The outcome of prenatal sonographic diagnosis of fetal talipes in the Cape Town Metro district

MMED

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DECLARATION

I, Dr. Elfriede Swarts, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to this or any other university.

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Date: 11/2/2017
Abstract

**Background:** Talipes equinovarus, also termed club foot, is a congenital deformity of the ankle joint. Despite its prevalence of approximately 1 per 1000 live births, fetal talipes is relatively poorly studied since the introduction of percutaneous tendo Achilles tenotomies.

**Objectives:** To document the associations, outcomes and prognosis of patients with antenatally diagnosed fetal talipes. The study aims to examine the association between, and prevalence of, fetal talipes and other abnormalities, structural and chromosomal, as well as the outcome in relation to postnatal surgery. The accuracy of prenatal ultrasound in diagnosing fetal talipes is also examined.

**Methods:** A retrospective observational study was made of all cases presenting to the Fetal Medicine Unit between 1 January 2009 and 31 December 2014. All the identified cases were analysed to identify isolated talipes, associated abnormalities, and chromosomal abnormalities. The pregnancy outcomes were determined using the Astraia database as well as maternity records. When the outcome resulted in a live infant, these infants were followed up using the files at the referral hospital to determine the treatment method used and the number requiring surgery.

**Results:** There were 155 cases, all referred to the Fetal Medicine Unit. Antenatal data included 75 who had other structural abnormalities and 75 who had isolated talipes. In five of the cases were no sufficient data could be found. Twenty-five cases were lost to follow-up, and 12 cases had no clubfoot at birth. Only one was labelled as having positional clubfoot. There were 91 live births. Of the cases of talipes with associated abnormalities, 21.19% were live births (excluding ENND). All terminations of pregnancy as well as 90.9% of intrauterine fetal deaths were complex talipes, and 94.52% of the cases of isolated talipes were live births. The most common associated abnormalities were of the central nervous system. Seventeen of the live births were lost to follow-up. Of the cases of isolated talipes, 53.19% had tenotomies and Ponseti treatment. The false positive rate of detecting fetal talipes on ultrasound was 7.74%.

**Conclusion:** The study made it evident that complex talipes is associated with a poor pregnancy outcome defined as pregnancy loss, where isolated talipes is usually associated with a good pregnancy outcome. Ultrasound is a good diagnostic tool when diagnosing talipes antenatally but cannot diagnose the severity of the clubfoot. False negatives were not studied. The introduction of tenotomy can make a difference in the outcome of clubfoot in comparison with previous studies where tenotomies were not performed. Medical professionals need to address the importance of counselling, and a multidisciplinary team should be involved in cases involving prenatal counselling.

**Keywords:** Talipes, talipes equinovarus, clubfoot, surgery, Ponseti, tenotomy, percutaneous tendo Achilles tenotomy, spina bifida, trisomy 18, trisomy 21.
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I gratefully acknowledge the guidance and assistance received from my supervisor Dr Chantal Stewart, my co-supervisor and statistical analyser Dr Gregory Petro, the maternity records staff at Groote Schuur Hospital, the Maitland Cottage Hospital Matron and administrative Clark, and the records staff at New Somerset Hospital, Mowbray Maternity Hospital and Red Cross War Memorial Children’s Hospital.
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List of abbreviations

CTEV  Congenital talipes equinovarus
ENND  Early neonatal death
GSH   Groote Schuur Hospital
IUD   Intrauterine fetal death
LB    Live birth surviving 1st week of life
MCH   Maitland Cottage Hospital
MOU   Midwife obstetric unit
PMNS  Peninsula Maternal and Neonatal Services
SB    Stillbirth
TOP   Termination of pregnancy
Part A: Study protocol and literature review

As approved by the Departmental Research Committee and Human Research Ethics Committee, University of Cape Town.
Project summary

The project aim is to assess the outcome of congenital talipes equinovarus (CTEV) when diagnosed by prenatal ultrasound at the Fetal Medicine Unit and Ultrasound Department of Groote Schuur Hospital. The object is to assess the accuracy of ultrasound diagnosis, compare the association between CTEV and other abnormalities, and record the outcomes concerning postnatal surgery or conservative treatment.

The population studied comprises all patients who presented to the Fetal Medicine Unit between 1 January 2009 and 31 December 2014, and is a retrospective cohort study. Data were collected from patient records and the Astraia database in the Ultrasound Department for the specified period. The infants' follow-up data were gathered from the Clubfoot Clinic at Maitland Cottage Hospital, Newlands, where the treatment to date was analysed and grouped into conservative treatment (the Ponseti method is mainly used), major surgery performed once, or two or more surgeries performed. Records confirm whether the deformities were structural or positional.

The information gathered in the present study will provide long-term outcome data in our current setting. The data can be used to complement current prenatal counselling and provide better information on the accuracy of diagnosis, percentage of patients requiring surgery and how many surgeries are needed, if necessary. The study also provides data on the proportion of cases associated with other abnormalities.
Research plan

Specific aims and objectives

The purpose of the study is to assess the outcome of congenital talipes equinovarus (CTEV) with postnatal surgery or conservative treatment and to examine the association between CTEV and other abnormalities as well as to establish the accuracy of prenatal ultrasound diagnosis.

Primary outcome

To determine the outcome of talipes diagnosed on ultrasound

Outcomes include:

- associated abnormalities v. isolated clubfoot
- treatment received, including conservative and surgical (including the number of surgeries needed for that outcome).

Secondary outcome

To determine the incidence of false positives on ultrasound diagnosis of talipes and use the data to accompany current prenatal counselling services.

Background and literature review

Antenatal ultrasound is the commonly used modality to diagnose structural fetal abnormalities. Although 18–20 weeks is the traditional time to screen for structural abnormalities, several abnormalities such as acrania, anterior abdominal wall defects and, in this context, talipes can be detected as early as 11–14 weeks of gestation. Structural abnormalities can be either associated with an underlying chromosomal abnormality or genetic syndromes, or isolated.¹

Most fetal abnormalities are encountered in women without risk factors. Earlier studies have shown that the sensitivity and specificity of ultrasound in detecting fetal anomalies in a
low-risk population are 40% and 85% respectively. It was also concluded that the sensitivity of diagnosis of major fetal anomalies was 35%. Other studies show a sensitivity of 74.4% and 85%-90% in a low-risk and relative-risk population. Many, but not all, women enrolled in the Peninsula Maternal and Neonatal Services (PMNS) have fetal anomaly scans at their midwife obstetric units (MOUs) or secondary hospital and are referred to the Fetal Medicine Unit if an abnormality is found.

The International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) has published recommendations for mid-trimester ultrasound. Equipment and training of the professionals who perform scans are addressed, as well as the timing and the minimum standards required for the examination regarding both fetal biometry and morphology. The requirements vary from one country to another. To achieve optimal results from routine screening examinations, individuals who perform scans should:

- perform fetal ultrasound scans regularly
- participate in continuing professional development activities
- be trained in the use of diagnostic ultrasonography and related safety issues
- have established adequate referral patterns for abnormal or suspicious findings
- routinely undertake control measures and quality assurance.

This current literature review focuses on the prenatal diagnosis of CTEV or clubfoot which remains one of the most common congenital limb deformities. CTEV is a severe congenital abnormality of the foot. Its incidence among white people is 1 per 1 000 live births. Racial differences occur, with an incidence among black South Africans of 1.55 in 1 000 births and Maori populations of 7 per 1 000 live births. CTEV is associated with other congenital abnormalities in about 20% of cases, the deformity is isolated in the majority of cases, and is described as idiopathic or non-complex. It is bilateral in around 50% of cases. The aetiology of clubfoot has not yet been clarified. Genetics plays a role as indicated by racial differences in incidence, familial pattern of inheritance and 32.5% concordance between monozygotic twins. Boys are more commonly affected than girls (M:F ratio 2:1), but affected females are more likely to transmit the disorder to their children and have siblings with clubfoot than are affected males. This probability suggests that the genetic component for susceptibility to clubfoot is polygenic and that females require a greater genetic liability to enable them to
develop the condition (the Carter effect). If there is a family history of clubfoot, the adjusted odds ratio for the baby having clubfoot is 6.52. Environmental factors also influence the risk; for example, if the mother smoked cigarettes during early pregnancy, the adjusted odds ratio for the baby having clubfoot is 1.34. If there is both a family history and the mother smoked cigarettes at the beginning of gestation, the adjusted odds ratio for the baby having clubfoot is 20.3. CTEV has also been linked to oligohydramnios, intraterine exposure to tubocurarine or sodium aminopterin, amniotic band syndrome and uterine tumours. Other associations include neural tube defects, arthrogryposis and syndrome complexes such as Smith-Lemli-Opiz syndrome or diastrophic dysplasia. A search for 'clubfoot susceptibility' genes is under way. Two transcription-factor genes, PITX1 and TBX4, have attracted attention. The PITX1-TBX4 transcriptional pathway is responsible for early limb development, with both playing a role in hind limb development but being minimally expressed in the forelimb.

Limb formation occurs at 4–8 weeks’ gestation, while primary ossification centres develop in all the long bones of the limbs by the 12th week of pregnancy. An aetiological approach to fetal limb abnormalities can be addressed by dividing them into four groups:

1. chromosomal diseases (T21, T13, T18)
2. single gene disorder
3. multifactorial conditions (congenital dislocation of the hips, clubfeet, scoliosis)
4. maternal diseases and teratogens (autoimmune diseases, valproic acid, cocaine, maternal insulin-dependent diabetes mellitus).

A thorough obstetric history, maternal medical history, family history of limb abnormalities and history of teratogens is needed when investigating the aetiology of all fetal abnormalities. The prenatal diagnosis of fetal limb abnormalities needs to involve a multidisciplinary team of obstetricians, clinical geneticists, radiologists/sonographers, orthopaedic surgeons and neonatologists to provide adequate information to the parents regarding prognosis, aetiology of the disorder, recurrence risk and options related to the current pregnancy.
The anatomical abnormality in CTEV is subluxation of the talo-calcaneo-navicular joint with underdevelopment of the soft tissues on the medial side of the foot. The foot is adducted and inverted and held in equinus at the ankle. In most cases, there is also a significant underdevelopment of the calf and peroneal muscles. The contracture of capsules and ligaments and consequent stiffness of the midtarsal and ankle joints can be explained by selective muscle degeneration causing a lack of intrauterine movement. There is evidence of neurogenic muscle disease, mainly type 1; this is predominant, and revealed by electron microscopic and histochemical studies of the leg muscles. This pathology might be why there is also a high association with neural tube defects; if the controlling muscles of the foot and ankle do not function normally and limit movement, movement at the joint may cease and contractures develop.

Of note is that an early study in 1963 by Irani et al., done on histological specimens from 147 fetuses at 8 - 21 weeks’ gestation, revealed that at 9 weeks in utero, the normal foot displays skeletal changes resembling clubfoot that completely resolve by 11 weeks. Normal embryonic development of the lower limb buds involves the foot first being abducted in a position resembling a CTEV deformity. It is thought to rotate in the second or third month to the supinated position. CTEV can be detected on transvaginal ultrasound at 13 weeks’ gestation, and at 16 weeks by transabdominal ultrasound. Jeanty and Romero suggested that the diagnosis of talipes on ultrasound be based on two criteria:

1. An inverted foot, in which the rays of the metatarsal are visible in the same plane as the tibia and fibula and roughly perpendicular to these two long bones.
2. The angle of the junction between the foot and lower leg is rounded. In the ordinary situation, the angle is more squared.

A study by Woodrow et al. in 1998 showed specific difficulties in the diagnosis when oligohydramnios is present. As discussed earlier, talipes has been described as being more prevalent in the presence of oligohydramnios, amniotic band syndrome and uterine tumours. Some instances are secondary to oligohydramnios but most are not. This observation calls into question whether it is a true structural abnormality or a postural
deformity secondary to intrauterine confinement. The diagnosis can be confirmed with repeat ultrasound or at birth.

In a study by Caroll et al. in 2001, the association between fetal talipes and other defects, and the outcome after postnatal surgery, was examined. The infants were followed up to determine the number of cases that had structural or positional talipes and the number of cases requiring surgery. There were 76 cases in total; postnatal follow-up details were available for 31 of the 40 live births. There were 3 neonates with unilateral talipes at birth who were thought to have bilateral talipes on prenatal ultrasound, and 1 neonate had bilateral talipes at birth who had been believed to have had unilateral talipes prenatally. The false positive rate was 6.4%; this indication also appears to be more likely to occur in the third trimester, possibly because of positional effects that are more likely in this trimester. Of the 29 neonates with confirmed talipes at birth, the defect was structural in 26 (90%) cases and positional in 3. Surgery was necessary in 21 (72%) of the 29 cases, and 18 (86%) of those undergoing surgery required only 1 operation.

Another study by Bakalis et al. in 2002 of 103,228 pregnancies undergoing routine ultrasound scanning at 18–23 weeks, found an incidence of 0.10% (107/103,228), where 64 (59.8%) were bilateral, and 43 (40.2%) were unilateral. In 48.6% (52) of cases, the talipes was associated with other abnormalities, and 51.4% (55) were isolated. In 19% of the cases, the diagnosis was changed to complex because of subsequent development of associated features.

In 2007, a prospective follow-up study spanning 18 years in Norway by Offerdal et al. recorded 113 fetuses or newborns with CTEV in a non-selected population. Isolated CTEV was found in 55/113 (49%) and complex CTEV in 58/113 (51%). Isolated CTEV was bilateral in 30/55 (55%) and unilateral in 25/55 (45%). Complex CTEV with associated abnormalities was found to have bilateral talipes in 34/58 (59%) and unilateral talipes in 24/58 (41%). The male-to-female ratio was 2:1. CTEV was detected on ultrasound at a median of 18+3 (range 12+0 to 30+6) weeks’ gestation. Prenatal diagnosis was made in 61% of cases in the 18-year period, and 39% were only diagnosed postnatally or on autopsy.
In the studies by Carroll et al. and Bakalis et al.\textsuperscript{11}, the median gestational age at diagnosis was 20 weeks (range 13–34). The two most common associated defects were chromosomal and those involving the central nervous system. Bakalis et al. showed a false positive rate of 3.7%. Adverse outcomes were seen more frequently with bilateral than with unilateral talipes (odds ratio 3.44; 95% confidence interval 1.50–7.90). The authors concluded that the prognosis of fetal talipes is related to the presence or absence of other defects. In cases of isolated talipes, 94% had a favourable outcome, but complex talipes resulted in stillbirth, TOP or long-term handicap in 90% of cases.\textsuperscript{12}

Offerdal et al.\textsuperscript{7} showed that, during the 18-year period, the prenatal detection rate improved from 43% (1987–1992) to 67% (1993–1998) to 77% (1999–2004). Regarding the outcome of live infants, serial plaster-cast treatment was performed in 96% of the cases, with the median time being 2 and 3 months. Surgical treatment, as well as serial plaster-cast treatment, was carried out on 86% (66/77). Eight (15%) of the isolated talipes cases required no surgical intervention, and only serial plaster-cast treatment. Thirty-one (57%) required 1 operation and 16 (30%) required 2 or more surgical procedures in addition to plaster-cast treatment.

Amniotic fluid levels were also investigated, and no association between amniotic fluid levels and talipes was found. Oligohydramnios and related bilateral talipes were diagnosed in 8 cases. In all these cases, there were associated abnormalities. There was a positive family history in 9/55 (16%) of the cases of isolated CTEV: 1 mother, 4 fathers, 1 uncle, 1 first cousin and 2 siblings. When the complex talipes was investigated, 17% (10/58) had a positive family history. Only 50% of the cases were karyotyped. An abnormal karyotype can therefore not be investigated as a risk factor for talipes.

The outcome of children born with talipes in South Africa was studied by Khan et al.\textsuperscript{13} in 2005 and found to have a good result using the Ponseti method. Most operations for clubfoot are avoidable. Khan et al. used the Harold and Walker classification. The Ponseti method was described by Ignacio V. Ponseti in 1992. The three most important components of the deformity are always corrected in the following order. First, the forefoot must be brought into rotational alignment with the hind foot; paradoxically, this is done by increasing the supination deformity of the forefoot so that it corresponds with the relatively
more supinated hind foot. Next, both hind foot and forefoot are together gradually brought out of varus and supination; correction is assisted by keeping the fulcrum on the lateral side of the head of the talus. Finally, equinus is corrected by bringing the heel down and dorsiflexing the ankle. This is achieved by serial manipulations and strapping for 8–12 weeks.\textsuperscript{14}

It is important to note that in South Africa the Ponseti method has been proven to be very successful for even grade III of the Harrold and Walker classification. The Harrold and Walker classification has been described in 1983 and indicate the severity of the clubfoot.

**HARROLD AND WALKER CLASSIFICATION OF CLUBFOOT**

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<td>I</td>
<td>Foot correctable beyond neutral</td>
</tr>
<tr>
<td>II</td>
<td>Pushed to neutral, but with fixed equinus or heel varus &lt; 20°</td>
</tr>
<tr>
<td>III</td>
<td>Fixed equinus or heel varus &gt; 20°</td>
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Other studies have shown that 57\% of patients have needed at least one surgery. Therefore, parents should be counselled about the Ponseti method as well as the possibility of surgery, depending on severity and response to the Ponseti method.

When we examine the treatment and outcomes of prenatally diagnosed talipes, it is important to look also at the severity of the deformity and the presence of other abnormalities. The severity of the deformity is not possible to diagnose on ultrasound. Postnatally, most classifications look at the degree of deformity and the amount of reducibility. A system proposed by Dimeglio has four groups:\textsuperscript{15} The classification should make it possible to distinguish between four categories of feet: benign feet, moderate feet, severe feet, and extremely severe feet. A scoring scale from 0 to 20 has been established:

1. From 0 to 5, benign or “soft=soft” feet: these are feet that can be entirely reduced.
2. From 5 to 10, moderate or “soft-stiff” feet: these feet can be reduced but are partially resistant.
3. From 10 to 15, severe or “stiff>soft” feet: these are resistant feet that can be partially reduced.
4. From 15 to 20, extremely severe or “stiff=stiff” feet: these are feet that virtually cannot be reduced.

Group 2 is by far the most common type, with 60% of cases in the study performed by Woodrow et al. Another classification has been used in the Maitland Cottage Hospital (MCH) where most of our subjects were being treated. The Pirani scoring system is composed of 6 clinical signs of contracture. Each component may score 0, 0.5 or 1.\textsuperscript{17}

Hind foot contracture score:

1. posterior crease
2. empty heel
3. rigid equinus.

Mid foot contracture score:

1. medial crease
2. curvature of lateral border
3. position of head of the talus.

These scoring systems are an essential part of the diagnosis and treatment of clubfoot. They are, however, beyond the scope of the present study. The severity of clubfoot in the present study can be assessed by the treatment needed.

Percutaneous tendon Achilles tenotomy is performed as a day-care procedure under local anaesthesia.\textsuperscript{16} This procedure had a great impact on the treatment of talipes as it is less invasive and probably has less morbidity. Tenotomy of the tendon Achillis is required in about 85% of cases of congenital talipes.\textsuperscript{17} Another study states that 85% of the feet received tenotomies.\textsuperscript{16}

**Research design and methods**

**Study design**

This is a retrospective cohort study. Data were collected from patient records in GSH, MMH and NSH as well as the Astraia database in the Ultrasound Department at GSH, University of Cape Town, South Africa, for the specified period. Neonatal data were obtained from the folders of patients referred to the MCH in Newlands, the NSH in Greenpoint, and the Red Cross War Memorial Children’s Hospital (RXH) in Rondebosch, Cape Town, South Africa.
Study subjects

The population studied is that of all cases of talipes that presented to the Fetal Medicine Unit between 1 January 2009 and 31 December 2014.

Exclusion criteria

There were no exclusion criteria in the study.

Data collection

Data were obtained from the Astraia database in the Ultrasound Department in GSH and follow-up data from the Clubfoot Clinic at MCH.

Data were entered on a datasheet (Appendix A). The variables include maternal age, parity and previous pregnancies with abnormalities. The ultrasound data collected include gestational age at diagnosis, other anomalies, karyotype, amniotic fluid index (AFI), body mass index (BMI) (this may be useful to determine the accuracy of the scan) and details about the talipes (unilateral or bilateral). Follow-up data include the postnatal diagnosis, as well as stillbirth/live birth or neonatal death, structural/positional and treatment to date.

This is a descriptive observational study where the principal investigator analysed the collected data to determine the outcome of talipes in our setting in South Africa. To statistically analyse the study, z-scores were determined by using the centre of the data, spread of the data points and the symmetry of the plotted graph. The chi-square test was used to determine if there were significant associations between categorical variables, as opposed to continuous variables.

Feasibility and time-frame

The collection of data did not carry any significant costs; any costs incurred were borne by the principal investigator. The estimated time-frame from start to finish was six months, owing to work obligations of the principal investigator.

Strengths

All relevant data are available on the Astraia database. Maternity records can also be used to fill in any gaps.

There was no need to recruit patients and obtain consent to conduct the study.

Limitations

This is a retrospective study, which relies on previously entered data to be correct. Follow-up data depend on the availability of baby folder numbers and birth registration. Follow-up data also depend on appropriate referral to MCH.
Ethics

Ethical approval for this study was requested from the University of Cape Town's Human Research Committee. Permission to collect data was obtained from the relevant authorities at GSH and MCH.

Confidentiality is important in collecting data and displaying results. The principal investigator collected data but used only folder numbers when referring to patients in the data collection and display of results, so as not to reveal the identities of research subjects.
The outcome of prenatal sonographic diagnosis of fetal talipes in the Cape Town Metro district

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Introduction

When any fetal anomaly is diagnosed, feelings of anxiety are invariably expressed by the parents. The prognosis and postnatal management is essential to helping the parents to deal with the event. Antenatal ultrasound is the commonly used modality to diagnose structural fetal anomalies. Congenital talipes equinovarus (CTEV) is one of the most common musculoskeletal congenital disabilities, affecting 1 in 250 to 1 in 1000 live births, depending on the population. It has in the past been described as being associated with congenital abnormalities in 20% of cases of congenital disability.5

The long-term outcome of talipes in relation to the need for surgery has been described by Carroll et al.11 for developed countries but not in South Africa. Conservative management has been described by Ponseti.14 Percutaneous tendo Achilles tenotomy was introduced in the Clubfoot Clinic at MCH in 2012 only.

The severity of the deformity is not possible to diagnose on ultrasound. Postnatally, most classifications look at the degree of deformity and the amount of reducibility. Classifications have been described by Diméglio15 and Pirani.24 A positional abnormality is easily corrected by manipulation and usually does not need treatment, whereas a structural abnormality can be rectified by serial manipulation, tenotomy or, in extreme circumstances, major surgery. (From this point on in the text, major surgery is referred to as surgery.) These considerations are important in the counselling of parents when clubfoot is diagnosed on ultrasound. The accuracy of ultrasound in the diagnosis of clubfoot is therefore also important. The aim of the present study is to provide information regarding the association of clubfoot with other abnormalities, as well as the current outcome of treatment of isolated clubfoot in South Africa. We also aimed to determine if there is a difference in the association of unilateral and bilateral clubfoot respectively when associated with other fetal abnormalities. The rate of live birth and pregnancy loss is also investigated.

Infants were treated by the Ponseti method only, by Ponseti and percutaneous tendo Achilles tenotomy (referred to as tenotomy hereafter), and surgery. The treatment goal is to rotate the foot laterally around a fixed talus, starting with weekly serial casts. The order of correction is summarised by the mnemonic CAVE: midfoot cavus, forefoot adductus, hindfoot varus and hindfoot equinus. Treatment starts between age 2 weeks and 3 months and can continue for up to 2 to 4 years. Eighty per cent of infants may require tendo Achilles lengthening which involves a tenotomy at week 8 of treatment. Foot abduction orthosis with Denis-Brown bar in external rotation (70° in clubfoot and 40° in the normal foot) can then be used 23 hours a day for 3 months after correction, and night time and nap time only until age 4 years.

Percutaneous tendo Achilles tenotomy is performed as a day-care procedure under local anaesthesia.16 After aseptic preparation of the posterior ankle and leg, the ankle is held in
maximal dorsiflexion by an assistant. The blade is introduced at the medial edge of the tendo Achilles above its calcaneal insertion, where the cutting surface of the tendon is pointing proximally. The tendon is then severed front to back when the dorsiflexion increases suddenly with an audible pop. A well-moulded leg cast is then used for maximum dorsiflexion of the ankle and maximum abduction of the foot for 3 weeks. Surgery is usually considered at age 2 years in 10%–20% of cases. Surgery usually involves tibialis anterior tendon transfer with or without repeat tendo Achillis lengthening. Infants were followed up to determine the number of cases that needed tenotomy as part of the conservative treatment as well as the number of tenotomies that were performed. Surgical intervention was also analysed in terms of the number of surgeries needed. Follow-up was from 2 years to 5 years of age.

**Methods**

Approval for the study was obtained from the Health Sciences Faculty Human Research Ethics Committee of the University of Cape Town (UCT) as well as the Clinical Directorate of GSH. This retrospective observational study was performed at the GSH Fetal Medicine Unit, Cape Town, South Africa.

The study population consists of patients making use of the Department of health services in Cape Town Metro West district. There is a private non-governmental service. These were not included in the study. The ultrasound scans are done by internationally accredited medical practitioners. The Astraia database is accredited by the UCT HREC and internationally.

Data were obtained from the Astraia database and patient folders between 1 January 2009 and 31 December 2014. All cases of talipes diagnosed on ultrasound were included in the initial search. The data were then entered into a spreadsheet where they were grouped into various categories. The main categories included talipes associated with other abnormalities and isolated talipes, gestational age at diagnosis, maternal age at diagnosis and outcome of the pregnancy. The outcome of gestation was measured in a live birth (LB), stillbirth (SB) (which included intrauterine fetal death (IUD)), termination of pregnancy (TOP) (which included cessation of the pregnancy with feticide), demographic data as well as the sex of the fetus. When the outcomes of pregnancies were not found on Astraia, maternity folders were used to fill the gaps. Where maternal folders were not found, the Clinicom system was used to determine the hospital of delivery and the infant's folder number. After delivery of a live infant with clubfoot, the infant is referred to the MCH clubfoot clinic or RXH, depending on the severity of associated abnormalities. Here the infants are evaluated, the diagnosis of clubfoot is confirmed, and treatment is commenced. Folders were used at the corresponding hospitals to determine the methods of treatment of the live infants.
Results

There were 155 cases identified, all of which were referred to the Fetal Medicine Unit at GSH from outside referral centres in the Cape Town Metro West district, as well as some of the rural areas around Cape Town (Table 1). Referrals were mainly due to abnormalities found on ultrasound in the primary centre. The mean maternal age at diagnosis was 28 (range 16–47) years. Maternal age at diagnosis was available for 151 cases which were grouped into 12–17 years, 18–34 years and 35–52 years, to determine if advanced maternal age were a factor in the diagnosis of clubfoot. It was found that 19.87% of the cases were in the advanced maternal age group and 79.47% of cases were in the middle group.

Table 1: Background demographic details.

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percentage</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age at diagnosis</td>
<td>28</td>
<td></td>
<td>6.44</td>
<td></td>
</tr>
<tr>
<td>12–17 yrs</td>
<td>1</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–34 yrs</td>
<td>120</td>
<td>79.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–52 yrs</td>
<td>30</td>
<td>19.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age at diagnosis</td>
<td>23</td>
<td></td>
<td>4.85</td>
<td></td>
</tr>
<tr>
<td>1–12 wks</td>
<td>5</td>
<td>3.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13–27 wks</td>
<td>120</td>
<td>82.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28–40 wks</td>
<td>20</td>
<td>13.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gravidity</td>
<td>2</td>
<td></td>
<td>1.58</td>
<td></td>
</tr>
<tr>
<td>Primigravida</td>
<td>36</td>
<td>30.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multigravida</td>
<td>83</td>
<td>69.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
<td>3.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>147</td>
<td>96.71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean gestational age at diagnosis was 22 (range 7–39) weeks. Gestational age at diagnosis was available for 145 of the cases and categorised into the first trimester (1–12 weeks), second trimester (13–27 weeks) and third trimester (28–40 weeks). Results showed that 5 (3.45%) of the cases were diagnosed in the first trimester, 82.76% (120) were diagnosed in the second trimester, and 13.79% (30) were diagnosed in the third trimester. Gravidity and parity were also analysed but were only available for 119 of the subjects, where 69.75% were multigravida and 30.25% were primigravida.
Of the 155 cases, 75 had isolated talipes, 75 were associated with structural abnormalities, and 5 were unknown because no further ultrasound data were available in the database. This resulted in 50% of cases associated with fetal abnormalities and 50% isolated. Of the 150 subjects, 88 (58.67%) had bilateral talipes and 62 (41.33%) had unilateral talipes. Table 2 presents the association between laterality (unilateral and bilateral) and associated abnormalities.

Table 2: Association between abnormalities and laterality.

<table>
<thead>
<tr>
<th>Laterality</th>
<th>Associated abnormalities</th>
<th>Isolated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>48 (32%)</td>
<td>40 (27%)</td>
<td>88</td>
</tr>
<tr>
<td>Unilateral</td>
<td>27 (18%)</td>
<td>35 (23%)</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>75</td>
<td>150</td>
</tr>
</tbody>
</table>

The findings were not statistically significant, with a p-value of 0.185. The odds ratio for the relationship was 1.56 (95% confidence interval (CI) 0.81–2.99).

The outcome of fetal talipes was grouped into live birth (LB), intrauterine death (IUD) or stillbirth (SB), as well as termination of pregnancy (TOP) referring to TOP before 24 weeks as well as feticide (after 24 weeks).

Figure 1 comprises a flowchart of the clinical development of talipes equinovarus diagnosed prenatally.

Live births are here defined as live babies after one week and ENND’s are excluded. The lost to follow up group includes, no birthing details or no record of the referral to the clubfoot clinic.
Figure 1: Clinical outcomes for talipes equinovarus diagnosed prenatally.

Talipes equinovarus
N=155

Lost to follow-up
n=25

No clubfoot at birth
n=12

Follow-up data available
n=118

Isolated TEV
n=51

Associated anomalies
n=67

Bilateral
n=28

Unilateral
n=23

Bilateral
n=45

Unilateral
n=22

IUFD
n=1

ENND
n=1

SB and IUD
n=12

SB AND IUD
n=8

TOP
n=21

TOP
n=6

Alive
n=46

Alive
n=15

IUFD
n=1

ENND
n=2

ENND
n=5

ENND
n=2

TOP
n=21

TOP
n=6

Alive
n=15

IUFD
n=1
Twelve cases were found not to have talipes at birth, giving a false positive rate of 7.74%. The diagnosis of talipes was made in the first trimester for 1 of these cases, in the second trimester for 9, and in the third trimester for 2.

A tabulation of the outcome of talipes confirmed at birth is shown in Table 3. There were 134 cases where the confirmation at birth was known. This indicates that all talipes not confirmed at birth were born alive. One of them had spina bifida and not clubfoot, with Arnold Chiari malformation on scan. The spina bifida was repaired on day one, but hydrocephalus necessitated a ventriculoperitoneal (VP) shunt, and complications led to the baby dying at age 5 months.

Talipes with associated abnormalities was classified into the most severe abnormality, as some of the cases had several anomalies. Chromosomal abnormalities were isolated as a separate entity as most of the cases with chromosomal abnormalities had several structural abnormalities. The most common fetal abnormalities observed were of the central nervous system. Table 4 refers to the 67 cases where fetal anomalies were found on prenatal ultrasound and the outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>True</th>
<th>False</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>False</td>
<td>12</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>True</td>
<td>66</td>
<td>21</td>
<td>88</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>21</td>
<td>99</td>
</tr>
</tbody>
</table>

The chromosomal abnormalities which were diagnosed with amniocentesis, as well as with postnatal genetic testing, included trisomy 21 (1), trisomy 18 (9/5.81%) and trisomy 13 (1). Others included Edwards-Klinefelter syndrome (1), trisomy 22 (1), tetrasomy 12p (Pallister-Killian syndrome) (1), mosaic isochromosome 20q, (1) and 46XY del 13q31 (1). Karyotyping was done in 47 of the cases where, in relation to all cases, 20% were normal and 69.7% did not have karyotyping. In the 47 cases where karyotyping was done, 34% were abnormal and 66% were normal. Of the 9 identified with trisomy 18, all 9 were associated with other abnormalities on ultrasound.

Associated abnormalities were grouped into spina bifida, spine other, CNS other, cardiac, face, renal, chromosomal, arthrogryposis, musculoskeletal, hydrops and other. The most commonly associated abnormalities were neurological in origin, comprising 25.5% (38/118). Of the CNS abnormalities, one had Dandy-Walker malformation with bilateral talipes. Other
CNS abnormalities included acrania, myelomeningocele, ventriculomegaly and microcephaly. There were 19 cases of spina bifida, of which 10 were terminated; 4 ended in IUD or SB. Half of the CNS abnormalities were spina bifida, with an incidence of 16.1% (19/118) in the study. For the present study, IUD and SB are grouped as one and are henceforth described as IUD. TOPs included TOP before 24 weeks and feticides after 24 weeks’ gestation. There were 27 TOPs in the study. Eight of the 27 TOPs were feticides.

Other fetal abnormalities that were observed were arthrogryposis, congenital infection, renal anomalies, cleft lip, other spinal or musculoskeletal abnormalities, Crisponi syndrome, cardiac abnormalities as well as one hydrops. The incidence of these abnormalities is shown in Table 4. The two congenital infections were of rubella and CMV, and were both confirmed on maternal blood testing. Arthrogryposis was mostly diagnosed antenatally owing to fetal akinesia syndrome on ultrasound.
Table 4: Associated fetal abnormalities diagnosed on prenatal ultrasound and outcomes in cases with talipes.

<table>
<thead>
<tr>
<th>Associated abnormality</th>
<th>Pregnancy outcome – number of defects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alive (n=91)</td>
</tr>
<tr>
<td>1. Chromosomal abnormality</td>
<td>3</td>
</tr>
<tr>
<td>Percentage</td>
<td>3.29%</td>
</tr>
<tr>
<td>2. Structural</td>
<td></td>
</tr>
<tr>
<td>Spina bifida</td>
<td>5</td>
</tr>
<tr>
<td>CNS other</td>
<td>5</td>
</tr>
<tr>
<td>Arthrogryposis</td>
<td>2</td>
</tr>
<tr>
<td>Renal</td>
<td>3</td>
</tr>
<tr>
<td>Face</td>
<td>1</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>3</td>
</tr>
<tr>
<td>Crisponi syndrome</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0</td>
</tr>
<tr>
<td>Hydrops</td>
<td>0</td>
</tr>
<tr>
<td>Congenital infection</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
</tr>
<tr>
<td>Percentage</td>
<td>21.19%</td>
</tr>
</tbody>
</table>

To analyse the outcome of the pregnancy when isolated talipes is diagnosed, a chi-square test was used. A p-value of 0.001 clearly confirms that talipes alone is not related to a poor outcome in the pregnancy. Poor outcome is defined as non live births.

Figure 2 summarises the outcome of isolated fetal talipes. Complex talipes is defined as talipes with associated abnormalities. The numbers in figure one exclude the cases lost to follow up, but for statistical purposes all cases with known outcome of pregnancy only are included in figure two.
There were 91 live births in the study, of which 12 were false positives. Seventeen patients were lost to follow-up, and follow-up data were available for 62 patients. The follow-up data were analysed in relation to the treatment received, if any, as well as the type of therapy which they were presented with. Most of the follow-ups were done at MCH where, since 2012, outpatient tenotomies have been offered in combination with the conservative treatment method devised by Ponseti. Treatment was investigated for all 62 patients. Table 5a sets out all live births and the treatment given. Where no treatment was given, it was either because there was no clubfoot (12 cases) or when associated abnormalities made treatment unnecessary. One patient had tibial aplasia syndrome and the leg with clubfoot was amputated; the other had spina bifida and paraplegia.

### Table 5a: Treatment of live births.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>14</td>
<td>18.92</td>
</tr>
<tr>
<td>Ponseti only</td>
<td>13</td>
<td>17.57</td>
</tr>
<tr>
<td>Ponseti and tenotomy</td>
<td>29</td>
<td>39.19</td>
</tr>
<tr>
<td>Surgery</td>
<td>18</td>
<td>24.32</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>74</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Figure 3: Postnatal treatment.

- Live birth: 91 cases
  - No clubfoot: 12 cases
  - Lost to follow-up: 17 cases
  - Follow-up available: 62 cases
  - Isolated: 47 cases
    - Conservative only: 33 cases
      - Ponseti only: 8 cases (17.02%)
      - Tenotomy and Ponseti: 25 cases (53.19%)
  - Associated abnormalities: 15 cases
    - Conservative only: 9 cases
    - Surgery: 4 cases (30.77%)
      - Ponseti only: 5 cases (38.46%)
      - Tenotomy and Ponseti: 4 cases (30.77%)
  - No treatment: 2 cases
  - Surgery: 14 cases (29.79%)
    - One surgery: 7 cases
      - One tenotomy: 2 cases
      - Two or more tenotomies: 3 cases
    - Two or more surgeries: 7 cases
Figure 3 is a flow diagram of the treatment received by both groups. Of the 62 patients where follow-up data were available, 47 had isolated talipes. Of these, 23 were unilateral and 28 were bilateral. Positional talipes was classified as not clubfoot. Only one of the patients with unconfirmed clubfoot at birth was classified as postural and not treated with any method, but only followed up and discharged. Unilateral talipes and bilateral talipes were compared with the treatment received. Statistically this was not significant, with a p-value of 0.995. Although this was not statistically significant, Table 6 and figure 4a shows that whether talipes is unilateral or bilateral may indicate the severity of the clubfoot. There was no significant difference in the treatment methods used for unilateral and bilateral talipes. The 17 cases lost to follow up in figure 3 were cases where no reference to follow up could be found at the referral hospital.

The focus was on the type of treatment received by the isolated talipes group. Tables 5b and 6a were recalculated to exclude complex talipes and only reveal the treatment of isolated talipes. Figure 4b and Table 6b presents the laterality associated with isolated talipes only. As previously mentioned, there were 47 children with isolated talipes; 29.79% (14/47) had surgery after Ponseti treatment failed as the primary treatment.

Table 5b: Treatment received for isolated talipes.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponseti only</td>
<td>8</td>
<td>17.02</td>
</tr>
<tr>
<td>Ponseti and tenotomy</td>
<td>25</td>
<td>53.19</td>
</tr>
<tr>
<td>Surgery</td>
<td>14</td>
<td>29.79</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 6a: Laterality of talipes in comparison with treatment received.

<table>
<thead>
<tr>
<th>Talipes laterality</th>
<th>Ponseti</th>
<th>Ponseti and tenotomy</th>
<th>Surgery</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>6</td>
<td>13</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>Percentage</td>
<td>46.15%</td>
<td>44.83</td>
<td>44.44</td>
<td>45</td>
</tr>
<tr>
<td>Bilateral</td>
<td>7</td>
<td>16</td>
<td>10</td>
<td>33</td>
</tr>
<tr>
<td>Percentage</td>
<td>53.85%</td>
<td>55.17</td>
<td>55.55</td>
<td>55</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>29</td>
<td>18</td>
<td>60</td>
</tr>
<tr>
<td>Percentage</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
Figure 4a: Laterality of talipes in comparison with treatment received.

Figure 4b: Isolated talipes associated with laterality.
Table 6b: Isolated talipes associated with laterality.

<table>
<thead>
<tr>
<th>Talipes laterality</th>
<th>Treatment</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ponseti</td>
<td>Ponseti and tenotomy</td>
<td>Surgery</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>3</td>
<td>11</td>
<td>7</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>37.5</td>
<td>44</td>
<td>50</td>
<td>44.6</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>5</td>
<td>14</td>
<td>7</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>62.5</td>
<td>56</td>
<td>50</td>
<td>55.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>25</td>
<td>14</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Treatment of patients was divided into conservative with or without tenotomy and surgery. The children who had surgery also had Ponseti treatment and one or two tenotomies before surgery was considered. Surgery was necessary in 14 (29.79%) of the patients with isolated clubfoot, and 7 needed 2 or more surgeries. Tenotomies were performed on 25 (53.19%) of the 47 patients, and 3 needed 2 or more tenotomies. Four had unilateral clubfoot and 2 or more surgeries on the same foot, 3 had bilateral clubfoot, and 1 patient had 3 surgeries on both feet. A comparison was made between the number of tenotomies performed and the number of surgeries performed (Table 7).

Table 7: Tenotomies done and surgeries needed.

<table>
<thead>
<tr>
<th>Tenotomy</th>
<th>Surgery</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>One</td>
<td>Two or more</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>107</td>
<td>6</td>
<td>6</td>
<td>119</td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>24</td>
<td>2</td>
<td>3</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Two or more</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>137</td>
<td>9</td>
<td>9</td>
<td>155</td>
<td></td>
</tr>
</tbody>
</table>

Table 7 shows that there were 29 tenotomy patients of whom 2 also had surgery, and 3 had two or more surgeries. Six had two or more tenotomies and had no surgeries. One had 2 or more tenotomies and 1 surgery. None had 2 or more tenotomies and 2 or more surgeries. Nine patients had 1 surgery and 6 had 1 surgery but no tenotomies. 29 (18.71%) had 1 tenotomy, 7 (4.52%) had 2 or more tenotomies. 9 (5.81%) had 1 surgery, and 9 (5.81%) had 2 or more surgeries.
Discussion

The present retrospective cohort study was done to provide accurate data for prenatal counselling when a pregnancy is diagnosed with talipes equinovarus on ultrasound. The study shows that isolated talipes is associated with 94.52% of live births (excluding ENND). Current prenatal counselling for talipes can be complemented by the outcome of this study when looking at the results in relation to conservative and surgical treatment in South Africa. Including paediatric surgeons as part of the team when a prenatal diagnosis of a surgical congenital malformation is diagnosed is a relatively new practice. It is important when an antenatal diagnosis such as this is made to actively involve them in counselling the parents, as it provides an opportunity to lessen the stress for prospective mothers and fathers. A study by Kemp et al. showed that parents experience a high degree of anxiety when a fetal anomaly is diagnosed on prenatal ultrasound. There was no correlation in their study between levels of anxiety and social class or age. Prenatal counselling can decrease the degree of anxiety experienced by parents. Much of the anxiety is experienced when there is a lack of specific information about the prognosis. Although a study by Skari et al. showed that anxiety was less in the diagnosis of an abnormality postnatally, it is hard to argue that postponing the process of informing the parents to the postnatal phase is ethical. In the present study, the prognosis of talipes in South Africa is evaluated by looking at complex and isolated talipes. This approach will provide information for the counselling of parents of progeny with antenatally diagnosed talipes equinovarus.

In our study, 155 patients were identified in the years 2009 to 2014. They were all referred to the Fetal Medicine Unit at GSH in Cape Town. Maternal age at diagnosis was evaluated. The mean maternal age at diagnosis was 28 where 79.47% of the cases were diagnosed in the age group of 18–34 years; this correlates with the standard age of most pregnant women. The advanced maternal age group had a 19.87% incidence. To evaluate if advanced maternal age is a factor in the incidence of clubfoot, a larger study will be needed that evaluates the entire population and the prevalence of clubfoot in the advanced maternal age group. In a study by Hollier et al., it was concluded that the incidence of cardiac defects, clubfoot and congenital diaphragmatic hernia increased with advanced maternal age.

CTEV can be detected on transvaginal ultrasound at 13 weeks’ gestation, and at 16 weeks by transabdominal ultrasound. The mean gestational age at diagnosis in the present study was 22 weeks, with a standard deviation of 4.85. This figure shows that there was a broad range in this variable of the group.

Table 2 explains the association between isolated talipes and the laterality of the talipes. In a study by Mammen et al., they found that bilateral talipes was associated with a greater incidence of fetal abnormalities than unilateral talipes. In our study, 32% of all talipes with abnormalities were related to bilateral talipes. Unilateral talipes was associated with abnormalities in only 18%. This was not statistically significant, with a p-value of 0.185. In a study by Bakalis et al., bilateral talipes was found more frequently in the group with
associated abnormalities. This was also evaluated in the survey by Mammen et al. where they found a significant p-value of \( p < 0.05 \). The fact that this value is not statistically significant in our study does not exclude the relevance of this finding. An odds ratio of 1.56 for this relationship may suggest a minor trend but is not significant. This is important in the evaluation and counselling of patients when the fetus is diagnosed with bilateral talipes as the association implies that bilateral talipes is more frequently associated with other structural abnormalities. The fact that it was statistically significant in these other studies cannot be attributed to the number of identified cases. The present study identified 155 cases, while the number in the study by Bakalis et al. was 107, and Mammen et al. identified 121 fetuses. However, there is still a notable difference when analysing these data, as described before.

Eight of the complex cases with bilateral talipes were associated with aneuploidy, and only 3 of those with aneuploidy were unilateral. Two-thirds of the aneuploidy cases were therefore associated with bilateral talipes. This was, however, not the case in another study where the incidence of aneuploidy was similar for both unilateral and bilateral talipes. There are many issues involving bilateral v. unilateral talipes when evaluating the outcome of birth, associated abnormalities and abnormal karyotyping, although isolated bilateral talipes and isolated unilateral talipes in our study had more or less the same outcomes. When accounting for all abnormal karyotyping, 12 of the cases with an abnormal karyotype had bilateral talipes and only 4 had unilateral talipes. This finding may strengthen the argument that invasive testing should be offered when bilateral talipes is diagnosed.

Isolated talipes had a 94.52% live birth rate while talipes with associated abnormalities or complex talipes had only a 27.78% live birth rate when including the ENND. These figures may be attributed to the incidence of feticide and TOP observed or to the fact that the abnormalities were lethal; 37.5% of complex talipes underwent TOP. Complex talipes was significantly associated with a poor outcome in pregnancy. This evaluation was statistically significant with a \( p \)-value of 0.001 when comparing outcomes of pregnancy with the presence or absence of associated abnormalities. With this analysis, it can be stated that talipes alone is not linked to adverse outcomes in pregnancy. In our study, 50% of talipes were complex and 50% were isolated, with 58.67% bilateral and 41.33% unilateral. These figures are different from those in the study by Caroll et al. which found that 69% of cases were associated with other abnormalities. This finding may be owing to the larger sample size in our study.

No cases with isolated talipes had an abnormal karyotype. This outcome was similar in two other studies where 76 cases and 121 cases were evaluated respectively. The issue of offering invasive testing when isolated talipes is diagnosed should therefore be based on other factors such as advanced maternal age or high-risk nuchal translucency (NT) scan.
As previously stated, complex talipes accounted for 50% of the cases. The most common associated abnormalities were those of the central nervous system. It is not surprising that spina bifida accounted for 50% of these cases, with other conditions including Dandy-Walker malformation, ventriculomegaly, acrania, microcephaly and myelomeningocele. The incidence of spina bifida in clubfoot has been described before\textsuperscript{22} and, along with arthrogryposis, is a causative factor. The relative weakness of the dorsiflexors and evertors is created by a muscle imbalance that can increase the risk of talipes formation \textit{in utero}. Therefore, spina bifida and arthrogryposis can be a causative factor in the formation of talipes \textit{in utero}. Arthrogryposis accounts for 5 (7% of the fetal abnormalities) in the study. Arthrogryposis, or arthrogryposis multiplex congenita, comprises non-progressive conditions characterised by multiple joint contractures found throughout the body at birth. As stated above, arthrogryposis was diagnosed as a result of the diagnosis of fetal akinesia syndrome. The lack of fetal movement causes excess connective tissue to develop around the joint, which worsens the contracture and can sometimes lead to clubfoot.

Complex talipes is compared with the outcomes of pregnancy in Table 4, which clearly reveals that complex talipes has a very poor prognosis. Of the complex talipes births, only 21.19% were live births (excluding the ENND). One hundred per cent of the TOPs were for complex talipes and 90.9% of the IUDs.

The incidence of false positives on ultrasound in our study was 7.74%. Other studies have found false positive rates of 29%, 6.4% and 3.7% respectively.\textsuperscript{11,12,21} The high false positive rate in Mammen et al. who studied 121 cases, can be attributed to the fact that they also included suspected and not confirmed clubfoot in their database. Another study had a false positive rate of 5.7% but only 35 patients.\textsuperscript{22} The false positive rate in our study shows that the diagnosis of talipes can be wrong and parents should be made aware of this finding. Eleven isolated cases had no diagnosis of clubfoot at birth, and one had spina bifida with no clubfoot. Most of the fetuses were diagnosed in the second trimester, only one in the third trimester, and one in the first trimester. In the study where a 6.4% false positive rate was found, the results showed that this is more likely to happen in the third trimester, but this was not evident in our study. The majority of cases were, however, scanned in the second trimester, with far fewer numbers in the first and third trimesters.\textsuperscript{10}

Several studies have mentioned amniotic fluid volume, uterine abnormality or fibroids as the cause of clubfoot \textit{in utero} owing to restricted intrauterine space. In our research in the literature, this was usually a cause of postural clubfoot, which usually resolves spontaneously without treatment after birth.\textsuperscript{10} In our study, however, this aspect was not investigated.

In the present study, the outcomes of the group with isolated talipes were analysed in more detail. The fact that isolated talipes is associated with a good pregnancy outcome does not mean that the morbidity is low as well. Knowledge of this consideration will inform the
counselling of parents not only on the prognosis of the pregnancy but also on the prognosis of the deformity and risk of major surgery.

Forty-seven of the live births had isolated talipes. The severity of the deformity was not possible to diagnose on ultrasound. We relied on postnatal examination and classifications to analyse the severity. Unfortunately, there are several classifications known in the literature, and the different classifications each have a different approach.

The Pirani scoring system is a classification that has been used in MCH where most of our subjects were being treated. Unfortunately, the notes of the subjects whom we followed up did not give a clear indication of the Pirani score.

The Pirani scoring system is essential in the diagnosis and treatment of clubfoot. The severity of clubfoot in our study can be assessed by the treatment needed. Treatment was investigated for isolated and complex talipes. After excluding those lost to follow-up and the false positives, 47 subjects had isolated talipes and 14 had complex talipes. This number also excluded the IUDs and TOPs in our study. Percutaneous teno Achill is tenotomy is performed as a day-care procedure under local anaesthesia16 and had a great impact on the treatment of talipes as it is less invasive and probably has less morbidity. Tenotomy of the teno Achill is required in about 85% of cases of congenital talipes.17 Another study quotes that 85% of the feet received tenotomies.16 This was not the case in our study, where 53.19% of the subjects with isolated talipes were treated with tenotomy in combination with Ponseti. The possible reason for these figures is that, in the timeframe of our study, there were 3 years when tenotomies were not performed in the hospital; this procedure was only introduced in 2012. Thus there were 2 years of data where the option of tenotomy was not offered and major surgery was performed where tenotomy might have been an option. Unfortunately, the fact that tenotomies were only introduced in 2 of the 5 years of our study is a great limitation of the survey. Another study needs to be done to properly analyse the effect that the introduction of tenotomy made in the treatment of talipes in the Cape Town Metro district.

When looking at the isolated group, there were 33/47 who only had conservative treatment, which included Ponseti and tenotomy. Eight out of 33 were treated with Ponseti only; this accounts for 17.02% who did not need any intervention other than Ponseti. Surgery was necessary for 14/47 (29.79%) of the children with isolated talipes. This figure contrasts with the study by Caroll where 60% required surgery11. During their study, no mention was made of the option of tenotomy for treatment of clubfoot; thus it can be assumed that tenotomies were not an option or not described yet. Tendo Achill is tenotomy was first described by Minkowitz in 200423 and the Caroll study was done in 2001. The fact that tenotomy was described after the Caroll study tenotomy was described after the Caroll study accounts for the reduction in the amount of major surgeries needed for clubfoot in our study.
Surgeries and tenotomies were grouped into one tenotomy v. two or more, as well as one surgery v. two or more. In both groups, it was evident that half had one surgery and half had two or more surgeries. Most of those who only required one surgery were diagnosed in the late second trimester. Two-thirds of those diagnosed in the second trimester needed two or more surgeries. Almost all the children who needed surgery were diagnosed in the late second or third trimester. Caroll et al. state that talipes diagnosed in the late second trimester is more likely to be positional; this was not the case in our study.

The comparison between the number of tenotomies and surgeries is analysed in Table 7. There were only six subjects who had no tenotomy and one surgery, and also six who had no tenotomy and two or more surgeries. These data show that tenotomy is not replacing surgery and, if surgery is needed, it will be the first option. Although tenotomy was a ground-breaking introduction to clubfoot treatment, it still does not replace major surgery.

**Conclusion**

The information obtained in the present study is useful for future counselling of women whose fetuses are diagnosed with CTEV on prenatal ultrasound. The study made it evident that complex talipes is associated with a poor pregnancy outcome defined as pregnancy loss, where isolated talipes is usually associated with a good pregnancy outcome. Ultrasound is a good diagnostic tool when diagnosing talipes antenatally but cannot diagnose the severity of the clubfoot. False negatives were not studied. The main treatment method and follow-up were statistically calculated, and these answers can help to provide information regarding the prognosis of talipes in South Africa. The introduction of tenotomy can make a difference in the outcome of clubfoot in comparison with previous studies where tenotomies were not performed. Medical professionals need to address the importance of counselling, and a multidisciplinary team should be involved in cases involving prenatal counselling.

CTEV is a debilitating abnormality but is treatable. The outcome of the present study is a clear product of this statement.
References


PART C: Supporting documents

Appendix A

Data collection sheet

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19 July 2016

HREC REF: 514/2016

Dr C Stewart
Department of Obstetrics & Gynaecology
H-Floor
OMB

Dear Dr Stewart

PROJECT TITLE: THE OUTCOME OF PARENTAL SONOGRAPHIC DIAGNOSIS OF FETAL TALIPES IN THE CAPE TOWN METRO DISTRICT (Masters-candidate-Dr E Swarts)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30 July 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

We acknowledge that the student, Dr Elfriede Swarts will also be involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 514/2016
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.