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Editorial

Risk stratification in congenital heart disease - A call for protocolised assessment and multicentre collaboration

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Mortality in patients with congenital heart disease (CHD) has dramatically decreased over the last decades. The main reasons for this trend include early CHD diagnosis, and the introduction and subsequent improvement of surgical and percutaneous interventions [1]. The increase in survival is evident in all groups of CHD. For example, cardiac surgery and intervention has transformed the natural history of patients with large ventricular septal defect (VSD) who, in the past, were destined to develop pulmonary hypertension, often severe enough to cause shunt reversal and cyanosis, the hallmarks of Eisenmenger syndrome [2]. Severe pulmonary vascular disease precludes repair of the defect and is, even today, associated with a very high morbidity and mortality [3,4]. Nowadays, the vast majority of patients born with a VSD in developed countries are diagnosed early and, when appropriate, undergo surgical or percutaneous repair. As a consequence, the incidence of Eisenmenger syndrome has dramatically decreased and the survival prospects of patients with VSD have been transformed [5,6]. The same is true of patients with atrial septal defects (ASDs), who nowadays undergo percutaneous repair or cardiac surgery. Their survival prospects are today comparable to that of the general population, while reports from the 60s and 70s clearly demonstrated that unrepaired ASDs were associated with the risk of premature death, with a mortality of 12% and 76% at the age of 20 and 50 years, respectively [7]. Even accounting for bias related to the limited diagnostic tools available 5 decades ago, the improvement in survival prospects for CHD patients is staggering.

Consequently, the number of adult patients with CHD is significantly increasing over the last decades and, in developed countries, there are currently more adults than children with CHD [8]. The vast majority of CHD patients require regular, life-long follow-up, provided or coordinated by tertiary CHD centres, with individualised management plans, taking into account cardiac anatomy, past interventions, comorbidities and lesion-specific complications. Indeed, heterogeneity in clinical presentation and outcome is high, even within subgroups of CHD patients. For example, while some adult patients with repaired tetralogy of Fallot (ToF) remain at risk of malignant tachycardias, premature death and/or heart failure [9], many are asymptomatic and may even become elite athletes, such as the snowboard star and three-time Olympic gold medallist, Shaun Roger White.

Classifying CHD patients for risk stratification solely on underlying anatomy is, thus, insufficient. More advanced risk stratification tools are needed, that are able to predict morbidity and mortality. Moreover, objective risk stratification tools are required to assist physicians when listing patients for heart transplant or ICD therapy.

In this issue of the International Journal of Cardiology, Baggen et al. describe a novel model for risk stratification in adult CHD patients. They assessed the prognostic value of 14 clinical parameters, selected by an expert panel, on a moderate-size (n = 602), single centre cohort of patients with CHD of moderate or severe anatomic complexity. They used a combined endpoint of death, heart failure or arrhythmia. The parameters independently contributing to risk stratification in the multivariable model were age, severity of CHD, NYHA class, cardiac medication, history of re-intervention for CHD, BMI and NT-proBNP.

This is important work, as most reports on risk stratification in CHD do not go beyond providing information on individual parameters. Baggen et al. take CHD risk stratification to the next essential step, by developing and validating their model on an external cohort of patients (n = 402). They used a multivariable logistic regression model for events within a 4 -years follow-up period. The externally validated C-statistic was satisfactory (0.78), albeit far from perfect, and confirms the discriminative ability of this model. This model allows for calculation of absolute risk and the authors provide an online web tool for this (https://achdwebcalculator.shinyapps.io/achdwebcalculator/). This is a very useful feature, as providing only odds ratios or hazard ratios, is of limited clinical value. Moreover, by inviting others to further

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collaboration and sharing their R-code script, they may help develop even more reliable models in the future.

Considering the significant heterogeneity of the CHD population and the limited prevalence of many lesions, collaboration studies are required to develop risk stratification models for the overall CHD cohort, and for individual CHD cohorts. Robust, but widely available clinical variables should be considered for use in such models. NYHA classification is widely used and was a component of the model proposed by Baggen et al. However, NYHA class alone lacks the discriminative value for predicting outcome and its interobserver variability is wide. Objective measures of exercise capacity, such as parameters derived from cardiopulmonary exercise testing, may be more reliable in defining the functional capacity of individual patients, but are not universally available and are not standardised across centres. Moreover, while patients receiving 'cardiac medication' (a parameter in the final risk model by Baggen et al.) are likely to have more advanced disease compared to those not on such medication, protocols and thresholds for administering medication vary greatly between centres, as evidence for their use in CHD is lacking.

An increased body mass index (BMI) was also a predictor of adverse outcome in the model by Baggen et al., and appears to reflect what is known for the general population. However, the prognostic value of BMI is likely to vary between countries, and also between subgroups of patients. CHD patients with complex and/or advance disease are likely to develop cachexia and, hence, a U-shaped relation between BMI and risk is expected in a population at risk of heart failure.

Clearly, there are still major challenges in developing reliable, universally applicable risk stratification tools for CHD. Models developed for the entire CHD population will always be limited by the inherent heterogeneity of this population, as well as substantial differences in demographic and clinical characteristics between CHD cohorts in different centres, as observed in the study by Baggen et al. An internationally shared protocolised approach to adult CHD care and follow-up is urgently needed, based on expert consensus and multicentre collaboration, in order to enhance our ability to optimise risk stratification models and improve the care of our patients.

Conflict of interest

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

References

[1] 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.

[2] P. Wood, The Eisenmenger syndrome or pulmonary hypertension with reversed central shunt, Br. Med. J. 2 (1958) 755–762.

[3] H. Baumgartner, P. Bonhoeffer, N.M. De Groot, F. de Haan, J.E. Deanfield, N. Galie, M.A. Gatzoulis, C. Gohlke-Baerwolf, H. Kaemmerer, P. Kilner, F. Meijboom, B.J. Mulder, E. Oechslin, J.M. Oliver, A. Serraf, A. Szatmari, E. Thaulow, P.R. Vouhe, E. Walma, A. Vahanian, A. Auricchio, J. Bax, C. Ceconi, V. Dean, G. Filippatos, C. Funck-Brentano, R. Hobbs, P. Kearney, T. McDonagh, B.A. Popescu, Z. Reiner, U. Sechtem, P.A. Sirnes, M. Tendera, P. Vardas, P. Widimsky, L. Swan, F. Andreotti, M. Beghetti, M. Borggrefe, A. Bozio, S. Brecker, W. Budts, J. Hess, R. Hirsch, G. Jondeau, J. Kokkonen, M. Kozelj, S. Kucukoglu, M. Laan, C. Lionis, I. Metreveli, P. Moons, P.G. Pieper, V. Pilossoff, J. Popelova, S. Price, J. Roos-Hesselink, M.S. Uva, P. Tornos, P.T. Trindade, H. Ukkonen, H. Walker, G.D. Webb, J. Westby, ESC Guidelines for the management of grown-up congenital heart disease (new version 2010), Eur. Heart J. 31 (2010) 2915–2957.

[4] A. Kempny, C.S. Hjortshoj, H. Gu, W. Li, A.R. Opotowsky, M. Landzberg, A.S. Jensen, L. Sondergaard, M.E. Estensen, U. Thilen, W. Budts, B.J. Mulder, I.M. Blok, L. Tomkiewicz-Pajak, K. Szostek, M. D'Alto, G. Scognamiglio, K. Prokselj, G.P. Diller, K. Dimopoulos, S.J. Wort, M.A. Gatzoulis, Predictors of death in contemporary adult patients with Eisenmenger syndrome: a multicentre study, Circulation 135 (2017) 1432–1440.

[5] C.S. Hjortshoj, A.S. Jensen, K. Sorensen, E. Nagy, B. Johansson, T. Kronvall, M. Dellborg, M.E. Estensen, H. Holmstrom, M. Turanlahti, U. Thilen, L. Sondergaard, Epidemiological changes in Eisenmenger syndrome in the Nordic region in 1977–2012, Heart 103 (2017) 1353–1358.

[6] J.W. Roos-Hesselink, F.J. Meijboom, S.E. Spitaels, R. Van Domburg, E.H. Van Rijen, E.M. Utens, A.J. Bogers, M.L. Simoons, Outcome of patients after surgical closure of ventricular septal defect at young age: longitudinal follow-up of 22–34 years, Eur. Heart J. 25 (2004) 1057–1062.

[7] M. Campbell, Natural history of cyanotic malformations and comparison of all common cardiac malformations, Br. Heart J. 34 (1972) 3–8.

[8] 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.

[9] G.P. Diller, A. Kempny, E. Liodakis, R. Alonso-Gonzalez, R. Inuzuka, A. Uebing, S. Orwat, K. Dimopoulos, L. Swan, W. Li, M.A. Gatzoulis, H. Baumgartner, Left ventricular longitudinal function predicts life-threatening ventricular arrhythmia and death in adults with repaired tetralogy of Fallot, Circulation 125 (2012) 2440–2446.