The survival rates after surgical intervention have improved over time. In a recent Australian study, the overall operative mortality was 13.5% over a 38-year period. However, they showed no operative mortality in 15 consecutive patients.
since 2001. They attributed improved results over the last 12 years of the study to a combination of increased surgical experience, the application of extensive branch pulmonary artery reduction techniques and a trend towards increased utilisation of valved conduits. The overall survival in this study was 81.4% ± 5.6% at 10 years.\(^{(8)}\)

There is currently no literature emanating from Africa that has been published on TOF with APVS. The aim of the study was to review the characteristics and outcomes of patients presenting with this condition at a tertiary African referral hospital.

**METHODS**

Data was sourced from the Chris Hani Baragwanath Academic Hospital (CHBAH), which is situated in the low-middle income South African township of Soweto, near Johannesburg. It serves a population of approximately 1.25 million people, including 128 000 children under 5-years of age.\(^{(11,12)}\) Using a paediatric cardiology electronic database, cases of TOF and APVS were identified over a 34-year period from January 1981 - April 2016. Additional information, not obtainable from the database, was sought from patient files and extracted onto a standardised data collection form. Data collected included: age, gender, details of initial presentation, maternal history, anthropometry, clinical examination, results of genetic tests, chest x-ray reports, electrocardiography reports, echocardiography reports, angiography reports, surgical complications and outcomes which included morbidity and mortality.

Permission to undertake this research was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand and the Medical Advisory Committee of CHBAH.

**RESULTS**

A total of 15 patients with TOF and APVS were seen over the 34-year study period (Table 1). APVS compromised 3% (15/514) of all TOF patients.

Of the 15 patients, over two-thirds (67%) were male. Ten (67%) patients presented before 1 year of age. The majority of patients (67%) had respiratory symptoms as their cause of presentation, of whom 6 (40%) were infants.

Fourteen (93%) patients were described to have the characteristic systolic and diastolic (to-and-fro) cardiac murmur on clinical examination at presentation.

Seven patients (47%) were recorded to be dysmorphic. The FISH analysis for 22q11.2 deletion was introduced at our institution in 1994, therefore documentation of testing was recorded from this period onwards. Five out of 11 (46%) patients which presented after 1994 were suspected to have had 22q11.1 deletion. Of these 5 patients, 2 patients were positive for 22q11.2 deletion, 1 patient was negative for 22q11.2 deletion, 1 patient’s blood was rejected by the laboratory and 1 patient was not tested. An additional patient showed phenotypical features of Noonan’s syndrome for which there is presently no genetic test available in South Africa (Table 1).

A number of patients with TOF and APVS had other associated cardiac features. Six patients (40%) were documented to have a right aortic arch. Both patients that were positive for 22q11.2 deletion had a left aortic arch. Of the other 3 patients that were suspected to have 22q11.2 deletion, only 2 patients had a right aortic arch. Patient 6 (Table 1) had a small secondum atrial septal defect (ASD) and a left superior vena cava (SVC) diagnosed on echocardiography. Patient 12 had a single right coronary artery and a left SVC draining into the coronary sinus. Patient 13 was documented to have a 4mm secundum ASD. Patient 14 had a quadricuspid aortic valve, but no aortic stenosis or regurgitation was noted.

Only 5 (33%) patients underwent surgical intervention (Table 1). The majority were done between 1981 and 1998, and in children older than a year of age.

Patient 1 had a transannular patch and ventricular septal defect (VSD) closure at 9 years of age, followed by placement of a pulmonary homograft and closure of a small residual VSD 2 years later. Patient 3 had a VSD closure at 11 years of age. According to the surgical notes reconstruction of the pulmonary outflow tract was not done because the pulmonary valve dysfunction was deemed to be mild at the time. Patient 8 had a pulmonary homograft and VSD closure at 8 years of age. Patient 12 had reconstruction of the main pulmonary artery and VSD closure at 2 years of age. Patient 14 had a pulmonary homograft and VSD closure at 6 months of age at a private hospital. Patient 9 planned to have surgery abroad and was lost to follow up. There were no records of surgical intervention in the other patients.

Recently a patient with TOF and APVS, who presented at 26 months of age with an incidental murmur, underwent bronchoscopy to assess the severity of bronchial compression pre-operatively. The bronchoscopy showed 90% compression of the right main bronchus and 30% of the left main bronchus. The patient has been lost to follow up without surgery being done.
Review of follow-up data showed that 7 (47%) patients were known to be alive at 1 year of age while 4 (27%) were known to be alive at 10 years of age. One patient died during the neonatal period. The follow up of patients improved over the last 3 years of the study period. Three out of the 4 patients that have presented since 2014, continue to be followed up at the cardiac clinic.

Figures 1 - 4 show 2 echocardiographic and 2 angiographic images for Patient 13 which demonstrate typical features of TOF with APVS.

### TABLE I: Characteristics of patients with TOF and APVS.

<table>
<thead>
<tr>
<th>No.</th>
<th>Year of presentation</th>
<th>Sex</th>
<th>Age of presentation</th>
<th>Symptoms on presentation</th>
<th>Syndromes</th>
<th>Surgical intervention</th>
<th>Alive</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1981</td>
<td>Male</td>
<td>2 months</td>
<td>Shortness of breath</td>
<td>Not dysmorphic</td>
<td>Transannular patch and VSD closure in 1990, Pulmonary homograft and closure of small residual VSD in 1992</td>
<td>Unsure</td>
<td>Last seen 2012</td>
</tr>
<tr>
<td>2</td>
<td>1982</td>
<td>Male</td>
<td>5 weeks</td>
<td>Incidental murmur</td>
<td>Phenotypical features of Noonan’s syndrome</td>
<td>Nil</td>
<td>Unsure</td>
<td>Last seen 1997</td>
</tr>
<tr>
<td>3</td>
<td>1983</td>
<td>Female</td>
<td>14 months</td>
<td>Respiratory distress</td>
<td>Not dysmorphic</td>
<td>VSD closure only in 1993, Pulmonary homograft not done</td>
<td>Unsure</td>
<td>Last seen 1997, Was awaiting pulmonary homograft</td>
</tr>
<tr>
<td>4</td>
<td>1994</td>
<td>Male</td>
<td>12 days</td>
<td>Respiratory distress</td>
<td>Not dysmorphic</td>
<td>Not done</td>
<td>Unsure</td>
<td>Last seen 1995</td>
</tr>
<tr>
<td>5</td>
<td>1994</td>
<td>Female</td>
<td>1 month</td>
<td>Incidental murmur</td>
<td>Clinically 22q11.2 deletion syndrome. Blood specimen rejected</td>
<td>Not done</td>
<td>Unsure</td>
<td>Last seen 1994, Plan was for cardiac catheterisation</td>
</tr>
<tr>
<td>6</td>
<td>1995</td>
<td>Male</td>
<td>Day 1 of life</td>
<td>Respiratory distress, distended abdomen</td>
<td>Suspected 22q11.2 deletion syndrome. Not tested</td>
<td>Nil</td>
<td>No</td>
<td>Died in ICU at 1 month of age, ventilated since birth</td>
</tr>
<tr>
<td>7</td>
<td>1997</td>
<td>Male</td>
<td>4 months</td>
<td>Cough and shortness of breath</td>
<td>Not dysmorphic</td>
<td>Not done</td>
<td>Unsure</td>
<td>Last seen cardiac clinic</td>
</tr>
<tr>
<td>8</td>
<td>1998</td>
<td>Female</td>
<td>7 years</td>
<td>Cough and incidental cardiac murmur</td>
<td>Not dysmorphic</td>
<td>Pulmonary homograft and VSD closure in 1998</td>
<td>Unsure</td>
<td>Last seen 1999</td>
</tr>
<tr>
<td>9</td>
<td>1998</td>
<td>Male</td>
<td>10 years</td>
<td>Incidental cardiac murmur</td>
<td>Not dysmorphic</td>
<td>Not done. For surgical intervention abroad as requested by family</td>
<td>Unsure</td>
<td>Last seen 1998</td>
</tr>
<tr>
<td>10</td>
<td>2005</td>
<td>Male</td>
<td>Day 1 of life</td>
<td>Mild respiratory distress with cardiac murmur</td>
<td>Not dysmorphic</td>
<td>Not done</td>
<td>Unsure</td>
<td>Last seen 2005, Was for cardiac catheterisation in 6 months’ time</td>
</tr>
<tr>
<td>11</td>
<td>2008</td>
<td>Female</td>
<td>2 months</td>
<td>Gastroenteritis, Incidental cardiac murmur</td>
<td>Positive for 22q11.2 deletion syndrome</td>
<td>Not done</td>
<td>Unsure</td>
<td>Last seen 2008</td>
</tr>
<tr>
<td>12</td>
<td>2014</td>
<td>Male</td>
<td>1 year 1 month</td>
<td>Respiratory distress</td>
<td>Positive for 22q11.2 deletion syndrome</td>
<td>Reconstruction of pulmonary artery and VSD closure in 2015, Transannular patch or pulmonary homograft not done</td>
<td>Yes</td>
<td>Last seen 2016</td>
</tr>
<tr>
<td>13</td>
<td>2015</td>
<td>Female</td>
<td>2 year 2 months</td>
<td>Cardiac murmur</td>
<td>Negative for 22q11.2 deletion syndrome</td>
<td>Awaiting surgery</td>
<td>Yes</td>
<td>Last seen 2016 – awaiting surgery</td>
</tr>
<tr>
<td>14</td>
<td>2015</td>
<td>Male</td>
<td>6 months</td>
<td>Respiratory distress with incidental cardiac murmur</td>
<td>Not dysmorphic</td>
<td>Pulmonary homograft and VSD closure in 2016</td>
<td>Unsure</td>
<td>Patient transferred to private hospital</td>
</tr>
<tr>
<td>15</td>
<td>2016</td>
<td>Male</td>
<td>8 months</td>
<td>Shortness of breath with incidental cardiac murmur</td>
<td>Dysmorphic</td>
<td>Not done yet</td>
<td>Yes</td>
<td>Last seen 2016</td>
</tr>
</tbody>
</table>
DISCUSSION

To our knowledge, this is the first African study on TOF with APVS. No literature pertaining to TOF and APVS in Africa could be found using an online literature search. Our data is in agreement with the published literature which shows that APVS is a rare congenital cardiac lesion, compromising 3% of all TOF patients.\(^1\) Ten (67%) patients presented before 1 year of age in our study. Typically, patients with TOF and APVS are divided into 2 categories: those who present early with respiratory symptoms (infant-type APVS) and those who present later (childhood-type).\(^5,13\) The majority of the study patients (67%) had respiratory symptoms as their cause of presentation, of which 6 (40%) were infants. A to-and-fro murmur (ejection systolic and early diastolic murmur) at the left sternal border is a characteristic clinical sign in TOF and APVS.\(^7,13\) The majority of our patients (93%) had a to-and-fro murmur on clinical examination which was diagnostic at presentation. Given the limited availability of prenatal ultrasound in a resource poor setting like ours, TOF and APVS should be suspected in a child less than 1 year presenting with respiratory symptoms and a characteristic to-and-fro murmur.

As 22q11.2 deletion is a common finding in patients with TOF and APVS, routine screening for this deletion should be
TOF with APVS may occasionally be associated with defects such as atrial septal defects and absent left pulmonary artery. Two patients had an ASD secundum and 2 patients had a left SVC. A right aortic arch has been previously documented in approximately 70% of patients who are positive for 22q11.2 deletion. In our study, 40% of patients were found to have a right aortic arch, however, both patients that were confirmed positive for 22q11.2 deletion had a left aortic arch. Of the other 3 patients that were suspected to have 22q11.2 deletion, 2 had a right aortic arch.

Adequate surgical data was available in only 5 patients. Of the 10 remaining un-operated patients, only 1 was confirmed to have died before 5 weeks of age. The other 9 patients were lost to follow up or may have died, or have had surgery at another institution. One patient was documented to have travelled abroad for surgery. Patients referred to our institution include patients from neighbouring provinces and countries who are difficult to trace.

Follow-up data of the study patients is poor, with only 4 (27%) of the 15 patients known to be alive at 10 years of age. One patient died in the neonatal period. Seven (47%) patients were alive at 1 year of age. The potential for good outcomes was documented in a study by Yong et al. in Australia over a 38-year period, which showed that the overall survival at 10 years was 81.4% ± 5.6%.

In conclusion, TOF with APVS is a rare condition compromising 3% of all TOF patients presenting to an African tertiary care centre, which correlates with the mainstream literature. The 22q11.2 deletion syndrome was suspected in 33% of patients but confirmed in a small number (13%), largely due to several of our patients presenting prior to the availability of routine testing. APVS should be suspected in a child less than 1 year presenting with respiratory symptoms and a characteristic to-and-fro murmur. A good outcome can be expected if diagnosed early and the appropriate surgical management provided.

The limitations of the study were that the data was analysed retrospectively at a single institution which has historically experienced numerous resource constraints, and where follow up of patients has been poor. As such, any inferences drawn from these data were limited.

Conflict of interest: none declared.

REFERENCES