, adult patients with CHD carry residual lesions and sequelae putting them at risk for premature death related to re-interventions or complications; most commonly heart failure and arrhythmia [2]. The scientific adult CHD (ACHD) community has been working hard to identify variables related to worse outcomes, modifying those where possible in order to improve survival. Indeed, survival in adults with CHD has increased, but consequently, on top of CHD-related complications, patients are increasingly exposed to the standard cardiovascular risk factors. Therefore, a program for lifelong coaching on health behavior and life style management becomes indispensable. More emerging is that a substantial number of patients, in particular those with complex heart defects, will eventually end up in a stage with hardly any medical or interventional options left. Our healthcare provision has to be prepared to organize care for this specific group of patients who will die prematurely and require the timely development and establishment of advanced care planning. Advanced care planning should preferentially be set-up in expert CHD centers. The long-lasting relationship in ACHD care with healthcare providers offers an excellent basis with regards to prognosis, advanced care planning and end-of-life issues.

1. Current opinion

1.1. Changing landscape of congenital heart disease

Congenital heart disease (CHD) remains the most frequently diagnosed congenital birth defect with an incidence of about 0.8% of live births [1]. Only in a minority of patients a known cause, chromosomal aneuploidy or single gene defect can be attributed to the CHD diagnosis. Prenatal diagnostics are capable of detecting up to 85% of complex lesions during pregnancy, facilitating prenatal counselling and delivery planning. Moreover, fetal diagnosis opens the door for a timely and couple-tailored discussion of pregnancy termination in case of irreversible infaust prognosis [3]. It is not clear to what extent the practice of prenatal diagnostics has changed over time and will impact the true prevalence of CHD defects in the late future [4–6]. However, some reports already suggest a clear shift in postnatal management of patients with CHD based on prenatal diagnostics [7,8].

Since the introduction of cardiac surgery in the fifties, intra-cardiac repair significantly improved the prognosis and survival of patients with CHD. The ongoing evolution and innovation of diagnostic tools, percutaneous and surgical interventions have profoundly changed the clinical spectrum of patients living with CHD [1]. As such, the number of adults with CHD is continuously growing and has already outnumbered the pediatric population [9]. This progressive shift from childhood over adolescence to adulthood led to the global awareness, in the medical and paramedical communities, that these patients need continued care and follow-up in highly specialized centers with adult CHD dedicated programs, particularly for complex lesions [10,11]. Indeed, although survival in early infancy and adolescence has improved significantly, many of these patients will need lifelong follow-up and,

* Corresponding author at: Congenital and Structural Cardiology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium.
E-mail address: werner.budts@uzleuven.be (W. Budts).

https://doi.org/10.1016/j.ijcard.2018.10.078
0167-5273/

despite all efforts, mortality risk increases with age, and is still significantly higher across all age groups when compared to the general population [12].

1.2. Causes of death in congenital heart disease

Data from the CONCOR registry have shown that the clinical course later in life is not uneventful and that many patients with CHD face a need for re-operation or re-interventions due to residual structural defects or sequelae. Hence, late complications such as the development of heart failure, arrhythmia, endocarditis, progressive pulmonary hypertension, increasing central cyanosis and valvular degeneration are common [5]. Two thirds of adults with CHD will prematurely die a '*CHD-related death*'. Most of these deaths can be attributed to *chronic heart failure* - peaking around the fifth decade of life - and to *sudden cardiac death* which rarely occurs during the first two decades of life but becomes a serious risk in some patients by the end of the third decade [13]. In 2000 Oechslin et al. reported that progressive heart failure (i.e., 21% of the studied population) was one of the three major causes of death in patients with CHD [14]. Depending on the underlying defect, the incidence increased up to 47%. Despite advances in medical treatment and improvement of surgical and interventional approaches, the prevalence and incidence of heart failure in patients with CHD do not appear to decrease. In contrast, as patients with CHD are getting older, they become prone to develop (terminal) heart failure. Therefore, heart failure impacts on morbidity and 20% of hospital admissions amongst patients with ACHD are related to heart failure [15]. Rodriguez and Marelli reported that heart failure related admissions of ACHD patients have increased by 82% from 1998 to 2005 (US data) [16].

The high incidence of *heart failure* stimulated the conduction of some small trials, but medical treatment options are still hampered by the lacking knowledge of the complex pathophysiological mechanisms leading to heart failure as well as the small numbers of adult patients with CHD included in heart failure studies so far. Nevertheless, the awareness of the high incidence of heart failure is clearly represented in a recent position paper from the Working Group of Grown-Up Congenital Heart Disease and the European Heart Failure Association summarizing existing data for this specific population [17].

The incidence of *arrhythmia* increases with age, affecting nearly 30% of patients from the age of 35 years and even up to 40 to 50% by the age of 65 to 70 years. Arrhythmias often cause very disabling symptoms and demand large efforts of cautiously balanced medical treatment, device therapy, catheter ablation, surgical procedures, and sometimes hybrid interventions performed in these patients who often present with a complex anatomy. Several studies tried to identify risk scores for specific populations that would benefit from preventive implantable cardioverter-defibrillator implantation in the case of syncope or documentation of non-sustained ventricular tachycardia [13,18]. Nevertheless, close follow-up of all patients with CHD is advised as even patients with a milder degree of CHD complexity may *die suddenly* and a larger number of prospective studies are necessary to elucidate these arrhythmia mechanisms.

In summary, adult patients with CHD are at risk of *sudden and/or premature death* mostly secondary related to *CHD complications*. Daily practice in expert CHD centers is mostly characterized by identifying and modifying parameters of worse outcome to *improve survival* and *maintain quality of life* as long as possible [19]. CHD-risk modelling, and subsequently improved treatment policies shift CHD survival patterns towards *classic cardiovascular mortality and/or non-cardiac related mortality*. Due to the general cardiovascular risk profile (i.e., smoking behavior, high blood pressure, dyslipidemia, diabetes, obesity, sedentary lifestyle), patients with CHD also develop atherosclerotic disease which, superimposed on the existing congenital substrate, negatively affects their prognosis. Some patients might have survived the potential complications related to their CHD and become exposed to the *risk for dying related to the natural aging process*. These emerging patients should be counselled on a timely basis about primary prevention in the context of cardiovascular risk factors or familial predisposition for acquired cardiovascular disease. Whereas in the beginning, counselling was mainly focused on strategies to avoid complications specifically related to the underlying CHD, later in life more attention will need to be paid to cardiovascular prevention in general. The need for well-informed advice can be found in guidelines or expert opinion papers both for the pediatric as well as the adult population [20–22]. Advanced Practice Nurses and CHD physicians have the utmost important mission to provide lifelong coaching for appropriate healthcare behavior [23]. This way of caregiving probably impacts outcome and *aging-related death*. Fig. 1 summarized this paragraph schematically.

1.3. Advanced care planning: a natural part of transitioning through life

Although ongoing investments in refining diagnosis and treatment options will result in an important growth of the ACHD population, this will be at the price of increasing numbers of patients with therapy-refractory heart failure or other non-treatable complications in some patients at rather young age. A growing number of patients will die when residual lesions are no longer amenable for repair and patients cannot be considered good transplant candidates for medical or surgical technical reasons. Healthcare providers need to be aware of the special care needs that should be addressed in these terminally ill patients facing an infaust prognosis. The concept of *advanced care planning* is gaining more attention in "classical" heart failure patients and should increasingly be introduced to end stage patients with CHD. The PAL-HF trial documented the benefit of interdisciplinary palliative care interventions in patients on top of conventional heart failure management regarding heart-failure related quality of life as well as overall quality of life parameters [24]. As specialists in CHD focus on treating the disease in this often-young population, it feels contra-intuitive that one would add an end-of-life approach before having exhausted all curative, or at least reparative, resources. This results in patients being deprived of psychological care for too long when coping with disabling symptoms and psychosocial distress [25]. Often a "trigger "event demonstrating the irreversible disease course serves as a surrogate to initiate palliative care and strengthens the belief of non-integrality of palliative and life-prolonging therapy. However, a longitudinal approach in the course of the disease with attention to improvement of symptoms, reducing pain and anxiety, and sustaining quality of life should be implemented at an earlier stage in addition to standard management and contributes to advance care planning. Efforts to preserve quality of life and to relieve symptoms could be the first step in a transitioning process towards end-of-life care, however, without discussing specific palliation issues at the beginning. Advanced care planning followed by end-of-life discussions has been well documented in some smaller studies performed in a tertiary care center [26,27]. Cornerstone is the need of patient-tailored counselling with respect to the course of the disease to improve patients' understanding of the prognosis and to create an opportunity for open communication and shared decision-making [28]. However, premature discussion about end-of-life might potentially be harmful for the well-being of patients with CHD. Care should therefore be organized as a continuous transition from curative strategies and gradually broadened towards symptom control and medical and psychosocial support as well. Nevertheless, further increasing awareness is needed to assist primary care providers and adult CHD specialists to adopt basic palliative skills. They need to identify those patients who should be referred to palliative care specialists in case of non-treatable symptoms and more complex issues such as end-of-life discussions, discordant patient-family goals, and unrealistic perspective of prognosis or treatments. Therefore, the introduction of primary or specialized palliative care will be different amongst patients depending on their specific needs and beliefs. The rationale for palliative care in end-stage heart disease or refractory heart failure has been inspired by studies on

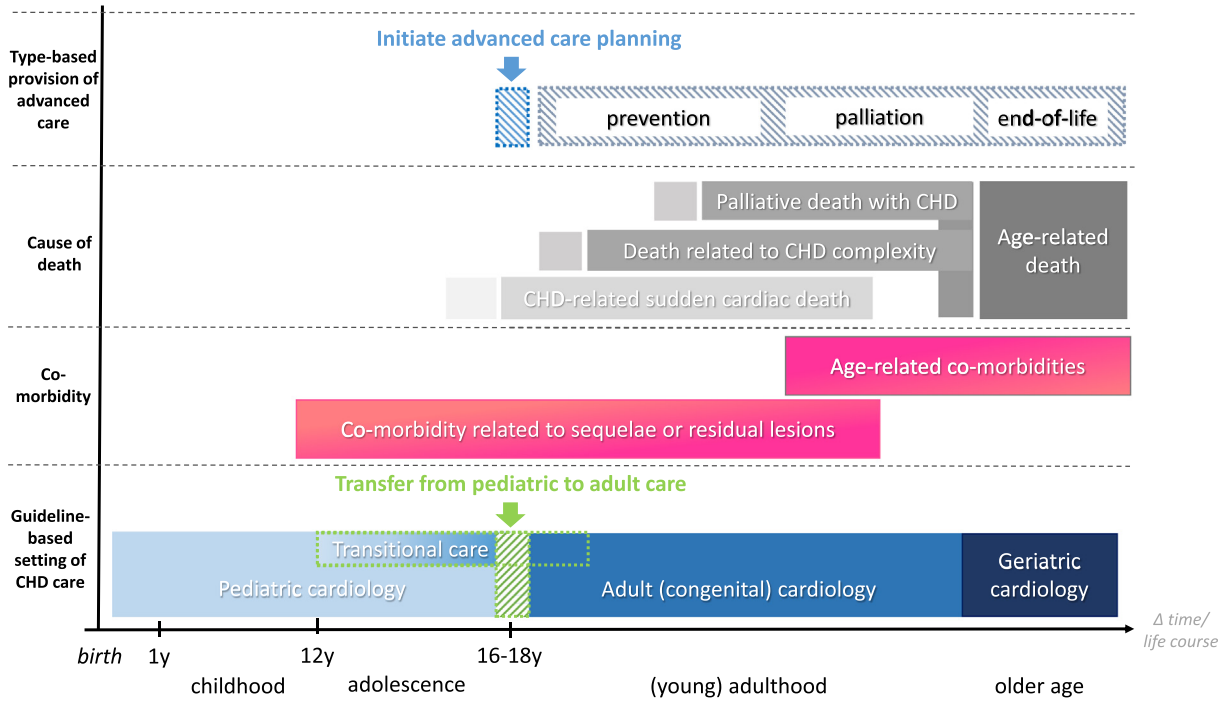

Fig. 1. Care planning and causes of death in congenital heart disease.

palliative care in oncology. Studies on in- and out-hospital palliative care in patients with heart failure, are still scarce, but may serve as a starting point to create a framework for future trials that focus on how and when palliative care should be integrated in end-stage heart disease [29,30].

Several societies such as the American Heart Association, the Heart Rhythm Society, the International Society for Heart and Lung Transplantation and the Heart Failure Association of the European Society of Cardiology, are progressively drawing attention to integration of palliative care in the treatment course of chronic heart failure. These recommendations are still greatly limited to the era of end-of-life evaluation when the implantation of mechanical circulatory pumps and the programming of implantable cardioverter defibrillators or cardiac resynchronization devices were discussed [31]. The PAL-HF trial, however, represents a milestone and showed the possible benefits of an earlier integration of palliative care in the disease course and accentuates the value of a more holistic approach of advanced heart failure. As the burden of chronic heart failure is expected to increase further on, this is an opportunity to broaden therapy not only with the purpose to sustain survival and reduce morbidity but also to ameliorate quality of life, relieve disease-related symptoms, and provide support in psychosocial issues. Further research is needed to design optimal treatment pathways and care strategies for patients with advanced circulatory failure throughout the course over the disease, from a more stable chronic phase over relapsing episodes of acute exacerbation and progressive decline to an end-stage care phase. This pathway should be made accessible for patients of all age groups, for all types of heart disease, including patients with CHD [32].

The unique characteristics of an often-long-standing patient-doctor relationship in adult patients with CHD provide an excellent basis for well-timed initiation of advanced care planning and end-of-life issues. However, as assessment of an individualized prognosis of the disease remains challenging; this might withhold many physicians to initiate such difficult discussions with their patients before they are admitted to the hospital in end-stage heart failure and/or with life threatening complications [28]. Contradictory, it has been documented that many patients with CHD, when asked, prefer to be informed about their disease course before they are facing life-threatening complications; remarkably, this was reported independently of the complexity of their disease or socio-economic variables [26,27].

Despite this widespread belief that communication on end-of-life issues should start earlier in the disease course, only 10% of patients in an ACHD group with advanced disease were reported in a retrospective review by Tobler et al. to have documented end-of-life discussions prior to their final hospital admission [25]. This means that for most patients such end-of-life discussions are conducted with their relatives or substitute decision-makers very near to their imminent death, causing thereby additional stress and anxiety in the family of these patients.

In addition, in the absence of any documented end-of-life preferences, these patients were more likely to receive aggressive treatment until the end and mostly died during attempted resuscitation [33]. These findings underline the need for improvement and early introduction of end-of-life discussions to incorporate patient preferences and to collaborate more closely with palliative care specialists [34]. A critical requirement before starting these discussions is a mutual understanding between doctors and patients about their concrete needs or desire for further information and partnership in decision-making. Ideally, in a long lasting patient-doctor relationship, such discussions should be incorporated in a dedicated and planned discussion, preferably in a programmed outpatient clinic around a future global care plan and life goals, after consent of the patient and in the presence of relatives the patient assigned to be part of these decisions [34]. It is only when clinicians find themselves confronted with a new patient in a life-threatening condition that this communication has to be held in an initial visit. Heart failure treatment and symptom relief go side by side and as such end-of-life care advice can be introduced even when heart failure treatment is still attempted. This reassures patients that this co-management between clinicians, heart failure specialists and palliative caregivers guarantees them continuous care and symptom relief in a gradual shift from repair towards palliation. More training in communication skills and end-of-life issues should therefore be introduced in the basic education of all healthcare professionals. The question is not only the timing of this communication but foremost making sure that such discussions are integrated in advanced care plan involving patients as much as possible as well as their partners in a discussion of their life goals.

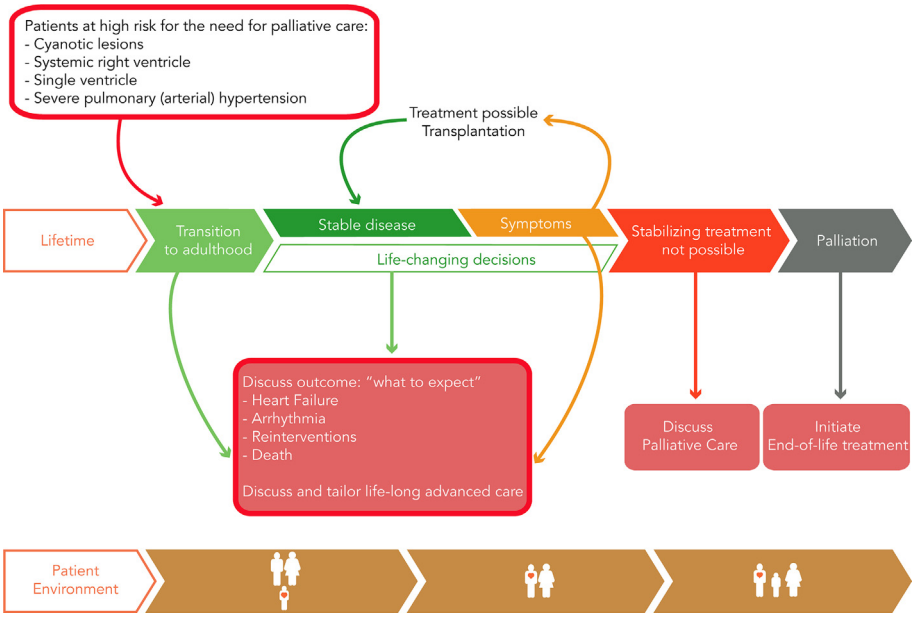

Fig. 2. Timeline advance care planning in congenital heart disease and suggested key moments for providing information about outcome and integration of a palliative treatment strategy.

Based on the theoretical discussion above and the experience of palliative care in patients with heart failure, we intended to set up and work-out a timeline of advanced care management for patients with CHD, as followed in our center (see Fig. 2). During the developmental transition from pediatric over adolescence to adulthood, it is important to identify these patients who are at higher risk (and hence might need palliative treatment) (Fig. 2). Specifically, during this transition phase it is important - depending on the maturity of the patient - to discuss the long-term outcome of the underlying disease and highlight the future risk for complications such as heart failure, arrhythmia, re-interventions, and death. It is, however, important to safeguard that discussing future prospects with patients at their visit in adult care, might have a significant emotional impact on patients and their environment, including parents and partners. As the main conversation partner starts to shift steadily from the parents to patient, the period of transitioning from pediatric to adult care seems the be an ideal moment to re-address the perspectives of life-long advanced care. The patient has to obtain an understanding of his/her condition, to realizing that a heart-healthy life style is of utmost importance, and that the future might be troubled with adverse events and complications. Regular follow-up is advocated, and its rationale should be discussed. During further follow-up, if the patient remains asymptomatic and has an uneventful course, we are not convinced that repeatedly focusing on the potential risks during long-term follow-up is required, unless patients indicate they want to discuss this matter. However, continuously recommending healthy life style remains mandatory. The ultimate aim is that patients live their life as carefree as possible. However, when the patient would ask spontaneously about risks and outcomes, similar information as communicated during transition, should be provided, potentially altered by the clinical course at that moment. New information needs to be discussed with the patient and if requested with his environment, where in the meantime a partner might have taken a more prominent role than parents might. However, each time symptoms re-occur, and treatment strategy has to be adapted, the discussion about outcome should be readdressed. During the patients' life course and depending on the underlying disease and its history, it might become clearer in what direction the treatment strategy will go. On one hand, it is possible that there is still room for hemodynamic and electrophysiological optimization, but on the other hand it might be clear that the patient becomes steadily more difficult to treat, finally leading to the need for a palliative approach and initiation of end-of-life management. It both cases, again outcomes require discussion and a shared decision-making process. Patients where hemodynamic and/or electrophysiological optimization is still possible, information has to focus on the new outcome data and the potential risks related to the adapted treatment strategy. If the patient remains asymptomatic thereafter and feels well with no need for further changing therapy, he/she could re-enter the timeline algorithm as indicated in Fig. 2. However, when the patient has entered the road of palliative treatment, patient and his/her environment need to be informed in detail. At this stage, it is realistic that the environment of the patients has changed from not only the partner but to partner and children. We consider it of utmost importance, especially at this stage, to not only inform the patient, but also his/her environment. The closer the patient comes to an end-of-life strategy, the involvement of the environment becomes more and more important. The road of a palliative approach is not necessarily short which opens the discussion when to initiate communication. In our opinion the option of a palliative treatment strategy can be communicated – always after discussion with the patient and his/her environment – relatively soon as indicated in Fig. 2. The longer the patient is on the road of palliative treatment to end-of-life care, the more also practical considerations become important besides communication. For practical issues, we do think that the policy does not have to differ from the ones that are applied for patients with heart failure. Updating about the clinical status, protecting quality of life as long as possible, dealing with anxiety, and implementing socio-familial and socio-juridical issues are key issues when entering end-of-life management. In most cases expertise from an interdisciplinary team is needed, including: treating physicians (including general practitioner), nurse practitioners, palliative support team, psychologists, social workers, and religious support team. We would like to stress that this approach described above is not validated but is purely based on our local experience. However, we are convinced that because of the growing need for advanced care planning in our patient population, each ACHD center has to develop their own tailored end-of-life care program. Nevertheless, the overall limited experience and the continuous changing epidemiology underline the need for further research investigating how to optimize patient care.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

References

[1] A.J. Marelli, A.S. Mackie, R. Ionescu-Ittu, E. Rahme, L. Pilote, Congenital heart disease in the general population: changing prevalence and age distribution, Circulation 115 (2007) 163–172.

[2] G.P. Diller, A. Kempny, R. Alonso-Gonzalez, L. Swan, A. Uebing, W. Li, S. Babu-Narayan, S.J. Wort, K. Dimopoulos, M.A. Gatzoulis, Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary centre, Circulation 132 (2015) 2118–2125.

[3] M. Thangaroopan, R.M. Wald, C.K. Silversides, J. Mason, J.F. Smallhorn, M. Sermer, J.M. Colman, S.C. Siu, Incremental diagnostic yield of pediatric cardiac assessment after fetal echocardiography in the offspring of women with congenital heart disease: a prospective study, Pediatrics 121 (2008) e660–e665.

[4] B.J. Bouma, B.J. Mulder, Changing landscape of congenital heart disease, Circ. Res. 120 (2017) 908–922.

[5] C.L. Verheugt, C.S. Uiterwaal, E.T. van der Velde, F.J. Meijboom, P.G. Pieper, A.P. van Dijk, H.W. Vliegen, D.E. Grobbee, B.J. Mulder, Mortality in adult congenital heart disease, Eur. Heart J. 31 (2010) 1220–1229.

[6] Pulmonary hypertension and pregnancy outcomes: data from the Registry Of Pregnancy and Cardiac Disease (ROPAC) of the European Society of Cardiology, Eur. J. Heart Fail. 19 (2017) 439.

[7] R.W. Weber, B. Stiasny, B. Ruecker, M. Fasnacht, A. Cavigelli-Brunner, E.R. Valsangiacomo Buechel, Prenatal diagnosis of single ventricle physiology impacts on cardiac morbidity and mortality, Pediatr. Cardiol. (Aug 18 2018), https://doi.org/10.1007/s00246-018-1961-1.

[8] R.S. Beroukhim, K. Gauvreau, O.J. Benavidez, C.W. Baird, T. LaFranchi, W. Tworetzky, Perinatal outcome after prenatal diagnosis of single-ventricle cardiac defects, Ultrasound Obstet. Gynecol. 45 (6) (2015 Jun) 657–663.

[9] A.J. Marelli, R. Ionescu-Ittu, A.S. Mackie, L. Guo, N. Dendukuri, M. Kaouache, Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010, Circulation 130 (2014) 749–756.

[10] P. Moons, F.J. Meijboom, H. Baumgartner, P.T. Trindade, E. Huyghe, H. Kaemmerer, Structure and activities of adult congenital heart disease programmes in Europe, Eur. Heart J. 31 (2010) 1305–1310.

[11] G. Webb, B.J. Mulder, J. Aboulhosn, C.J. Daniels, M.A. Elizari, G. Hong, E. Horlick, M.J. Landzberg, A.J. Marelli, C.P. O'Donnell, E.N. Oechslin, D.D. Pearson, E.P. Pieper, A. Saxena, M. Schwerzmann, K.K. Stout, C.A. Warnes, P. Khairy, The care of adults with congenital heart disease across the globe: current assessment and future perspective: A position statement from the International Society for Adult Congenital Heart Disease (ISACHD), Int. J. Cardiol. 195 (2015) 326–333.

[12] T. van der Bom, B.J. Mulder, F.J. Meijboom, A.P. van Dijk, P.G. Pieper, H.W. Vliegen, T.C. Konings, A.H. Zwinderman, B.J. Bouma, Contemporary survival of adults with congenital heart disease, Heart 101 (2015) 1989–1995.

[13] Z. Koyak, L. Harris, J.R. de Groot, C.K. Silversides, E.N. Oechslin, B.J. Bouma, W. Budts, A.H. Zwinderman, I.C. Van Gelder, B.J. Mulder, Sudden cardiac death in adult congenital heart disease, Circulation 126 (2012) 1944–1954.

[14] E. Oechslin, D.A. Harrison, M.S. Connelly, G.D. Webb, S.C. Siu, Mode of death in adults with congenital heart disease, Am. J. Cardiol. 86 (10) (Nov 15 2000) 1111–1116.

[15] D. Ntiloudi, G. Giannakoulas, D. Parcharidou, T. Panagiotidis, M.A. Gatzoulis, H. Karvounis, Adult congenital heart disease: a paradigm of epidemiological change, Int. J. Cardiol. 218 (Sep 1 2016) 269–274.

[16] F.H. Rodriguez III, A.J. Marelli, The epidemiology of heart failure in adults with congenital heart disease, Heart Fail. Clin. 10 (1) (2014) 1–7.

[17] W. Budts, J. Roos-Hesselink, T. Radle-Hurst, A. Eicken, T.A. McDonagh, E. Lambrinou, M.G. Crespo-Leiro, F. Walker, A.A. Frogoudaki, Treatment of heart failure in adult congenital heart disease: a position paper of the Working Group of Grown-Up Congenital Heart Disease and the Heart Failure Association of the European Society of Cardiology, Eur. Heart J. 37 (2016) 1419–1427.

[18] P. Khairy, J. Aboulhosn, M.Z. Gurvitz, A.R. Opotowsky, F.P. Mongeon, J. Kay, A.M. Valente, M.G. Earing, G. Lui, D.R. Gersony, S. Cook, J.G. Ting, M.J. Nickolaus, G. Webb, M.J. Landzberg, C.S. Broberg, Alliance for Adult Research in Congenital C. Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study, Circulation 122 (2010) 868–875.

[19] S. Apers, A.H. Kovacs, K. Luyckx, C. Thomet, W. Budts, J. Enomoto, M.A. Sluman, J.K. Wang, J.L. Jackson, P. Khairy, S.C. Cook, S. Chidambarathanu, L. Alday, K. Eriksen, M. Dellborg, M. Berghammer, E. Mattsson, A.S. Mackie, S. Menahem, M. Caruana, G. Veldtman, A. Soufi, A.W. Romfh, K. White, E. Callus, S. Kutty, S. Fieuws, P. Moons, Consortium A-I and Isachd, Quality of life of adults with congenital heart disease in 15 countries: evaluating country-specific characteristics, J. Am. Coll. Cardiol. 67 (2016) 2237–2245.

[20] P. Moons, D. Hilderson, K. Van Deyk, Implementation of transition programs can prevent another lost generation of patients with congenital heart disease, Eur. J. Cardiovasc. Nurs. 7 (2008) 259–263.

[21] T. Takken, A. Giardini, T. Reybrouck, M. Gewillig, H.H. Hovels-Gurich, P.E. Longmuir, B.W. McCrindle, S.M. Paridon, A. Hager, Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: a report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology, Eur. J. Prev. Cardiol. 19 (2012) 1034–1065.

[22] W. Budts, M. Börjesson, M. Chessa, F. van Buuren, P. Trigo Trindade, D. Corrado, H. Heidbuchel, G. Webb, J. Holm, M. Papadakis, Physical activity in adolescents and adults with congenital heart defects: individualized exercise prescription, Eur. Heart J. 34 (2013) 3669–3674.

[23] P. Moons, W. Scholte op Reimer, S. De Geest, B. Fridlund, J. Heikkila, T. Jaarsma, J. Martensson, K. Smith, S. Stewart, A. Stromberg, D.R. Thompson, Undertaking Nursing Interventions Throughout Europe Research G. Nurse specialists in adult congenital heart disease: the current status in Europe, Eur. J. Cardiovasc. Nurs. 5 (2006) 60–67.

[24] J.G. Rogers, C.B. Patel, R.J. Mentz, B.B. Granger, K.E. Steinhauser, M. Fiuzat, P.A. Adams, A. Speck, K.S. Johnson, A. Krishnamoorthy, H. Yang, K.J. Anstrom, G.C. Dodson, D.H. Taylor Jr., J.L. Kirchner, D.B. Mark, C.M. O'Connor, J.A. Tulsky, Palliative Care in Heart Failure: the PAL-HF randomized, controlled clinical trial, J. Am. Coll. Cardiol. 70 (2017) 331–341.

[25] D. Tobler, M. Greutmann, J.M. Colman, M. Greutmann-Yantiri, L.S. Librach, A.H. Kovacs, End-of-life care in hospitalized adults with complex congenital heart disease: care delayed, care denied, Palliat. Med. 26 (2012) 72–79.

[26] D. Tobler, M. Greutmann, J.M. Colman, M. Greutmann-Yantiri, L.S. Librach, A.H. Kovacs, End-of-life in adults with congenital heart disease: a call for early communication, Int. J. Cardiol. 155 (2012) 383–387.

[27] D. Tobler, M. Greutmann, J.M. Colman, M. Greutmann-Yantiri, S.L. Librach, A.H. Kovacs, Knowledge of and preference for advance care planning by adults with congenital heart disease, Am. J. Cardiol. 109 (2012) 1797–1800.

[28] M. Greutmann, D. Tobler, J.M. Colman, M. Greutmann-Yantiri, S.L. Librach, A.H. Kovacs, Facilitators of and barriers to advance care planning in adult congenital heart disease, Congenit. Heart Dis. 8 (2013) 281–288.

[29] D. Kavalieratos, L.P. Gelfman, L.E. Tycon, B. Riegel, D.B. Bekelman, D.Z. Ikejiani, N. Goldstein, S.E. Kimmel, M.A. Bakitas, R.M. Arnold, Palliative care in heart failure: rationale, evidence, and future priorities, J. Am. Coll. Cardiol. 70 (2017) 1919–1930.

[30] S.E. Bowater, J.K. Speakman, S.A. Thorne, End-of-life care in adults with congenital heart disease: now is the time to act, Curr. Opin. Support. Palliat. Care 7 (2013) 8–13.

[31] T. Jaarsma, J.M. Beattie, M. Ryder, F.H. Rutten, T. McDonagh, P. Mohacsi, S.A. Murray, T. Grodzicki, I. Bergh, M. Metra, I. Ekman, C. Angermann, M. Leventhal, A. Pitsis, S.D. Anker, A. Gavazzi, P. Ponikowski, K. Dickstein, E. Delacretaz, L. Blue, F. Strasser, J. McMurray, Advanced Heart Failure Study Group of the HFAotESC, Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology, Eur. J. Heart Fail. 11 (2009) 433–443.

[32] D. Tobler, N. de Stoutz, M. Greutmann, Supportive and palliative care for adults dying from congenital heart defect, Curr. Opin. Support. Palliat. Care 5 (2011) 291–296.

[33] T. Van Puyvelde, K. Ameloot, M. Roggen, E. Troost, M. Gewillig, W. Budts, A. Van De Bruaene, Outcome after cardiopulmonary resuscitation in patients with congenital heart disease, Eur. Heart J. Acute Cardiovasc. Care 7 (5) (Aug 2018) 459–466.

[34] A.H. Kovacs, M.J. Landzberg, S.J. Goodlin, Advance care planning and end-of-life management of adult patients with congenital heart disease, World J. Pediatr. Congenit. Heart Surg. 4 (2013) 62–69.