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ORIGINAL ARTICLE

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A first population-based long-term outcome study in adults with repaired tetralogy of Fallot in Malta

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Abstract

Objectives: To determine overall and reintervention-free survival for repaired Maltese tetralogy of Fallot patients and to investigate the potential impact of gender, age at repair, genetic syndromes, previous palliation, and type of repair on these outcomes.

Design: All 130 tetralogy of Fallot patients born before the end of 1997 included in the local database were extracted. Surgical repair type, age at repair and operative survival were analyzed among the 103/130 repaired patients. Kaplan–Meier survival analyses were performed on the 75 repair survivors with complete follow-up data (mean follow-up 26.37 ± 9.27 (range 9.95–51.21) years).

Results: Patients born after 1985 were operated at a younger age (median 1.28 years) compared with patients born before 1985 (median 9.64 years) ($P < .001$). Transannular patch repair was the commonest operation among patients born after 1985 (43.90%), while repair without transannular patch use prevailed among those born before 1985 (66.13%). 90.24% of patients born after 1985 survived reparative surgery compared with 70.37% of those born before 1985. Of the 75 repair survivors, 7 (9.33%) died of cardiac causes and 22 (29.33%) needed reintervention during follow-up. Overall estimated mean survival was 45.56 years (95% CI 41.67–49.24) with estimated survival rate of 77.5% at 40 years from repair. Estimated mean reintervention-free survival was 37.71 years (95% CI 33.75–41.66) with estimated reintervention-free survival rate of 59.2% at 40 years. Patients with genetic syndromes had significantly lower overall survival after repair. Transannular patch repair was associated with significantly lower reintervention-free survival (median 32.37 years (95% CI 12.75–51.99)) compared with repair without transannular patch [median 44.21 years (95% CI 43.06–45.35); $P = .03$].

Conclusions: Although survival after tetralogy of Fallot repair in contemporary patients is very good, cardiac death can occur at any stage and structural reintervention is common. Regular follow-up with imaging and rhythm monitoring remains of utmost importance in all patients.

KEYWORDS

follow-up studies, population-based, survival analysis, tetralogy of Fallot

1 | INTRODUCTION

Tetralogy of Fallot (TOF) is the commonest cyanotic congenital cardiac defect. Several variants of TOF are recognized including TOF with double-outlet right ventricle (DORV), TOF with pulmonary atresia, and TOF with absent pulmonary valve. TOF is slightly commoner in males and can be associated with a number of genetic syndromes, the commonest being 22q11.2 microdeletion syndrome.[1] Most contemporary adults with TOF will have had surgical repair when younger. Repair involves relief of right ventricular outflow tract obstruction (RVOTO), ventricular septal defect (VSD) closure, and correction of any other associated lesions.[2] Reparative surgery has evolved significantly since its origins in the mid-1950s,[3] with a move toward repair in infancy particularly since the mid-1970s, lesser use of palliative shunts, less repairs via right ventriculotomy and efforts to maintain integrity of the pulmonary valve annulus when possible.[4] It is well-recognized that reparative surgery is not curative and that repeat surgery and/or intervention are often required to correct residual or reacquired hemodynamically significant

lesions, particularly RVOTO recurrence, and pulmonary regurgitation (PR).[5]

Malta is a group of islands in the Mediterranean Sea located 93 km south of the Italian island of Sicily. The vast majority of inhabitants are native Maltese, who are genetically of Eastern Mediterranean descent with Greco-Roman and Arabic influences and a later European influence. The islands have a population of around 425 000 and a crude birth rate of 9.5/1000 in 2013.[6] Epidemiological studies in the 1990s quantified the birth prevalence of different congenital heart defects (CHD) in Malta and found the overall incidence of CHD to be comparable to that in other European countries at 0.8%. It was however noted that the prevalence for TOF in Malta between 1990 and 1994 was 0.8/1000 (95% CI 0.46–1.15) live births, which was significantly higher than that reported in similar studies at the time.[7] A dedicated database, Maltese Pediatric Cardiology Database (MAPCAD), was instituted at the time and all known CHD cases were included both prospectively and retrospectively.[8] Virtually all congenital cardiac surgery on children and adults born in Malta is carried out in overseas tertiary referral centers, in the United Kingdom, through a reciprocal national health service agreement, while a number of structural cardiac interventions are carried out locally by visiting specialists. Transfer of care from pediatric to adult services takes place at the age of 14–16 years. Transthoracic echocardiography became available in the mid-1980s. An on-site pediatric cardiology service started operating in the early 1990s, with adult congenital heart disease (ACHD) services starting a few years later. This study is the first to report the long-term outcomes of Maltese repaired TOF patients and also one of the few in the international literature with follow-up in excess of 40 years. The aims were to determine overall survival and reintervention-free survival from time of reparative surgery, to analyze the potential impact of patient gender, age at repair, prior palliation and presence of genetic syndromes on these outcomes, and to assess differences in outcomes based on type of reparative surgery.

2 | METHODS

2.1 | Study protocol

All patients with a primary diagnosis of TOF, including all variants listed above, who were born before December 31, 1997, followed within the Maltese health care system and included in MAPCAD by the end of year 2013, were extracted. For the purposes of long-term outcome analysis, only patients known to have survived reparative surgery and with complete follow-up data were included. Perioperative mortality was defined as death at, or within the first 30 days after, reparative surgery. The study protocol was approved by the University of Malta Research Ethics Committee, after being granted institutional data protection clearance, and conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all participants or authorized representatives.

Clinical data obtained from MAPCAD was supplemented with information gathered from hospital paper and digital notes. Mortality data was obtained from the National Mortality Registry. The term "reparative surgery" refers to the surgical procedure during which biventricular repair was performed with RVOTO relief, VSD closure, and correction of any other significant lesions when necessary. For comparison purposes, reparative surgery was subdivided into five categories: (1) repair involving relief of infundibular and/or pulmonary valvular stenosis without the use of a transannular patch, and thus without sacrificing the pulmonary valve annulus (non-TAP repair), (2) repair using a transannular patch (TAP repair), (3) repair with implantation of a right ventricle to pulmonary artery (RV-PA) conduit, (4) repair including implantation of a new tissue pulmonary valve, or (5) other surgery, which included cases in which surgical details were incomplete or absent. While studying type and timing of reparative surgery and perioperative mortality, repaired patients were divided into two categories based on whether they were born before or after 1985. This subdivision was based on the improvements in the diagnosis that accompanied the introduction of echocardiography and changes in surgical management of TOF that started to take place sometime before.[4]

During long-term survival analysis, "cardiac death" was defined as death from any cardiac cause as declared on the death certificate or confirmed at postmortem studies. This included death directly related to reinterventions but excluded perioperative mortality related to the original repair. The term "reintervention" was used to denote any surgical or transcatheter procedure performed to tackle any hemodynamically significant residual or recurrent structural lesions, for example, recurrence of RVOTO and PR. All reinterventions were performed following consensus at multidisciplinary team discussion and timing of procedures was in line with international recommendations.[1] In the case of patients requiring more than one reintervention, only the first procedure was taken into consideration. Repeat surgery within a few weeks from, and directly related to, the reparative operation, aimed to treat a complication of the repair itself, was not considered as a reintervention. Electrophysiological studies and radiofrequency ablation of arrhythmias, implantation of permanent pacemakers and percutaneous coronary interventions or coronary artery bypass grafting needed to manage acquired coronary artery disease were not taken into account as relevant reinterventions for the purposes of this study. "Reintervention-free survival" refers to time in years between reparative surgery and the first reintervention. Prior palliation refers to interventions performed before the reparative procedure, in the main represented by surgical systemic-to-pulmonary shunt to augment pulmonary blood flow.

In a first outcome analysis, overall survival and reintervention-free survival for all TOF patients that survived reparative surgery were generated. Subsequently, the potential impact of four separate factors—patient gender, prior palliative surgery, timing of reparative surgery (before or after age 16 years) and presence of a genetic syndrome—on these long-term outcomes was studied. Finally, differences in outcomes between the two commonest reparative surgical procedures (TAP repair and non-TAP repair) were analyzed.

2.2 | Statistical methods

Categorical variables were analyzed using chi-square tests. Fisher's exact test was applied in the case of smaller sample sizes. Comparison

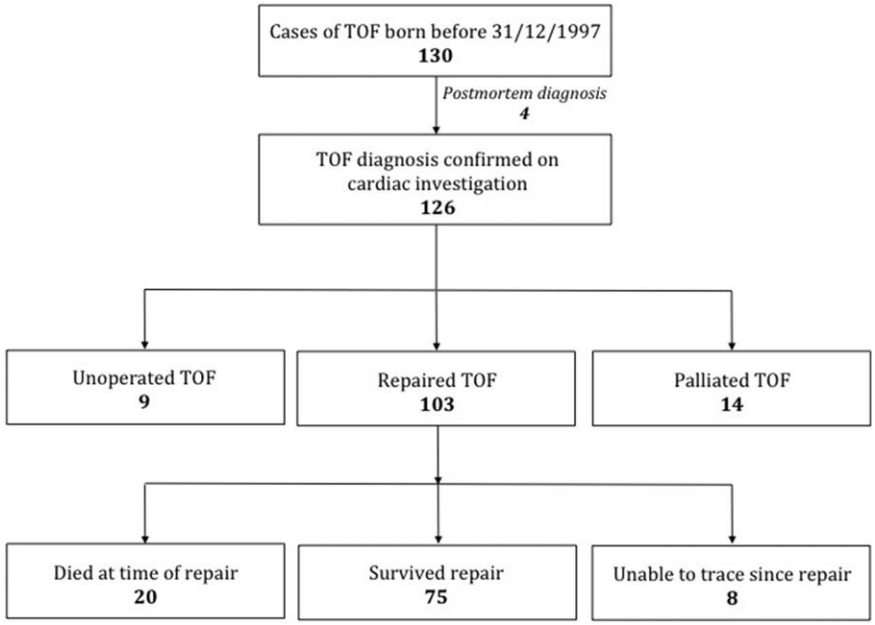

FIGURE 1 Cohort of known Maltese patients with tetralogy of Fallot (TOF). In our study, unoperated TOF patients or those that underwent palliation only were excluded. For the purposes of long-term outcome analyses, only repair survivors with complete follow-up data were included ($n = 75$).

of all continuous variables was performed using Mann–Whitney *U* test after Shapiro–Wilk test determined a non-normal distribution for all. Kaplan–Meier methodology was used to determine estimates of overall and reintervention-free survival for repaired TOF patients. The statistical significance of comparisons between Kaplan–Meier curves was calculated using a log-rank test. All analyses were performed using SPSS 21 (IBM SPSS 21, SPSS Inc., Chicago, IL). Statistical significance was defined as $P \leq .05$.

3 | RESULTS

A total of 130 TOF patients were extracted, of which 103 had undergone reparative surgery. All cases were operated in the United Kingdom, with the cases being divided between a number of centers in London or Birmingham. Sixty-two of the 103 repaired patients (60.19%) were male. In 14 patients (13.59%), TOF was part of a genetic syndrome, with trisomy 21 (4 patients) and 22q11.2 microdeletion syndrome (3 patients) being the most commonly encountered. Long-term follow-up data among TOF repair survivors was complete for 75 patients (90.36%) (47 males). In 8/103 repaired patients (9.64%), no follow-up data was available beyond repair and these were subsequently excluded from long-term outcome analyses (Figure 1).

3.1 | Differences in surgical trends with time

Age at reparative surgery for the 41/103 repaired patients born after 1985 (median 1.28 years; range 0.19–10.81) was significantly lower than that among the 62 patients born before 1985 (median 9.64 years; range 0.55–56.06) ($P < .001$). While non-TAP repair was the commonest form of repair in patients born before 1985 (66.13%), TAP repair was the commonest operation among patients born after 1985 (43.90%), with other forms of repair representing a minority in both subgroups. These differences in surgical strategies between the 2 age subgroups were statistically significant ($P = .02$) (Figure 2). There was a trend toward less palliation use prior to reparative surgery among younger patients (26.83%) compared with patients in the older subgroup (45.16%) ($P = .07$). Survival after reparative surgery improved significantly with time, with 90.24% of patients born after 1985 surviving the repair compared with 70.37% of those born before 1985 ($P = .02$).

3.2 | Long-term outcome analysis for all repaired TOF patients

The 75 patients that survived reparative surgery and for whom complete follow-up data was available were operated between 1962 and 2000. Non-TAP repair was undertaken in 41 patients (54.7%), TAP repair in 25 (33.3%), repair with RV-PA conduit in 5 (6.7%), repair with implantation of new pulmonary valve in 1 (1.3%), and other forms of repair in 3 patients (4%). The mean duration of follow-up was 26.37 ± 9.27 years (median 23.84 years; range 9.95–51.21 years). A follow-up of at least 10 years was available for all but one patient (98.67%), at least 20-year follow-up for 61 patients (81.33%), at least 30-year follow-up for 21 patients (28%), and 40-year follow-up and over for 9/75 patients (12%). There were 7 cardiac deaths (9.33%) during follow-up, with an overall estimated mean survival from repair of 45.56 years (95% CI 41.67–49.24). There were no cardiac deaths in the first 10 years following reparative surgery. Kaplan–Meier estimates of survival rates were 98.6% at 20 years, 88.2% at 30 years, and 77.5% at 40 years from repair (Figure 3). Repaired TOF patients with genetic

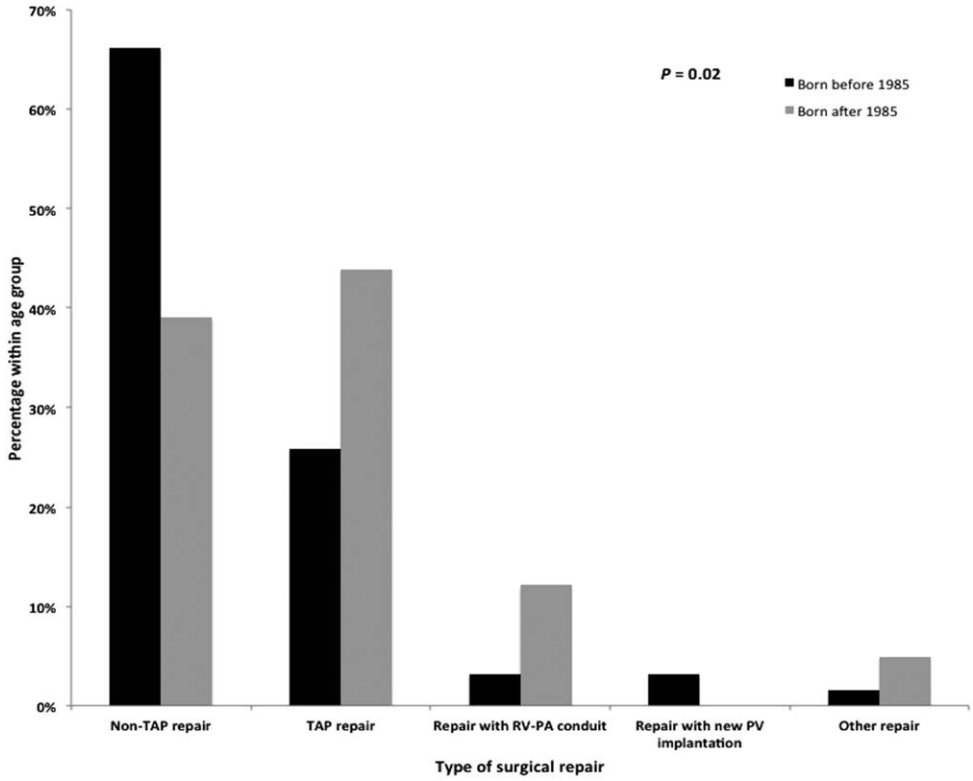

FIGURE 2 Comparison of trends in surgical reparative techniques for patients born before and after 1985. Chi-square analysis of all surgical strategies used in the two patient subgroups showed a significant difference ($P = .02$) Abbreviations: PV, pulmonary valve; RV-PA, right ventricle to pulmonary artery; TAP, transannular patch.

syndromes had a significantly lower estimated survival [mean 31.17 years (95% CI 26.34–36.00)] compared with non-syndromic patients [mean survival 46.17 years (95% CI 42.31–50.04); $P = .048$]. Patient gender, age at reparative surgery and prior palliation had no significant impact on long-term survival.

Twenty-two of the 75 patients (29.33%) required reintervention during follow-up: 8 were in patients with non-TAP repair, 10 in patients with TAP repair, 2 in patients with a repair using an RV-PA conduit and 2 in patients with other forms of repair. The estimated mean reintervention-free survival was 37.71 years (95% CI 33.75–41.66). No patients required reintervention in the first 10 years after follow-up. The estimates of reintervention-free survival rates were 84.6% at 20 years, 69.1% at 30 years, and 59.2% at 40 years. In 3 patients, reintervention was required after more than 40 years after repair (Figure 4). Reintervention-free survival was not affected by patient gender, age at reparative surgery, previous palliation, or presence of genetic syndromes. Analysis of impact of the four studied

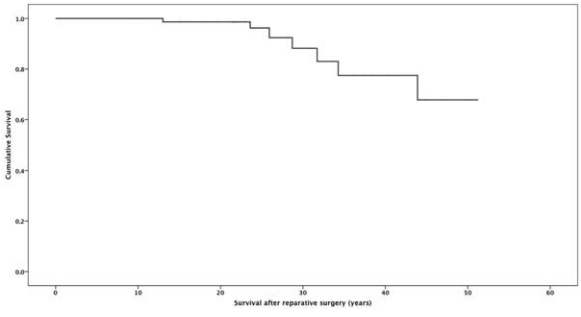

FIGURE 3 Kaplan–Meier curve showing cumulative overall survival after reparative surgery for repair survivors in the Maltese TOF cohort ($n = 75$). Estimated survival rates after surgical TOF repair are 98.6% at 20 years, 88.2% at 30 years, and 77.5% at 40 years.

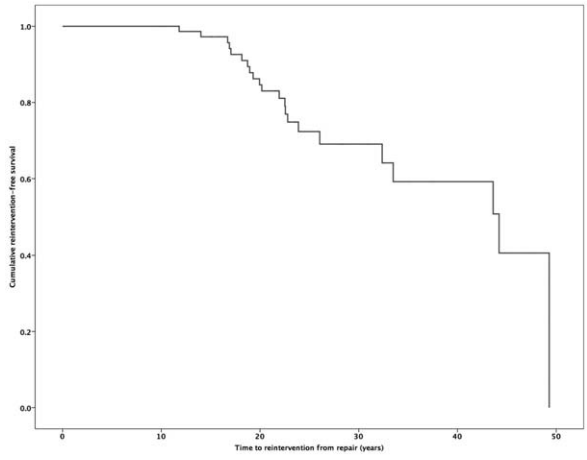

FIGURE 4 Kaplan–Meier curve showing cumulative reintervention-free survival after reparative surgery for repair survivors in the Maltese TOF cohort ($n = 75$). The majority of structural reinterventions were needed between 20 and 30 years from repair, with an accompanying decline in reintervention-free survival rate estimates from 84.6% at 20 years to 59.2% at 40 years.

TABLE 1 Analysis of impact of patient gender, prior palliative surgery, timing of reparative surgery, and genetic syndromes on long-term and reintervention-free survival among the 75 TOF repair survivors

(a) Patient gender	Male ($n = 47$)	Female ($n = 28$)	*P* value
Long-term survival (years)	43.70 (95% CI 38.80–48.60)	48.71 (95% CI 46.16–51.25)	.29
Reintervention-free survival (years)	38.55 (95% CI 33.49–43.60)	35.03 (95% CI 29.74–40.33)	.47
(b) Prior palliation	**Prior palliation ($n = 23$)**	**No prior palliation ($n = 52$)**	***P* value**
Long-term survival (years)	46.49 (95% CI 40.53–52.45)	42.40 (95% CI 38.69–46.12)	.73
Reintervention-free survival (years)	37.92 (95% CI 31.06–44.77)	37.12 (95% CI 32.72–41.51)	.97
(c) Age at reparative surgery	<16 years of age ($n = 64$)	≥16 years of age ($n = 11$)	*P* value
Long-term survival (years)	44.27 (95% CI 39.42–49.12)	45.01 (95% CI 40.99–49.02)	.32
Reintervention-free survival (years)	36.62 (95% CI 31.87–41.38)	41.23 (95% CI 35.01–47.44)	.34
(d) Genetic syndrome	**Syndrome ($n = 12$)**	**No syndrome ($n = 63$)**	***P* value**
Long-term survival (years)	31.17 (95% CI 26.34–36.00)	46.17 (95% CI 42.31–50.04)	**.048**
Reintervention-free survival (years)	31.76 (95% CI 27.65–35.86)	37.33 (95% CI 33.10–41.57)	.60

Survival estimates are expressed as mean years from reparative surgery followed by 95% confidence intervals. Significant *P* values are shown in bold.

factors on overall and reintervention-free survival are summarized in Table 1.

3.3 | Comparison of long-term outcomes of TOF repair with and without transannular patch use

TAP repair (25/75) and non-TAP repair (41/75) were the commonest two types of repair and together accounted for 88% of all repairs with long-term follow-up. Follow-up for these two types of surgical repair were comparable: mean follow-up for TAP repair patients was 25.11 ± 7.29 years (median 23.80 years; range 15.00–47.22) and mean follow-up for non-TAP repair patients was 27.55 ± 9.75 years (median 24.30 years; range 13.01–50.03). There were five deaths due to cardiac causes among the 41 patients who had non-TAP repair and 1 death in the 25-patient TAP repair subgroup. Reinterventions were required in 10/25 (40%) TAP repair patients and in 8/41 (19.5%) non-TAP repair patients. Kaplan–Meier survival estimates for the two subgroups were comparable (mean survival for TAP repair subgroup 45.53 years (95% CI 42.35–48.72) versus mean survival for non-TAP repair subgroup 44.28 years (95% CI 39.83–48.73); $P = .56$). There were significant differences in the type of reintervention needed as well as the timing of reintervention. While 9/10 patients (90%) with TAP repair required surgical PVR to correct significant residual PR, the commonest reintervention for non-TAP repair patients was transcatheter relief of RVOTO recurrence (37.5%) and only 2/8 patients (25%) requiring reintervention needed a surgical PVR for PR ($P = .01$). The estimated median reintervention-free survival for patients with a history of TAP repair was 32.37 years (95% CI 12.75–51.99) which was significantly lower compared with that for non-TAP repair patients [median 44.21 years (95% CI 43.06–45.35)] ($P = .03$). At 20, 30, and 40 years from reparative surgery, Kaplan–Meier estimates of reintervention-free survival rates for non-TAP repair were 94.4%, 82.8%, and 73.6%, respectively, compared with 73.1%, 57.0%, and 42.7%, respectively, for patients following TAP repair (Figure 5).

4 | DISCUSSION

The long-term outcomes of TOF repair have been reported by several institutions, from as early as the late 1970s.[2,3,9–13] Most studies report experiences from a single or, at most, a few centers from the same country. In the last years, multicenter collaborations have created registries for patients with repaired TOF, in an attempt to generate larger cohorts and more robust data.[14,15] The overall small size of the Maltese population and the national health care set-up has made it possible to carry out numerous population-based studies over the years. The current study is the first to investigate long-term outcomes following TOF repair in the Maltese population. In our literature search, we found only one previous population-based outcome study in repaired TOF, conducted in Finland.[10]

The increasing access to transthoracic echocardiography, which locally became available in the mid-1980s, and advances in cardiac surgery resulted in a move toward earlier diagnosis and surgical repair of TOF.[16,17] A shift toward earlier diagnosis of TOF and other CHD in Malta has already been reported.[18,19] Our study also demonstrated a shift toward earlier repair with a significant difference in age at repair between patients born before and after 1985. We also observed less scatter of ages at reparative surgery for those born after 1985 (range 0.19–10.81 years, IQR 1.90 years) compared with patients born before 1985 (range 0.55–56.06 years, IQR 10.88 years). Furthermore, we

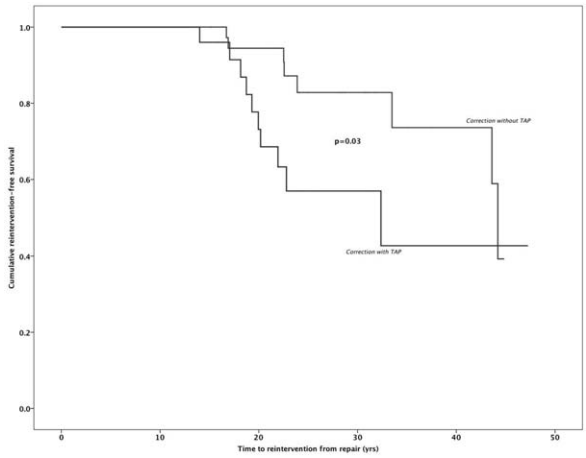

FIGURE 5 Comparison of reintervention-free survival between patients with reparative surgery with ($n = 25$) and without ($n = 41$) use of transannular patch (TAP). Patients undergoing TAP repair needed structural reinterventions earlier compared with patients where the pulmonary valve annulus was preserved at surgery.

noted a significant improvement in survival after reparative surgery for patients born after 1985.

The overall survival after reparative TOF surgery reported in recent series is encouraging.[9,10,12,13] Though the data emerging from our population-based study is overall positive, our patients' survival appears to be somewhat lower than that reported in two recent European studies with follow-up in excess of 40 years. Among our TOF patients that survived reparative surgery, estimated cumulative survival was 100% at 10 years and 98.6% at 20 years, going down to 88.2% at 30 years and 77.5% at 40 years. In their population-based Finnish study, Ylitalo et al.[10] reported survivals of 90% at 10 years, 88% at 20 years, and 83% at 40 years, while in the Dutch study by Cuypers et al.[13] survivals of 98% at 10 years, 96% at 20 years, 92% at 30 years, and 86% at 40 years were reported. This difference could in part be explained by the fact that, whereas our cohort included all long-term survivors of reparative surgery irrespective of age at repair, both other studies only included patients repaired before the age of 15 years, thus excluding patients that might have been exposed to longer periods of cyanosis. Furthermore, our cohort incorporated all TOF variants, including three patients with the more surgically-challenging anatomy of TOF with pulmonary atresia, whereas the latter was specifically excluded by Ylitalo et al.[10] The majority of cardiac deaths in our cohort (5/7) occurred between 20 and 35 years from repair (Figure 3), with one death occurring at 13 years and another at 43 years. This finding suggests the period between the second and fourth decades after repair as a time when patients might be at higher risk of cardiac death. At the same time, and possibly more importantly, this graph underlines the importance of vigilant follow-up at all ages after repair, particularly in patients with residual structural disease which could predispose to a higher arrhythmia burden.[20]

In our cohort, reinterventions were required in 22 patients during long-term follow-up, with the majority of structural procedures (17/22) being carried out between 10 and 30 years after repair (Figure 4). This finding suggests this period of time from TOF repair as that when reintervention is more likely to be required. At the same time, in some cases, reinterventions were needed even over 40 years from repair, again highlighting the importance of life-long follow-up with imaging to detect residua that need addressing later on in life.

Two of the four factors that we investigated for their potential impact on overall and reintervention-free survival were reported separately in different publications in recent years. In 2006, Michelion et al. suggested that repaired TOF patients with certain genetic syndromes had a poorer overall survival compared with nonsyndromic patients.[21] Similarly, genetic syndromes appeared to have a negative impact on overall survival but no effect on reintervention-free survival in our patients (Table 1). In our cohort, previous palliation did not affect overall or reintervention-free survival. This contrasts with what is documented in the literature. In fact, two studies quoted earlier, both of which included patients operated in a similar era to our group, demonstrated previous palliative shunt surgery to have a negative impact on survival: Cuypers et al. showed previous shunt surgery to be a predictor for late mortality,[13] and Ylitalo et al. found patients with primary palliation to have both an inferior late survival as well as higher reoperation rates.[10] Although Ylitalo et al.[10] investigated the impact of operative age on survival and event-free survival and demonstrated better survival in patients operated earlier, all the patients included in their cohort were operated before the age of 15 years. This differs from our study cohort, which included all operated patients, irrespective of age at repair. We found no significant differences in long-term outcomes between patients operated before age 16 years and those operated later, despite the latter having possibly been exposed to the deleterious effects of cyanosis for a longer time. To our knowledge, ours is the only study with late long-term follow-up that investigated patient gender as a possible factor impacting outcomes. We documented no significant differences between male and female patients (Table 1).

Comparison of the two main forms of repair represented in our cohort, namely TAP repair and non-TAP repair, showed a significant difference in reintervention-related outcomes but no difference in mortality. We demonstrated that TAP repair patients are likely to require reintervention, most commonly in the form of pulmonary valve replacement, significantly earlier than non-TAP repair patients (Figure 5). Ylitalo et al. reported similar findings, with TAP repair patients having a higher reintervention rate but similar mortality to those with a non-TAP repair.[10] Luijten et al.[22] also demonstrated poorer event-free survival for TAP repair patients, though this cohort consisted of patients exclusively operated after 1970. Thus, all non-TAP repairs were done via a transatrial–transpulmonary approach as opposed to patients in our group, where non-TAP repairs included earlier versions of the operation done via a right ventriculotomy as well as improvements on the technique that emerged later.

5 | LIMITATIONS

The small size of the Maltese population, and consequently of its CHD patient population, is a main limitation of this study. The number of

subgroups in which our patients were divided for some analyses was purposefully restricted to avoid reducing the numbers further. Efforts were made to retrieve all patients with a history of TOF repair so as to draw as truthful a population-based picture as possible. Despite this, some patients on MAPCAD could not be traced, in some instances as they had relocated abroad since their repair. In itself, this point highlights what is likely to represent a universal problem encountered with such retrospective studies, and which a small population with specialist medical care concentrated in one main institution like Malta's might not be enough to overcome. Data on mortality in our study depended on the reporting of the primary cause of death on death certificates, which, in most cases, was not guided by a prior post-mortem examination. As a consequence, with some patients who died out of hospital, it is not possible to determine the nature of cardiac death with certainty.

Although the patients in our study were all followed up in Malta, reparative surgery was carried out in different centers in the United Kingdom, with the majority in one of four centers. Most outcome studies in the literature concentrated on single or a limited number of surgical centers, and, subsequently, of congenital cardiac surgeons. In their article from the Melbourne TOF repair series, d'Udekem et al. showed that intersurgeon variability in transatrial TOF repair technique results in differences in outcomes[23] and this factor could be relevant to our population. It is likely that patients with a less favorable anatomy, for example, TOF with pulmonary atresia, are under-represented in our older patient group due to limited access to timely diagnosis and surgery before the 1980s. Similarly, the 11/75 repair survivors in our cohort that underwent surgery at 16 years of age or older are likely to have had a more favorable and balanced anatomy that allowed them to survive to an older age before they had their repair. The authors are aware that this aspect could have introduced a degree of bias in comparison of outcomes between these two subgroups due to disparity in the severity of the underlying congenital anatomy. The rapid decline in reintervention-free survival estimates particularly after 45 years from reparative surgery in Figure 4 should be interpreted with caution due to the small number of patients in that follow-up bracket.

6 | CONCLUSIONS

This study shows very good overall survival after TOF repair among Maltese patients, though cardiac death remains a possibility at any stage following successful surgery. Several of our findings, including the poorer survival for TOF patients with genetic syndromes and transannular patch use leading to earlier and higher rates of reintervention, are in line with what has been previously reported. Our study also presents findings which contrast with those in the literature, particularly in failing to show a significant disadvantage in overall and reintervention-free survival for patients with a history of previous palliative surgery or for those operated at an older age. With an ever-growing population of repaired TOF survivors operated early on in life, the lesser use of TAP repair in favor of a transatrial-transpulmonary approach with preservation of the pulmonary valve annulus and a trend toward earlier reintervention in the hope of maintaining normal RV function,[24] outcomes remain very dynamic and repeat studies in the future might yield different results. In the meantime, regular clinical follow-up including imaging and rhythm monitoring in all patients remains of utmost importance. It is hoped that the findings from this study can help guide and plan future service provision for this growing patient population.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Both authors were jointly involved in the concept and design of the study and the statistical analysis of the data. The final article was approved by both authors.

Data collection, analysis and interpretation and drafting: Dr. Maryanne Caruana.

Critical revision: Prof. Victor Grech

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