ORCHESTRA

Title: **ORCHidopexy: does Earlier Surgery affect TesticulaR Atrophy?**

Short title: **ORCHESTRA**

A multicenter, trainee-led study co-ordinated by the Paediatric Surgery Trainees Research Network (PSTRN)

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Abstract

Background: In September 2011 the British Association of Paediatric Urologists wrote a consensus statement including the recommendation that orchidopexy should be performed from as early as 3 months of age although between 6 and 12 months is acceptable. However it is not known whether operating at earlier age may affect the rate of testicular atrophy following orchidopexy. It is also not known whether current referral patterns would permit such early intervention.

Aim: To establish the testicular atrophy rate at 6 to 12 months post surgery and to define current practice with regards to the age at orchidopexy in a multicentre international audit.

Endpoints:

1) Rate of testicular atrophy
2) Rate of re-operation/ testicular ascent
3) Wound infection rates
4) Anaesthetic complications/ overnight stays

Hypothesis: Reducing the age at orchidopexy may affect the rate of testicular atrophy following surgery.

Standards: Currently accepted rate of atrophy is 5% for single stage orchidopexy. (1)

Sample Size Calculation: To detect an increase in atrophy to 10%. Power 0.8, alpha 0.05 will require 185 patients in each of two groups (to detect increase in atrophy to 8% sample size would be 478 in each group):

1. Age at orchidopexy < 1yr
2. Age at orchidopexy >1 yr

We aim to recruit a minimum of 370 children in this study.

Methods: The audit will be performed over a 3 month period. Participation from at least 10 paediatric surgical centres and 20 district general hospitals performing general surgery of childhood is estimated to recruit 400 patients. The audit will be performed using a standardised pre-determined protocol and online data collection tool. The audit standards are taken from published literature including: <5% atrophy rate post orchidopexy, < 2% testicular ascent requiring re-operation, < 2% wound infection rate, <2% overnight stay following planned daycase surgery. The audit report will be prepared in accordance to guidelines set by the STROBE statement for observational studies.

Potential Bias: Adult surgeons/ urologists with an interest in general surgery of childhood may not operate on small infants due to anaesthetic considerations in district general hospitals therefore those operated at a younger age may be more likely to be performed by paediatric surgeons.

Introduction

Orchidopexy is one of the most common operations performed in paediatric surgery. Around 7% of boys are born with cryptorchidism. This declines within the first year of life to around 1-2% as in a proportion of boys the testis continues to descend postnatally. This is especially true for those babies born prematurely- the testis traverses the inguinal canal from the 26th week and usually reaches a scrotal position by 34 weeks of gestation. (2)

The guidelines for the optimal age at orchidopexy have changed over time. Prior to 2000 it was considered acceptable to perform orchidopexy between the ages of 2 to 4 years of age. From 2000 the recommended age was considered to be less than 18 months. Recent evidence suggests that the best chance of preserving normal spermatocyte production in later life and reducing future maliganant risk depends on bringing the testis down into a normal scrotal position as early as 3 months of age. (3) The BAPU conference in 2011 proposed that the ideal age would be between 3 to 6 months of age although under 1 year of age would be acceptable.(4)

This recommendation raises several potential issues:

1. There is a paucity of evidence on the rate of testicular atrophy after orchidopexy with estimates ranging from 1 to 5%. (1,5) It would be important to know this before initiating a change in practice to ensure that reducing the age at orchidopexy is not associated with an increase in atrophy rate.

2. It is not known whether the current pattern of referral would allow this change in practice as there are not good national data on the age of referral for orchidopexy.

3. Orchidopexy is often performed by adult surgeons with an interest in paediatric surgery. It is not known whether reducing the age of orchidopexy would be feasible in hospitals without a specialised paediatric anaesthetic service. There is limited data on how much of the workload is performed born by adult surgeons and it is not clear whether tertiary paediatric centres would have the capacity to take on this work if required for anaesthetic or surgical reasons.

This (inter)national multicenter audit has been proposed to address these questions.

Methods

Overview

This is a multicentre prospective audit that will record data from an inception cohort of boys undergoing orchidopexy for unilateral palpable undescended testis during a 3 month period in 2014. Outcome data will be recorded up to 1 year following orchidopexy. The study will be co-ordinated by

the Paediatric Surgery Trainees Research Network, a trainee research collaborative with a proven track record of multicentre audit such as this study.

Eligible Centres

Any hospital which provides elective general surgery of childhood service is eligible to enter patients. A consultant will be named as the principal investigator on the audit registration form and data collection will be completed by a surgical trainee working at that hospital. This audit of current practice must be registered with each individual hospital's clinical audit department.

Patient eligibility

All boys (<16yrs of age) in whom orchidopexy is performed for unilateral palpable undescended testis can be entered into this audit. The testis may be considered palpable either during routine clinical examination or during examination under anaesthesia (Figure 1).

Boys with a known endocrine or genetic condition that may adversely affect testicular growth will be excluded.

Study outcomes

Primary outcome:

1. The rate of testicular atrophy at 6-12 months following orchidopexy.

Secondary outcomes:

1. Rate of (need for) re-operation/ testicular ascent
2. Wound infection rate
3. Anaesthetic complications/ overnight stays

Audit Standards

The standard against which data arising from this audit will be compared has been taken from published literature and for the primary outcome will be:

- Rate of testicular atrophy less than 5% at >6 months post orchidopexy. (1)

For the secondary outcomes the standards are also taken from published literature:

1. Rate of re-operation/ testicular ascent less than 2% (6)
2. Wound infection rate less than 2% (7)
3. Overnight stay less than 2% (8)

We will also compare actual age at referral with a standard we have defined of 100% referral before 34 weeks of age which is the age necessary to allow surgery before 1 year of age (assuming a maximum 18 week wait for elective surgery).

Audit Phases

- Registration for centres to enroll in the audit will begin during late April 2014
- Each centre will register the audit with their institutional audit department during May-August 2014.

- A pilot data collection period will take place in 3 to 4 centres in July 2014.
- Recruitment will run from September 1st 2014 to Novermber 30th 2014.
- Follow-up data will be collected during routine clinic attendance for 1 year following orchidopexy.
- The final patient will reach follow-up December 31st 2015 to allow for flexibility in arranging the 12 months outpatient follow-up appointment.

Projected numbers

A local audit run at the lead centre (Oxford Children's Hospital) recorded approximately 100 orchidopexies per year. Assuming 20% were intra-abdominal or bilateral undescended testes then approximately 80 orchidopexies are being performed for unilateral undescended testis each year. This equates to 20 over a 3 month period.
Morriston Hospital, Swansea reported 125 orchidopexies over a 3 and a half year period equating to 35 orchidopexies / year in a district general hospital. Therefore approximately 10 in a 3 month period. We aim to enroll at least 10 paediatric surgical centres (anticipated 200 patients) and at least 20 district general hospitals (200 patients) with no maximum number of centres. This will allows for a 7.5% drop out rate on follow-up to obtain a minimum sample size for analysis of 370. There will no maximum number of patients included.

Data collection

- *Variables to be recorded:* The patient level data to be recorded are shown in Appendix 2 according to the definitions used in Appendix 1.
- *Method of data collection:* Data will be collected on each eligible patient using a standardised online electronic proforma. Only patient anonymised data will be entered via secure webpage entry.
- *Hospital related variables:* hospital level variables will be collected through an online questionnaire relating to each hospital's local policies, including the preferred age at orchidopexy of each consultatnt. These data will be collected at the commencement of the audit.

Data collection timepoints:

1. *Patient identification*: Patients should be identified on a weekly basis from planned elective lists.
2. *Pre-operative data:* A trainee will fill this in before the operation.
3. *Operative data:* This should be completed either by or with the operating surgeon at the end of the procedure.
4. *Post-operative data:* All patients will be followed up between 6 to 12 months after their operation. For a centre to be included in the audit their consultant body should agree to follow their patients up in the outpatient clinic until at least 6 months post-operatively. There is known to be variability in reported atrophy rate which may be ascribed to insufficient length of follow-up.

Data collation

Anonymised data will be entered via a secure webpage online database. Each patient will be assigned a study number. The trainees entering the data will keep a secure record on a hard drive of an NHS computer linking the study to a hospital number which can then be referenced for follow-up. The data collated by the lead investigator assisted by members of the steering committee.

Statistical Analysis

The report of this audit will be prepared in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies. The analysis will be performed by the study team. Data will be tested using unpaired t-tests, Mann-Whitney U tests and Chi squared tests as appropriate.

Ethical considerations

Since this is an audit, research ethics approval is not necessary. Each centre must register the audit with their institutional audit department and follow all local regulations regarding the implementation of the audit at their institution.

Publication policy

The study will be published according to the policy of the PSTRN which is available in Appendix 3 and online at www.PSTRN.org.uk

Local centre arrangements

This study is designed to be run and delivered by trainees. Each centre will also have a consultant level lead investigator who will oversee the study at that centre. The consultant will approve the final dataset released from any centre to ensure its accuracy.

APPENDIX 1 – Definitions to be used in this study

The following definitions will be used for this study:

- Palpable testis- undescended testis found to be palpable either pre-operatively or at examination under anaesthetic before commencing surgery

- Site of undescended testis=
  1) canalicular- within the inguinal canal
  2) superficial inguinal pouch- inferior to external ring of inguinal canal along course of normal testicular descent
  3) ectopic- outside of inguinal canal, may be in a variety of locations: on perineum lateral to scrotum, thigh or crossed ectopia in contralateral hemiscrotum

- Testicular re-ascent – testis already operated on no longer in scrotal position at follow-up requiring further surgery

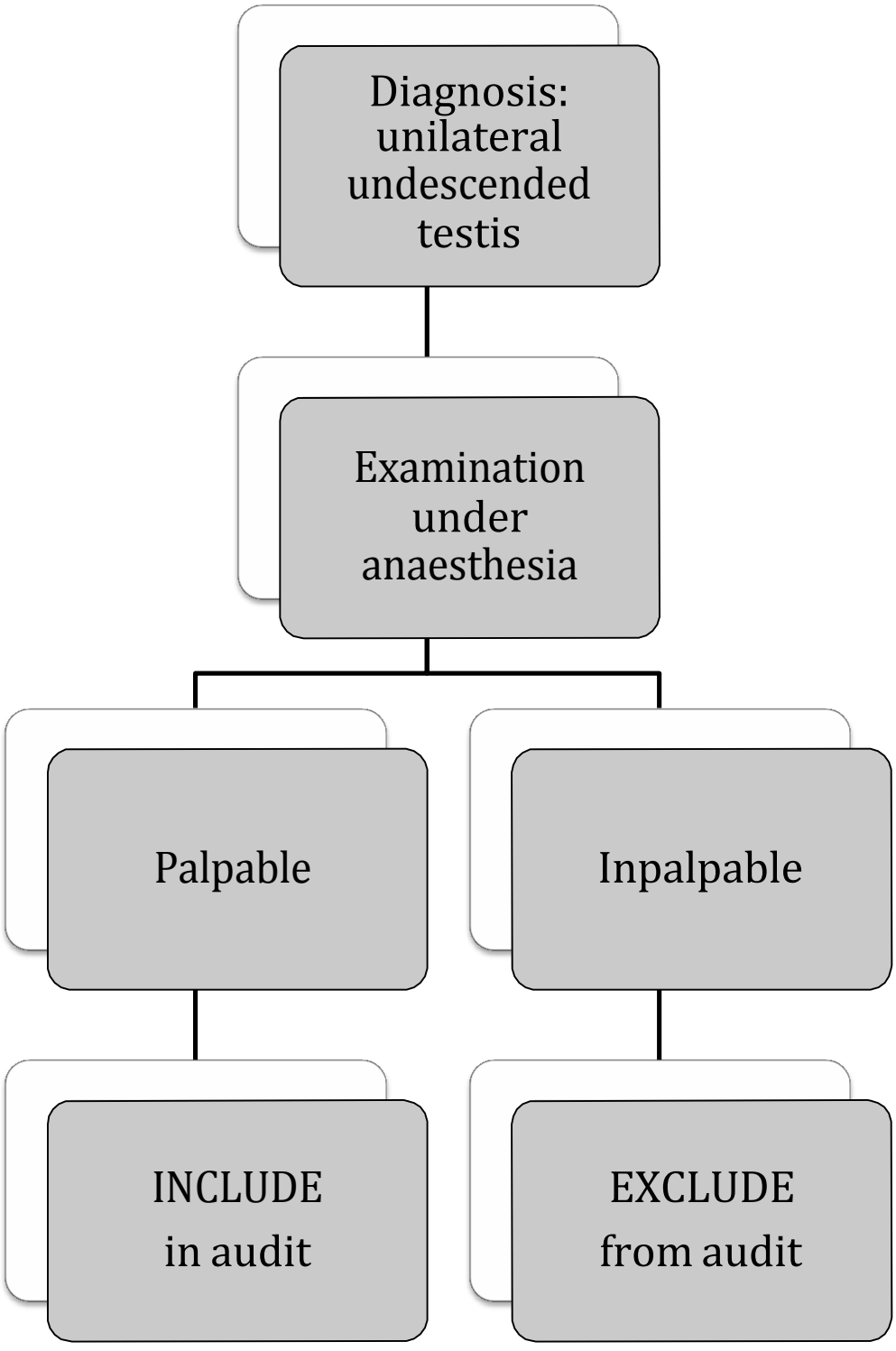
- Complete testicular atrophy- no palpable testicular tissue in scrotum; testis not thought to have re-ascended.

- Partial testicular atrophy- testis documented to be smaller at follow-up than at orchidopexy

- Wound infection- any one of:
  1) Purulent drainage from the incision
  2) At least two of: pain or tenderness, localised swelling, redness, heat, fever AND the clinician diagnoses a surgical site infection
  3) Organisms AND pus cells from aspirate/swab.

  Data will also be collected on whether patients were given antibiotic treatment post-operatively for presumed wound infection in the absence of a defined infection.

Figure 1: FLOW CHART TO CONFIRM ELIGIBILITY



APPENDIX 2 - Data collection forms

Table 1 - Centre Characteristics

Centre Characteristics	
Audit registration number	
Is your centre a :	Paediatric Surgical Centre University Hospital District General Hospital
How many consultants perform orchidopexies?	
How many orchidopexies/year are performed?	Answer in number (3 digit)
Orchidopexy Policies (anonymous, for each consultant performing orchidopexy)	
Are they: (and numbers)	General Paediatric Surgeons Paediatric Urologists Adult general surgeons with interest in general surgery of childhood Adult urologists
What age does each consultant consider optimal for performing orchidopexies?	Answer in months
Does your consultant perform same day bilateral orchidopexies?	Yes/ no
What is your consultant's policy for retractile testes in older boys?	Free text
Does your consultant perform any pre-operative investigations for unilateral palpable UDT (e.g. ultrasound, hormonal testing)	Yes/no another box for what- Ultrasound (free text)
Would the consultant be interested in participating in a randomised controlled trial of age at orchidopexy?	Yes/no

Table 2 - Patient Characteristics

Patient Characteristics	
Age at surgery	(months and days)
Age at referral	(months and days)
Was the testis ever documented as being intra-scrotal? Until what age?	Yes/ no
Date of surgery	
Side of undescended testis	Right/ left
Co-morbidities including previous groin surgery	Yes/ no Free text
Pre-operative findings	Palpable /impalpable
Pre-operative ultrasound	Yes/ no
If yes, was testis correctly identified?	Yes/ no
Surgery	
Grade of primary operating surgeon	FY1/2 CT1-3 Clinical fellow ST3-8 Associate specialist Consultant
If operator was a trainee were they supervised?	Yes/ no
Was the supervisor scrubbed?	Yes/no
Site of testis (one of following)	-superficial inguinal pouch - canalicular -ectopic – free text for site
Size (compared to contralateral)	<25% volume 25-50% volume 50-75% volume 75-100% volume 100% volume larger than contralateral
Appearance of testis Is the vas dissociated from the testis?	Free text Yes/no
Procedure:	Standard inguinal approach Transcrotal incision Other- free text to explain
Anaesthetic complications	Yes/ no If yes- free text to expand
Overnight stay	Yes/no
Reason for overnight stay	Pain/ vomiting/ other- free text

Follow-up plans	
Number of planned follow-up	1 or 2
Timing of 1st follow –up	X months
Timing of 2nd follow-up	X months

Table 3 - 6- 12 month follow-up

6- 12 month follow-up	
Wound infection	Yes/ no
Antibiotic course	Yes/ no
Given by	GP/ hospital
Other post-surgical complication	Yes/ no Free text for yes
Size of testis (compared to contralateral)	- no detectable testis - <25% volume - >25%<50% volume - >50<75% volume - >75% < 100% - 100% - greater than contralateral
Site of testis	- low scrotal - high scrotal - ascended
Further surgery performed within 12 months? Further surgery planned?	Yes/ no Yes/ no
Details of further surgery	Free text
Keep under review	Yes/ no Reason for yes

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