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Clinical Trials-Protocol Assignment due for Section II:

Research Question:

Is the one stage Fowler-Stephens laparoscopic orchiopexy superior to the two stage Fowler-Stephens laparoscopic orchiopexy: Comparison in a Randomized Control Trial

Aim:
Children who present with non-palpable intra-abdominal testicles require surgical management to bring the testicle into the scrotum by one year of age in order to best preserve fertility. In most cases the blood supply is long enough and the testicle is of an adequate size to bring it down in a standard laparoscopic orchiopexy. However, sometimes the blood supply is too short to adequately place the testicle in the scrotum. In this instance the standard of care is to transect the artery and the vein, wait 6 months for development of the collateral blood supply and then place the testicle in the scrotum in a second procedure. This technique has been shown to be feasible laparoscopicaly. More recently people have begun to skip the 6-month waiting period, transect the vessels and during the same anesthetic place the testicle in the scrotum. Studies have shown that this is also a feasible technique and while it may spare the child a second surgery there may be some decrease in testicle size post-operatively. There are no randomized trials comparing the outcomes of the two techniques

Target Study Population:
All pediatric males with a non-palpable, intra-abdominal testicle.

Accessible Study Population:
All pediatric males presenting to a participating pediatric urology clinic with a non-palpable, intra-abdominal testicle.

Inclusion criteria:
All male children >4months and <10years old
The testicle remains non-palpable after anesthesia induction and the blood supply to the testicle is too short for a standard laparoscopic orchiopexy.
(The testicle when placed on stretch does not reach the contralateral side. This can be performed by grasping the gubernaculum or by using an instrument to passively push the testicle across the abdomen.)

Exclusion criteria: Children with Prune Belly Syndrome
Children with a nubbin or no testicle

Children on whom the surgeon has attempted the standard laparoscopic orchiopexy without transection of the testicular artery and vein
The testicle reaches the contralateral side and is amendable to a standard lap orchiopexy.

Study Design:
Double Blind Clinical Trial.
The patients and parents will be recruited and consented at the clinic visit prior to surgery. Surgery will be scheduled as it normally would be for this condition as an exploratory laparoscopy and possible orchiopexy versus excision of nubbin. The child will be randomized once the decision has been made to transect the testicular artery and vein, see below in the randomization section. The child will be randomized to one anesthetic laparoscopic Fowler-Stephens or a two anesthetic laparoscopic Fowler-Stephens. If they are randomized to the one anesthetic then they will follow up at two weeks and 3 months. The three-month visit will include a scrotal US in Radiology for measurement of the testicle size. The two anesthetic patient will follow up at two weeks for a wound check and then six months for the second procedure, which is usual care. Then after the second procedure the child will follow up at two weeks and 3 months. The three-month visit will include a scrotal US in Radiology for measurement of the testicle size. The person collecting the post-op measurements will be blinded to the procedure performed, and the person doing the analysis will be blinded to the procedure performed.

Outcomes:
Primary:
Testicle atrophy:
This is defined by a testicle that is no longer present in the scrotum by palpation or by scrotal or inguinal Ultrasound.

Secondary:
Change in Testicle size
Ascent of the Testicle
Good Scrotal Placement
Infection
Post Op surgical complication
Post Op anesthetic complication
Predictors-
- Location the testicle is found in the abdomen
- Location the testicle stretches to before the vessels are transected
- Looping Vas
- Vas separate to the testicle
- Size of testicle

Randomization:

This will need to be a multicenter study. Therefore we will do block randomization for each center in groups of 4. Using AABB, ABAB, BABA, BBAA, ABBA, BAAB etc.… There will be a predetermined set of envelopes that will go to each study site and will only be opened during surgery once the decision has been made by the surgeon to transect the vessels. If the sample size calculation suggests that each site will only do six procedures we may need to change the group size for each block to make it less predictable.

Blinding:

Blinding will need to occur at the level of data collection and data analysis, as it will be impossible to blind the surgeon or the patient since one arm has only one procedure and the other arm has two procedures and it is unethical to take a child to surgery for a sham procedure. The surgeon will use an ultrasound during surgery to measure the testicle size prior to transecting the vessels. The child will be sent for an ultrasound at the three-month post op visit to measure the testicle size. The person doing the ultrasound will be blinded to the procedure. The person collecting the data and analyzing the data will also be blinded to which procedure was performed.

Control Group:

The control group will be the group getting the two procedure Fowler-Stephens as this is considered the standard by most urologists when the blood supply is short.

Intervention:

The intervention is the single anesthetic Fowler-Stephens and is different to the standard as the testicle is placed in the scrotum at the same time the vessels are transected.

Method to maximize adherence:

Adherence is challenging on a provider level more than it is on a patient level. Providers who have a bias as to which procedure is better may want to just perform the two procedure Fowler-Stephens approach, they may not want to randomize a patient if the testicle appears small or abnormal. Education in regards to the literature and a discussion with the PIs will be crucial to maintaining provider adherence. We will also need to monitor the providers and if they are not sticking to the randomization they and their patients may need to be excluded from the study.

Patients will more likely adhere, since this is a required surgery for the undescended testicle and standard of care is to place it in the scrotum around 1 year of age. Parents rarely no show to follow up surgeries and returning for the second procedure is necessary for placement in the scrotum. If we can get funding we can provide financial incentive to return for the 3-month US and post op visit.

Adverse event and side effect measures:

We will also follow adverse events as it relates to surgery itself.

1. Anesthetic complications: aspiration, respiratory failure, cardiac failure
2. Wound Infection
3. Complications from laparoscopic such as bowel injury or bladder injury or vasculature injury

Plans for interim monitoring:

1. We anticipate that the study will take at least 3 years to accumulate enough patients to have the power to detect a difference in atrophy
2. We also anticipate differences between sites
3. The investigator will need to adjudicate the data every 3 months to make sure there is no missing data from each site
4. Then every year there will need to be a review of the data to make sure that there is no excessive harm or excessive benefit in one of the two arms.
5. We will need a separate Board that can analyze the data and determine if there needs to be a change in the protocol
6. I prefer the Lan-Demet technique with a predetermined number of reviews (3 over the following 3 years- or is it 2 since the third review will be the end of the study)

Ethical issues:

The main ethical issue I see here is that you are comparing two different types of surgery without a placebo arm. The reason I feel a placebo arm is not necessary is that the gold standard is the open two stage Fowler-Stevens. The newer techniques have already been shown in previous studies to have equivalent success rates of 75% and atrophy rates of 15%, which are the same as the open technique. No one has compared them to each other. This is also what makes this study very important because if we determine that there is no difference between the two procedures in regards to our primary and secondary outcomes then we are unlikely to do the two stage procedure in the future in order to minimize the risk of a second procedure. Likewise if we determine that indeed the testicles are larger and less likely to atrophy with the two procedure technique then we will be more likely to perform the second procedure.