Testing the undescended testis

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Citation for published version (APA):
de Vries, A. (2014). Testing the undescended testis

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Summary and future perspectives
SUMMARY

CHAPTER ONE
It is stated that a boy with a non-palpable testis should be treated with a diagnostic laparoscopy and pre-operative ultrasound would not be of any value. Analyzing the ultrasonographic and operative findings of 117 non-palpable testes, we found that a pre-operative ultrasound has a positive predictive value of 91% in localizing the testis in the inguinal canal. When these inguinally localized testes are treated with an inguinal exploration primarily, an unnecessary laparoscopy can be avoided in 9 out of 10 cases. Therefore, we advice pre-operative ultrasound for all boys with a non-palpable testis.

CHAPTER TWO
When an undescended testis is diagnosed as acquired it is unclear whether and when it should be orchidopexied. From 1996 until 2012 we followed 410 boys with 487 acquired undescended testes following a conservative policy until Tanner stage 3. Annually, we performed physical examination and ultrasonography with testis volume measurements. We observed that nearly 80% of the acquired undescended testes descended spontaneously and so, did not need surgery. Furthermore, analysis of 1404 volume measurements showed that acquired undescended testes were small but not smaller than acquired undescended testes orchidopexied at diagnosis (chapter 7). Therefore, we believe a conservative approach until puberty is warranted.

CHAPTER THREE
The same conservative policy and annual follow-up was carried out for the undescended testis after inguinoscrotal surgery. From 2003 until 2010 we followed 24 boys with 26 undescended testes. Of these 26 undescended testes, 12 were after inguinal hernia repair and 14 after orchidopexy, which descended spontaneously in 57% and 75%, respectively. Furthermore, the volumes of these testes are illustrated in the curve of normative values. The most important message of this chapter is that spontaneous descent of undescended testes after inguinoscrotal surgery does occur.

CHAPTER FOUR
Some authors state a testis should not be left in an inguinal position because of the high risk of torsion (with possible detrimental consequences) and hence, an orchidopexy at
diagnosis is needed. We evaluated this risk of torsion in a cohort of 458 patients with 544 acquired undescended testes during 2664 testis-years of follow-up. During these years we did not see any torsion of an acquired undescended testis. Therefore, we dispute that the risk of torsion is an argument for performing orchidopexy at diagnosis.

CHAPTER FIVE
The question is whether the congenital and the acquired undescended testis are truly two different entities or if they represent the same disorder, but at another side of the spectrum. In search of an answer to this question we studied the differences in anatomy at surgery. We compared findings of 76 congenital and 30 acquired undescended testes and found the acquired form more likely to be situated in the superficial pouch (63 vs 15%), and to have a closed processus vaginalis (70 vs 17%) and a normal insertion of the gubernaculum (40 vs 17%). Therefore, we concluded there are distinct anatomical differences between congenital and acquired testes, although congenital aspects are present in the acquired undescended testis.

CHAPTER SIX
As we have treated 335 acquired undescended testes with an orchidopexy at diagnosis from 1986 until 1999 we were able to study the long-term consequences of this policy. Upon request, 105 men with a mean age of 25.7 ± 3.3 years and 137 acquired undescended testes were seen in follow-up. Their mean age at orchidopexy was 9.2 ± 2.8 years. All, but one, testes were situated low-scrotally. Further, the mean volume of the acquired undescended testes orchidopexied at diagnosis was 10.3 ± 3.5 ml, which was smaller than the contralateral testis and smaller than the normative values, described in literature.

CHAPTER SEVEN
In the men seen in follow-up, described in the former chapter, we found a prevalence of 8.6% of intratesticular varicoceles, whereas in the literature prevalences up to 2% have been reported. All intratesticular varicoceles were left-sided after a left-sided orchidopexy. So, after right-sided orchidopexy, no intratesticular varicocele was found. In addition, the testes with intratesticular varicoceles were smaller than the testes without.
CHAPTER EIGHT
In the formerly described study group, in combination with another cohort of 155 acquired undescended testes orchidopexied at diagnosis at the median age of 8.5, from 1996 – 2009, a prevalence of 6.5% of testicular microlithiasis was found. This is higher compared to the prevalence in both asymptomatic boys (2.4 - 5.6%) and boys with acquired undescended testes in whom a conservative policy had been applied (2.8%).

CHAPTER NINE
The $^{18}$F-FDG-uptake of 40 healthy testes of 20 men with a mean age of 26.5 ± 3.9 years were assessed on PET/CT-scan by three independent observers and twice by one of them. The FDG-uptake was expressed as $\text{SUV}_{\text{max}}$, $\text{SUV}_{\text{peak}}$ and $\text{SUV}_{\text{mean}}$ and was 3.42 ± 0.61, 3.06 ± 0.54 and 2.44 ± 0.44, respectively. For all SUV values, the laterality indices were low and interobserver and intraobserver reliability high (ICC 0.992 - 1.0). Therefore, we believe the $^{18}$F-FDG PET/CT has the potential to become a useful instrument in the evaluation of the function of the individual testis.

CHAPTER TEN
This chapter describes the first study evaluating the function of orchidopexied testes on PET/CT. We included eleven men at the mean age of 24.1 ± 2.3 years, who underwent an orchidopexy for a unilateral congenital undescended testis at the age of 1.9 ± 1.4 years. The mean $\text{SUV}_{\text{peak}}$ of the orchidopexied testis was 2.74 ± 0.48 (2.13 − 3.47), which was significantly lower than its descended counterpart. Nonetheless, congenital undescended testes orchidopexied in childhood function to some degree.

The findings of chapters two, three, six, seven and eight illustrate that a randomized controlled trial comparing orchidopexy at diagnosis with a conservative policy until puberty, is desirable to reach consensus on the treatment of the acquired undescended testis.
FUTURE PERSPECTIVES

Clinical practice; a boy, eight years of age, notices his left testis has been ascended out of its scrotum into his groin. He tries to pull it back into the scrotum, but it turns back into his groin directly. The boy feels ashamed and is full of questions. Did I do something wrong? Will it stay there? Is it dangerous to leave it there? Will I ever become a dad? Do I need to go to the hospital? And, do they need to operate on me then!? Sooner or later he will be worried enough to tell his mother and/or father. His parents are concerned as well, and cannot answer his questions. They go and see the general practitioner who tells them (s)he thinks an operation is needed. Full of expectations, they arrive at the pediatrician or pediatric surgeon.

The specialist explains the boy has an acquired undescended testis. And then; instead of answering their questions, a story full of uncertainties follows: “it is unknown whether this testis will descend back into the scrotum itself. Probably not the next coming years, but maybe when your puberty starts. We can operate on it now, but we can wait as well. Your testis will most likely become smaller than the other one, both if we operate on it and if we do not. Probably you will become a father, but we cannot guarantee it. We do not know whether it is better for your future semen to operate now or to wait first. And, we do not think it is dangerous to leave it in your groin, but when it hurts, you need to go to the hospital immediately, otherwise it is possible you lose your testis.”

Subsequently, the specialist explains that because we do not know which treatment – to operate on it now or to await possible spontaneous descent at puberty - is best, we are doing research on it. This means that - if the boy and his parents consent - the boy will be randomized to a certain treatment protocol. Furthermore, it is important that - if he participates - he will come back when he has reached the age of 18 years to participate in the follow-up examinations.

One can imagine the boy and his parents might feel even more unsure, also to choose whether to leave it to chance which treatment he will be given.

Besides this difficulty to include boys with acquired undescended testes in a randomized controlled trial, we have to be aware of more struggles. The study population will be rather heterogenic. Age at referral, duration of non-scrotal position, uni/bilaterality, location of the acquired undescended testis, will all differ. Further, most outcome parameters, like the function of the testis, will only be possible to evaluate at the long-term. Therefore, the follow-up period will take decades.
Last but not least, the outcome parameters of the randomized controlled trial should be chosen accurately. Psychological consequences, risk of testicular torsion, degree of malignant degeneration and the function of the testis should all be taken into account. The assessment of the function of the testis is, as portrayed in the introduction, far from simple. Ultrasonographically measured testicular volumes, hormone levels and semen analysis, could be considered as outcome parameters. However, we suggest to use the PET/CT-scan, as illustrated in the latter two chapters of this thesis, to quantify this counterpart-independent function. The position of the testes, far from other FDG-active organs, makes it possible to scan with a low dose of FDG and radiation and the costs of these scans will probably become less in time.

So, if we ever want to have a clear evidence-based explanation to the boys with acquired undescended testes and their parents, we should sit together and make plans for a multi-center randomized controlled trial. In the Netherlands, we have 1500 new patients per year, many dedicated clinicians and a continuing centralization of care. Therefore, in our opinion, the optimal method to reach consensus on the best treatment of acquired undescended testes, a multi-center randomized controlled trial, is feasible.