

Letters

Role of Acquired Cardiovascular Disease in Tetralogy of Fallot Patients >50 Years of Age



Acquired cardiovascular diseases, such as coronary artery disease (CAD) and cerebrovascular accident (CVA) or transient ischemic attack (TIA), were reported main determinants of mortality in elderly patients with mainly anatomically classified simple congenital heart disease (CHD) (1,2). However, whether this is similar in patients born with severe cyanotic lesions remains unknown. Patients with tetralogy of Fallot (TOF) are the first specific group with cyanotic CHD, on average reaching >50 years of age (3). We sought to determine the role of acquired cardiovascular disease in mortality and morbidity of elderly TOF patients.

Out of 794 adult TOF patients within 6 participating centers in the prospective Dutch nationwide CONCOR (Congenital Corvicia) registry, a total of 167 patients >50 years of age were included (55% men, 40% previous shunt, 32% >18 years of age at correction, 42% previous sustained ventricular tachycardia, 11% previous ventricular tachycardia, 25% previous pulmonary valve replacement, 7% previous CVA or TIA, 2% previous CAD, QRS duration 150 ± 27 ms). Follow-up (6.4 ± 3.8 years) started at CONCOR registry inclusion ($n = 65$, age >50 years) or at the 50th birthday ($n = 102$, 50th birthday after CONCOR registry inclusion). Mortality was compared to a reference cohort (100:1 TOF patient) of age- and gender-matched Dutch inhabitants using data from the Dutch Central Bureau of Statistics.

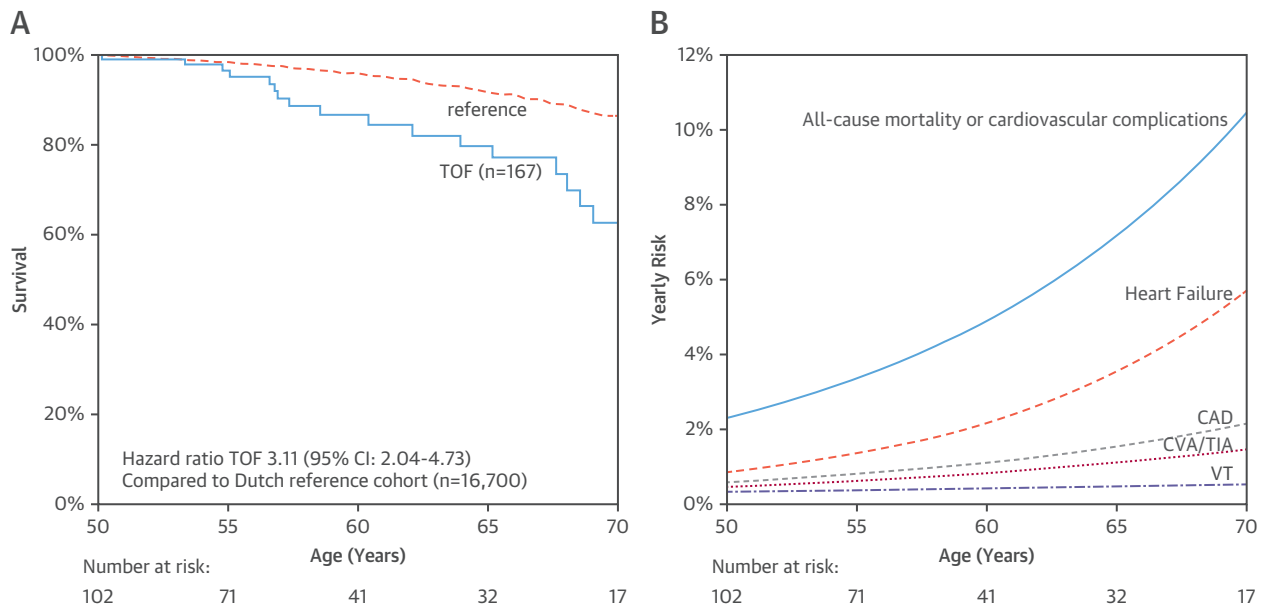
TOF patients had an increased mortality risk compared to the reference cohort (hazard ratio: 3.11; 95% confidence interval: 2.04 to 4.73) (Figure 1A). There was a cardiovascular cause of death in 64% (14 of 22) patients (heart failure: 12, sudden cardiac death: 1, CVA: 1) versus 20% in a comparable Dutch population. Heart failure progression was observed in 24 patients (11 right ventricular failure, 11 right ventricular + left ventricular failure, 2 left ventricular failure). Furthermore, 11 patients had

CAD (2 coronary revascularization, 3 myocardial infarction, 6 stable CAD) and 8 patients had CVA ($n = 4$) or TIA ($n = 4$) during follow-up. CVA or TIA was more prevalent than expected ($n = 4.6$), while myocardial infarction occurred at the expected rate. Only 4 patients had VT during follow-up. The estimated yearly risk of heart failure increased from 0.8% per year in patients 50 years of age to 5.7% in patients 70 years of age (Figure 1B). The risk of acquired cardiovascular disease (CAD and CVA or TIA) was substantially lower but also increased yearly (from 0.5% and 0.4% at 50 years of age to 2.1% and 1.5% at 70 years of age, respectively). The estimated yearly risk of all morbidity or mortality increased to 10.5% (95% confidence interval: 6.7% to 16.4%) at 70 years of age (Figure 1B).

The present study demonstrated a markedly increased mortality of TOF patients, after reaching the 50th birthday. Heart failure was the cause of death in 55%, likely attributed to TOF-related factors. This is in line with TOF patients from other age categories but in contrast with previous studies focusing on elderly CHD patients, which found acquired cardiovascular diseases as main determinants of mortality in elderly (mainly non-severe) CHD patients (1-3). Presumably due to residual lesions and longstanding childhood cyanosis in TOF, heart failure outweighs typical acquired cardiovascular diseases throughout late follow-up. The rate of myocardial infarction was similar to the general population. CVA/TIA, which were approximately 2-fold increased, may be attributed to both TOF-related factors such as residual septal defects or supraventricular arrhythmias, and acquired cardiovascular disease.

This study is limited by its design; a retrospective analysis of patients enrolled in a prospective registry. Advantages include the large, multicenter nature of the registry with inclusive enrollment at each site (which may reduce selection bias) and prospective follow-up data. However, data were retrospectively acquired and outcomes could be missed if not noted in hospital database or CONCOR registry. The results are applicable to late survivors of TOF born before 1965. Currently, most children are operated on earlier with altered techniques.

In conclusion, TOF patients >50 years of age had an approximately 3-fold higher mortality risk compared

FIGURE 1 Overall Survival and Yearly Risk of Cardiovascular Disease in Tetralogy of Fallot

(A) Overall survival in tetralogy of Fallot (TOF) versus Dutch reference population. Survival curves were created using a delayed entry method with age as time scale for left-truncated, right-censored data to display overall survival of TOF patients compared to the matched (1:100) Dutch reference cohort. **(B)** Estimated yearly risk of cardiovascular disease in tetralogy of Fallot. Estimated yearly risk of cardiovascular disease with age as time scale using smoothed estimates based on B-splines (bshazard package, R Project for Statistical Computing, Vienna, Austria). CAD = coronary artery disease; CVA = cerebrovascular accident; TIA = transient ischemic attack; VT = ventricular tachycardia.

to the general population. Acquired cardiovascular diseases such as myocardial infarction and CVA had a limited role when compared to heart failure.

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<http://dx.doi.org/10.1016/j.jacc.2017.03.529>

Please note: This work was supported by the Netherlands Heart Institute (NL-HI) and Nuts Ohra foundation. The work described in this study was carried out in the context of the Parelsnoer Institute. Parelsnoer Institute is part of and funded by the Dutch Federation of University Medical Centers. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Truncating Variants in Titin Independently Predict Early Arrhythmias in Patients With Dilated Cardiomyopathy



Dilated cardiomyopathy (DCM) has a population prevalence of ~1 in 500 and is associated with prognostically adverse arrhythmias at initial disease presentation in up to one-third of patients (1). While