EIJA MÄKELÄ

Torsion of the Spermatic Cord in Childhood and Adolescence

ACADEMIC DISSERTATION
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UNIVERSITY OF TAMPERE

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YMPÄRISTÖMERKKI
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To my family

ABSTRACT

Aim

One aim of this thesis was to examine spermatic cord torsion (SCT) and compare its distribution, symptoms and signs with those of other causes of acute scrotum in infancy, childhood and adolescence. A further aim was to investigate the feasibility of two new diagnostic techniques, dynamic contrast-enhanced (CE) and diffusion-weighted (DW) magnetic resonance imaging (MRI), for the detection of SCT and acute scrotum.

Materials and Methods

The medical records of 388 consecutive boys under 17 years of age, who had been treated for acute scrotum at the Hospital for Children and Adolescents in Helsinki in 1977–1995 were reviewed. Ninety-one of them had been under one year of age. At that time all patients with acute scrotum were operated on urgently regardless of any imaging findings. The duration and characteristics of the symptoms and signs prior to operation and the ages of the patients were recorded.

The possibility of using dynamic CE-MRI for the detection of SCT-induced hypoperfusion was investigated first with adult Sprague-Dawley rats subjected to unilateral testicular torsion of 360 or 720 degrees followed one hour later by dynamic CE-MRI performed with a 1.5 T MRI scanner. The region of interest (ROI) values for the ischaemic and control testicles in the apparent diffusion coefficient (ADC) images were then compared. Gadolinium uptake in the ROI of the dynamic CE-MRI images was presented in the form of curves, from which the maximal slopes were calculated and compared. The ROI values in testicles with normal blood circulation increased as a function of time.

The MRI method tested with rats was then used in a prospective study at Tampere University Hospital in 2001–2005 involving 17 boys and young men with acute scrotum symptoms. The protocol prior to MRI included a physical examination by a surgeon, laboratory tests and Doppler ultrasound (DUS). Nine patients were operated on because SCT could not be excluded on the grounds of either the clinical or the DUS findings.

Results

The scrotal operations performed in Helsinki revealed 100 cases (26%) of SCT, 174 cases (45%) of torsion of the testicular appendage (TAT), 38 cases (10%) of epididymitis

(ED), 32 cases (8%) of incarcerated inguinal hernias and 44 (11%) other conditions. The peak incidences of SCT were during the first month of life and in puberty. Almost half of the boys with TAT were nine to 12 years of age (median 11 years). The acute symptoms reported by patients other than infants were chiefly pain (SCT 88%, TAT 94%, ED 76%). Swelling in the hemiscrotum was found in 44% of the SCT cases, 39% of the TAT cases and 50% of the ED cases. Epididymitis was also accompanied by erythema (37%), but less often by fever (in 16%). Scrotal erythema was found in 55 (32%), but the "blue dot sign" was found to be positive in only 17 of the boys with TAT (10%). In infants, a dark or hard testicle was detected in 91% of the SCT patients.

Three quarters of the boys who were operated on within six hours of the onset of symptoms had testicular torsion. All the testicles were saved when detorsion was performed within six hours, but salvage was possible in only half of the cases in which the symptoms had lasted 6–12 hours. Only 4% of the twisted testicles recovered after symptoms lasting more than 12 hours. The salvage rate for SCTs was 48% in the whole cohort series and 11,4% among the infants.

The maximal slope of contrast enhancement in the experimental rat model employing 360° SCT was 0.072%/s vs. 0.47%/s in the contralateral control testicle ($p<0.001$). With 720° SCT the slope diminished to 0.046%/s vs. 0.37%/s, respectively. Decreased ADC values, implying hypoperfusion, were also measured on the affected side in both groups the decrease being 12.4% ($p<0.05$) in the group with 360° SCT and 10.8% ($p<0.001$) in the group with 720° SCT.

In the clinical trial all the normal testicles gave increasing ROI values, while all SCTs gave constantly low values, indicating no perfusion. The enhancement curves for the other causes of acute scrotum, such as TAT and ED, showed normal or increased perfusion relative to the contralateral testicle.

Conclusions

Acute scrotum was caused by SCT in a quarter of the patients with incidence peaks to be found in neonates and pubertal boys. A review of acute scrotum studies demonstrated that the clinical signs used in the various diagnoses overlap considerably. The crucial finding for SCT is a sudden pain that brings the patient to the emergency room within six hours of onset. Such cases mostly require immediate surgical exploration. There is still a need for reliable diagnostic tools, however, and our investigations demonstrated that hypoperfusion caused by SCT can be detected and quantified easily by means of dynamic CE-MRI. In combination with DW-MRI this can also be used for selecting acute scrotum patients for urgent surgery.

TIIVISTELMÄ

Tavoitteet

Väitöskirjatyön tavoitteena oli tutkia kiveksen kiertymää ja verrata sen esiintymistä, oireita, niiden kestoa sekä kliinisiä löydöksiä muihin äkillistä kiveskipua aiheuttaviin tauteihin lapsuus- ja nuoruusiässä. Toisena tavoitteena oli pyrkiä kehittämään taudin diagnostiikkaa. Varjoainetehosteisen ja diffuusio painotteisen magneettitutkimuksen (MRI) soveltuvuutta akuutin kivesiskemian havaitsemiseen tutkittiin eläinkokein ja potilastyössä.

Aineisto ja menetelmät

Potilasaineisto kerättiin Lasten ja Nuorten Sairaalasta Helsingistä ja siihen kuului 388 peräkkäistä alle 17-vuotiasta potilasta, jotka oli hoidettu 1977–1995. Näistä 91 oli alle yksivuotiaita. Tuolloin kaikki potilaat, joilla todettiin äkillisesti kipeytynyt kives, leikattiin. Sairaskertomuksista etsittiin tiedot potilaan iästä, oireista ja niiden kestosta sekä löydöksistä ennen leikkausta. Alle yksivuotiaita tarkasteltiin myös omana ryhmänään.

MRI tutkimukset toteutettiin Tampereen yliopistossa ensiksi Sprague-Dawley rotilla, jolle tehtiin kokeellinen kiveksen kiertymä anestesiassa leikkauksella. Toista kivestä käytettiin verrokkina. Kivestä kierrettiin 360 tai 720 astetta ja nukutettuna tunti leikkauksen jälkeen rottien kivekset kuvattiin 1.5 Teslan MRI laitteella dynaamisesti varjoainetehosteisena. Diffuusio MRI kuvista määritettiin tutkimuksen kohde, ROI (region of interest), kierretystä kiveksestä ja terveestä viereisestä vertailukiveksestä. MRI kuvista havainnollistettiin varjoaineen kertyminen siten että, ROI-arvoista muodostettiin käyrä ajan funktiona. Käyrien jyrkkyys kuvasi varjoaineen kertymistä ja sitä voitiin mitata ja vertailla.

Rotilla kokeellisesti testattu dynaaminen varjoainetehosteinen MRI ja diffuusio MRI tutkimus sovellettiin potilaskäyttöön prospektiivisessa tutkimuksessa, joka toteutettiin TAYS:ssa 2001–2005. Pilottitutkimukseen saatiin mukaan ensiavusta 17 poikaa ja nuorta miestä, joilla oli äkillisesti kipeytynyt kives. Potilaat tutkittiin normaalin hoitokäytännön mukaisesti kirurgin toimesta, laboratoriokokein ja doppler ultraäänitutkimuksella ennen MRI tutkimusta. MRI ei saanut pitkittää leikkaukseen pääsyä. Yhdeksän potilasta hoidettiin leikkaamalla, koska kiveksen kiertymää ei voitu poissulkea kliinisen tai ultraääni arvion perusteella.

Tulokset

Helsingissä leikatut akuutit kiveskipuiset potilaat jakautuivat seuraaviin diagnoosiryhmiin: 100 (26 %) kiveksen kiertymää, 174 (45 %) kiveslisäkkeen kiertymää, 38 (10 %) lisäkivestulehdusta, 32 (8 %) kureutunutta nivustyrää ja 44 (11 %) muuta syytä. Kiveskiertymiä oli eniten alle yhden kuukauden ikäisillä vauvoilla ja murrosikäisillä pojilla. Lähes puolet pojista, joilla oli kiveslisäkkeen kiertymä, oli 9–12 vuoden ikäisiä (mediaani 11). Kipuoire yli yksivuotiailla todettiin 88 %:lla kiveskiertymä potilaista, 94 %:lla kiveslisäkkeen kiertymä potilaista ja 74 %:lla lisäkivestulehdus potilaista. Turvotusta todettiin 44 %:lla, 39 %:lla ja 50 %:lla vastaavasti. Lisäkivestulehdus potilailla todettiin punoitusta 37 %:lla ja kuumetta 16 %:lla. Kiveslisäkkeen kiertymä potilailla todettiin punoitusta 32 %:lla ja spesifinen löydös ”blue dot sign” todettiin 17:llä (10 %) pojalla. Alle yksivuotiaiden kiveskiertymäpotilaiden tyypillinen löydös oli tumma tai kova kives (91 %:lla).

Kolmella neljäsosalla potilaista, jotka leikattiin kuuden tunnin kuluessa oireiden alusta, löydettiin kiveksen kiertymä. Jos kiveksen kiertymä saatiin purettua leikkauksessa alle kuuden tunnin oireiden alusta, kives aina säästyi. Kuuden ja 12 tunnin välillä puolet kiveksistä voitiin säästää. 12 tunnin jälkeen vain 4 % kiveksistä toipui. Kaikkiaan 48 %:ssa leikatuista kiertyneistä kiveksistä verenkierto palautui, mutta alle yksivuotiaiden kiveksistä vain 11,4 % säästyi.

Kokeellisessa eläintyössä todettiin selkeä ero ROI-käyrien kulmakertoimissa. Kun kiveskiertymä oli 360 astetta, maksimaalinen jyrkkyys oli 0.072 %/s ja terveellä verrokkipuolella 0.47 % ($p<0.001$). Vastaavasti 720:een kiertymä ryhmässä luvut olivat 0.046 %/s ja 0.37 %/s. Molemmissa ryhmissä todettiin myös jonkin verran alentuneet arvot diffuusiokuvauksissa verrattuna terveeseen puoleen.

Prospektiivisessa potilastyössä MRI tutkimuksessa voitiin osoittaa nousevat ROI-käyrät kaikissa terveissä kiveksissä, kun taas kiertyneiden kivesten ROI-arvot pysyivät matalana kertoen hypoperfuusiosta. Kiveslisäkkeen kiertymä ja lisäkivestulehdus aiheuttivat normaalisti tai voimakkaammin nousevat perfuusiokäyrät terveen kiveksen ROI-alueen arvoihin verrattuna.

Yhteenveto

Äkillisen kiveskivun kliiniset löydökset ovat hyvin samantapaiset eri tautiryhmissä, eikä niiden perusteella pelkästään voi tehdä leikkauspäätöstä tai jättää leikkaamatta. Kiveksen kiertymän aiheuttama kipu näyttää kuitenkin tuovan potilaat nopeammin ensiapuun kuin muiden tautiryhmien aiheuttamat oireet. Jos oireiden alusta on kulunut alle kuusi tuntia, tulee kivespussi eksploroida nopeasti. Oireiden pitkittyessä kiveskiertymän diagnostikkaa vaikeutuu ja tuolloin tarvitaan luotettavia apuvälineitä arvioimaan kiveksen verenkiertoa. Tutkimuksemme osoitti, että kiveksen kiertymän aiheuttama hypoperfuusio voidaan myös todentaa ja mitata dynaamisella CE MRI tutkimuksella. Yhdistettynä DW MRI löydöksiin, magneettitutkimusta voidaan käyttää apuvälineenä äkillisten kiveskipuisten potilaiden leikkausarviossa.

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ABBREVIATIONS

ADC	apparent diffusion coefficient
ASL	arterial spin-labeling
CE	contrast enhanced
CEUS	contrast enhanced ultrasound
DUS	doppler ultrasonography
DW	diffusion-weighted
ED	epididymitis
EPI	echo planar imaging
FSE	fast spin echo
FSH	follicle-stimulating hormone
FSPGR	fast spoiled gradient-recalled echo
GnRH	gonadotropin-releasing hormone
HCG	human chorionic gonadotropin
LH	luteinising hormone
MIS	müllerian-inhibiting substance
MRI	magnetic resonance imaging
NEX	number of excitations
NIRS	near-infrared spectroscopy
NS	nuclear scintigraphy
PCT	perfusion computer tomography
ROI	region of interest
SCT	spermatic cord torsion
SRY	sex-determining region of the Y-chromosome
TAT	torsion of the testicular appendage
TE	time of echo
TR	time of repetition
US	ultrasonography

1 INTRODUCTION

Torsion of the spermatic cord (SCT) is a sporadic phenomenon which may result in organ loss and can potentially influence fertility. Testicular torsion occurs when the spermatic cord becomes twisted and the blood circulation to the testicle is cut off. It was first described by Delasiauve in 1840 in a patient with an undescended testicle while Taylor published the first report of an infant who had a normally descended testis with torsion in 1897 (Leape 1979). Since then testicular torsion has been found in all age groups up to 78 years of age. Since its incidence in men under 25 years of age is about one in 4000, one man in every 160 will suffer from this condition by that age 25 (Burgher 1998). In particular, many authors have found SCT to be the most common reason for acute scrotum during the first year of life (Yang et al. 2011).

SCTs are divided into two groups: extravaginal torsion, where the entire spermatic cord is twisted, and intravaginal torsion, where the cord twists within the tunica vaginalis. Intravaginal torsion is more common and is found among prepubertal and pubertal boys, whereas extravaginal torsion is typical among neonatal patients. (Skoglund et al. 1970.) The lack of fixation of the testis and epididymis to the tunica vaginalis, called the "bell-clapper" deformity or elongated mesorchium may allow testicular torsion to take place. This abnormality is usually bilateral. Although SCT is typically sporadic, familial torsion occurs in about 10% of cases (Cubillos et al. 2011, Shteynshlyuger et al. 2013). Torsion initially occludes the veins, causing oedema of the testis, which may ultimately lead to haemorrhagic infarction of the testicle. Experimental findings have demonstrated that in addition to the degree and tightness of the torsion, the duration of occlusion can affect the degree of damage and ischaemia that the testis suffers and clinical experience has revealed that the duration of the symptoms is a crucial factor when evaluating the vitality of the affected testicle. Although there is no absolute time limit for operative salvage, it has been shown that the salvage rate for a human testicle declines sharply after 6 hours of ischaemia (Lewis et al. 1995). Detorsion within 6, 12 and 24 hours of the onset of symptoms will results in salvage rates of 90%, 50% and less than 10%, respectively (Ringdahl and Teague 2006). Thus early recognition of SCT is essential in order to save the testis.

SCT is a urological emergency and leads to acute scrotum, but it is not the only cause of this challenging condition. Acute scrotum is characterized by a swollen, hard, tender,

red, dark and painful scrotum with a sudden onset of symptoms. Although SCT may be fatal for the testis, there are other reasons for acute scrotum that mimic its signs and symptoms. Common causes are epididymitis (ED) and torsion of the testicular appendage (TAT), but these do not need operative treatment. The challenge is to diagnose and operate on the SCT cases urgently while avoiding unnecessary operations. Since SCT is the cause of only about quarter of acute scrotum cases (Murphy et al. 2006), surgical exploration is not considered to be mandatory for all patients with acute scrotal symptoms (Kass et al. 1993).

Although the cornerstones of SCT diagnostics are a thorough case history and clearly identified clinical symptoms and signs, imaging modalities are a valuable help in any examination. Radiology and nuclear medicine offer several options for imaging the scrotum area, and new, more accuarate modalities are being developed. Nuclear scintigraphy (NS) is an isotope imaging method for evaluating the vascularity of the testicle (Hörmann et al. 2004) while ultrasound is the most commonly used modality for imaging acute scrotum in children and Doppler ultrasonography (DUS) is especially helpful in detecting the blood flow in the small vessels of an affected testis and comparing it with that of the contralateral testicle. The sensitivity of scintigraphy for SCT in children is 84–100%, with an accuracy of 95% (Babcock 1995). The limitations of NS are the delay in immediate availability for 24 hours a day and an inability to detect anatomical structures. DUS is more readily available in acute care hospitals and is useful modality for diagnosing other forms of scrotal pathology as well. The sensitivity and specificity of DUS may be as high as 90%, but the evaluation of the scrotum is dependent on the size and co-operation of the patient and the experience of the radiologist (Baker et al. 2000). In addition to NS and DUS, magnetic resonance imaging (MRI) has emerged as a promising new modality with increasing acute availability (Trambert et al. 1990).

The operative treatment of SCT is an urgent matter. The affected testicle is usually explored by means of a midline incision in the scrotum, and if SCT is verified, it is derotated and orchiopexy is performed on both sides. Should the blood circulation not recover, the necrotic testicle has to be removed. As first aid in the emergency room, manual detorsion may be attempted, or else cooling of the affected testicle (Kallerhoff et al. 1996, Miller et al. 1990).

The salvage rates in cases of SCT have improved in recent times, so that where the rate was 55% in the 1960s and 1970s, it was 60–70% in 1980s and 1990s, presumably due to improved diagnostics and acute surgical service availability. Detorsion within 6 hours saves nearly 100% of testicles, 70% within 6 to 12 hours and 20% beyond 12 hours (Burgher 1998).

2 REVIEW OF THE LITERATURE

2.1 History of testicular torsion

Testicular torsion, or more precisely termed torsion of the spermatic cord (SCT), was first mentioned by Delasiauve in 1840, affecting an undescended testicle. In 1881 Langton, at St Bartholomew's Hospital in London, reported the first torsion case affecting a normally descended testicle (Williamson 1976). The torsion could not be released, however, and the testis was lost. By 1901 Scudder had found 32 cases of SCT in the world's medical literature, but it was still considered to be a rarity. Wheeler and Clark (1952) and Deming and Clarke (1953) reported 9 and 20 cases of SCT respectively in the 1950's, but it was suspected by Scott (1956) that there must have been more undiagnosed or untreated cases which had led to testicular atrophy. It was not until the 1970's that SCT became more frequently recognized, with over 1000 cases reported (Skoglund 1970). In addition, it was discovered that torsion occurred mainly in infancy and adolescence.

2.2 Development of the testicle

2.2.1 Embryology

Morphologically the developing embryo is at first bisexual. Germ cells migrate to the hindgut and retroperitoneum, where they condense in the urogenital ridge to become either a testis or an ovary. The Y-chromosome is needed for testicular development. Sinclair et al. (1990) found the sex-determining region of the Y-chromosome (SRY), which encodes a DNA-binding protein responsible for testis differentiation in all mammals. At the seventh week of embryogenesis the fetal testis develops seminiferous tubules with Sertoli cells surrounding the germ cells, and Leydig cells differentiate from the interstitial mesenchyme (Elder 1988). The Sertoli cells produce Müllerian-inhibiting substance (MIS), which causes regression of the female duct elements. At the 10th weeks of gestation the Leydig cells start to produce testosterone, which is needed

for the Wolffian ducts to develop into the epididymis, vas deferens and seminal vesicles. Testosterone has to be reduced to dihydrotestosterone by 5α-reductase in order for the male external genitalia to differentiate to the phallus and scrotum (Imperato-McGinley 1974). This takes place during the 10th and 15th weeks of gestation. The descent of the testis starts after sexual differentiation, at 8–10 weeks and by the 15th week the testes arrive in the inguinal area, passing the inguinal ring by the 28th week. The testis normally reaches the scrotum at 35–40 weeks. The gubernaculum, which develops during the fifth week of gestation, plays an important role in guiding the testis down to the scrotum (Heyns and Hutson 1995). It is attached to the caudal end of the Wolffian duct, the gonad, and to the inguinal abdominal wall and the cauda epididymis. It is swelling of the gubernaculums that leads to migration of the testis, which descends within an outpouching of the peritoneum, the processus vaginalis, which covers the testis and epididymis except for the posterior attachment of the epididymis to the scrotal wall. The testes are suspended by the spermatic cord, which contains the spermatic artery and vein. The connection of the processus vaginalis to the peritoneum closes by the end of the first year (Friedman and Sheynkin 1995). There is evidence that abdominal pressure also has an important role in the descent of the testis (Frey 1984). A normal epididymis is needed for proper attachment of the gubernaculum.

2.2.2 Hormonal factors and puberty

The concentration of testosterone in the serum of a newborn boy is as high as in puberty. It then diminishes for a short while, but arises again for about six months. Thus the Leydig cells are activated from the very beginning, but it is regulation by gonadotropin-releasing hormone (GnRH) from the hypothalamus and the gonadotrophins luteinising hormone (LH) and follicle-stimulating hormone (FSH) from the hypophysis that completes this arousal of puberty over a period of ten years.

The first signs of puberty appear at the age of 10–14 years. Endocrinological arousal takes place and the boy starts to take on a more masculine appearance. The testes grow to 4–5.5 cm in length in response to the secretion of LH and FSH, which is preceded by GnRH pulsation. The Leydig cells and Sertoli cells in the testes are activated and spermatogenesis (involving Sertoli cells) starts in puberty due to the enhancement of steroid production (Dunkel 2000).

2.3 Anatomy of the scrotum

Both testes are suspended in the scrotum by a fibrovascular string, the spermatic cord, which leaves the inguinal canal through the external inguinal ring. The left testicle usually hangs somewhat lower than the right one. The temperature in the scrotum is lower than in the abdomen, which is necessary for spermatogenesis (Williams et al. 1966). Between the compartments of the scrotum is the septum and a midline seam called the raphe of the scrotum.

The testicle is plum-shaped and about one cm in length in a newborn baby and 4–5.5 cm long when mature. The testicle is firm in consistency. On the posterior side, in the mediastinum of the testis, the blood vessels, nerves and the ductus deferens reach the epididymis through the spermatic cord. The epididymis is like a tail above the testis, and it has three parts: the caput, corpus and cauda epididymis. There may be up to four small anatomical sctructures or vesicles on the surface of the testicle and the epididymis and 90% of men have an 1–10 mm-long appendix on cranial surface of testis, which is a remnant of the Müllerian duct. The appendix of the epididymis is found on the caput epididymis, and is a remnant of the Wolffian duct while smaller vesicles are the paradidymis, above the epididymis, and the vas aberrans on the cauda epididymis (Waldayer and Mayet 1980) (Figure 1).

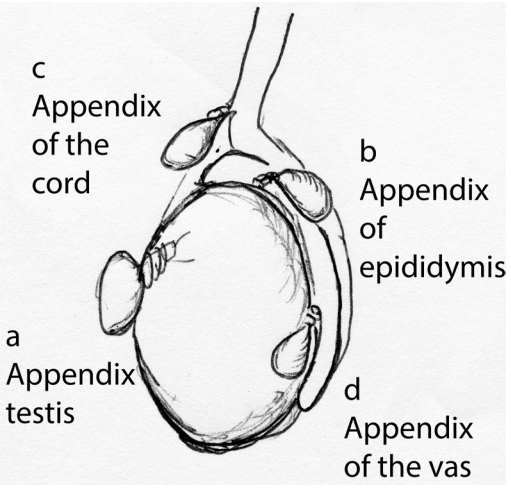


Figure 1. The appendages of testis: a) Appendix testis (hydatis of Morgagni), b) Appendix of epididymis, c) Appendix of the cord (organ of Giraldes) and d) Appendix of the vas (vas aberrans of Haller).

The testis and epididymis are largely covered in the scrotal sac by the visceral layer of a peritoneal sheath, the tunica vaginalis, the parietal layer of which surrounds these and encloses the scrotal sac. The next layers around the testes are the internal spermatic fascia, the cremaster muscle and fascia and the external spermatic fascia. The cremaster muscle arises from the internal oblique and oblique transverse abdominal muscles and

is able to elevate the testicle by contraction, known as the cremaster reflex. The outer layer of the scrotum consists of thin skin with hair and sebaceous glands. Instead of fat, the subcutaneous tissue contains smooth muscle cells, the tunica dartos contractions of which serve to regulate the volume and the temperature of the scrotal sac.

The spermatic cord, which follows the testicle through the inguinal canal to the scrotum contains the testicular artery and veins, nerves and ductus deferens, with fibers of cremasteric muscle and its connective tissue around them. The testicular artery originates from the aorta, below the renal arteries, and continues through the inguinal canal to end up in the testicle. The testis also has a collateral blood supply from the cremasteric artery (a branch of the inferior epigastric artery, which in turn is a branch of the external iliac artery) and the artery leading to the ductus deferens (a branch of the inferior vesical artery, which in turn is a branch of the internal iliac artery). All these arteries enter through the spermatic cord. The testicular veins follow testicular arteries at first, after which the right testicular vein drains into the inferior vena cava and the left testicular vein into the left renal vein. The lymphatic vessels of the scrotum follow the testicular arteries and the lymphatic fluid drains into the lumbar lymph nodes on the inferior vena cava and the abdominal aorta. The genital branch of the genitofemoral nerve comes from the celiac plexus and supplies the cremaster muscle and the scrotal skin (Kahle 1986). The testicle is supplied by the testicular plexus, which is derived from the renal plexus, receiving branches from the aortic plexus. It accompanies the internal spermatic artery to the testis (Waldeyer and Mayet 1980).

The testicle is tightly surrounded by a thick, white capsule, the tunica albuginea, which radiates from the outer surface to the mediastinum of the testis and subdivides the tissue into hundreds of lobules, the lobuli testis. Each lobule contains a few seminiferous tubules, which lead to the mediastinum of the testis and create the rete testis. From there the tubules drain into the efferent ductules, which conduct the sperm (spermatozoa) to the ductus epididymis. The structure outside of epididymis is called the ductus deferens.

There is a basal membrane which separates the tubules from the surrounding connective tissue. The seminiferous tubules are lined with peritubular myoid cells, which surround Sertoli cells. Here in the seminiferous tubules germ cells develop into spermatogonia, spermatocytes, spermatids and spermatozoon through the process of spermatogenesis. The Sertoli cells are connected with tight junctions building a blood-testis barrier for the maturing spermatocytes and they support, nourish and surround the developing spermatogonia. Moreover, the hormonal signals (FSH, testosterone) to the developing spermatogonia come across the Sertoli cells, which produce inhibin hormone. The Leydig interstitial cells are located between the seminiferous tubules and around the blood vessels. It is these that produce the male sex hormone, testosterone,

Figure 2. Anatomy of scrotum with license from netterimages.com.

Figure 3. Anatomy of scrotum and testis with license from netterimages.com.

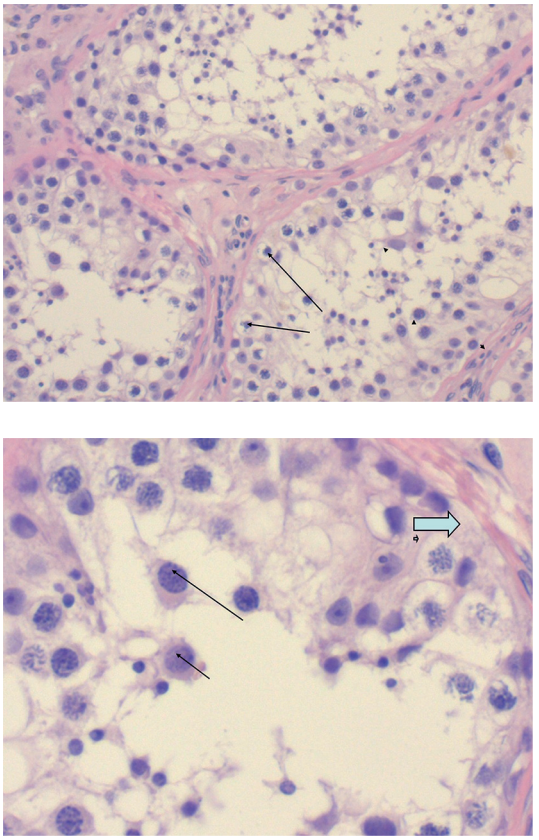


Figure 4A. Normal histology of a testicle (enlargement of 100 and 200 times) showing seminiferous tubules and Sertoli cells with dark nucleus (black arrows) and Leydig cells close to blood vessels (blue arrow).

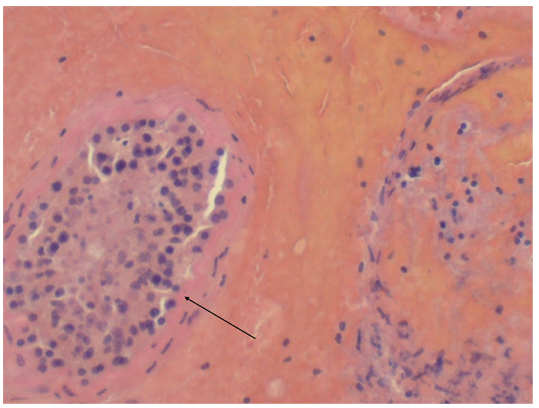


Figure 4B. Almost destroyed seminiferous tubule after torsion and necrosis of a testicle. (200x).

important for sexual depelopment and a small amount of female hormone, oestrogen. Also interstitial macrophages and epithelial cells are found (Figure 4).

From the rete testis the spermatozoa move to the epididymis through the efferent ductules, which make up the greater part of the head of the epididymis. From there on, the duct of epididymis is highly tortuous tube about 5m long ending in the cauda epididymis, where the spermatozoa are stored. While still in the testis the spermatozoa are immobile and reach the epididymis with the stream of fluid. The ductus deferens is a continuation of the ductus epididymis and it transports the spermatozoa from the epididymis via the spermatic cord through the inguinal canal. The end of the ductus deferens widens to form the ampulla, into which the seminal vesicle drains continuing as an ejaculatory duct which passes through the prostate.

2.4 Pathogenesis of spermatic cord torsion

2.4.1 Intravaginal torsion

The visceral and parietal layers of the tunica vaginalis cover the testicle and epididymis, except at the posterior attachment of the epididymis to the scrotal wall (Ceasar 1994). There is also a strong attachment between the testis and the epididymis, which is similarily tightly connected to the posterior scrotal wall. This anatomy should prevent free rotation of the testis. However, Muschat (1932) described the "bell-clapper" deformity, in which the tunica vaginalis totally covers the testicle and the epididymis without any posterior attachment and the tunica vaginalis has a high investment in the spermatic cord. This exceptional anatomy allows the testis to rotate more freely intravaginally and so that it often lies horizontally in the scrotal sac rather than vertically as the normal testis does (Figure 5). The deformity is usually bilateral (Jones 1991). In a recent series of 47 boys operated on for SCT or intermittent cord torsion this anatomical anomaly was found in all cases, and contralaterally in 88% and 90%, respectively (Hayn et al. 2008). The left side is slightly more often affected, since the spermatic cord is longer on this side (Anderson et al. 1989). A rare possibility for testicular torsion is a loose connection between the testicle and epididymis by means of the mesorchium, which may lead to torsion between the testis and epididymis. An autopsy series analysed by Caesar (1994) demonstrated that up to 12% of the male population have an abnormal testicular attachment, although the incidence of SCT is not that high.

The event that triggers SCT is poorly understood, but contraction of the cremasteric muscle may be one contributory factor (Burgher 1998). The muscle contracts secondarily to trauma, physical exercise, an erection or a sudden drop in temperature (Cuckow

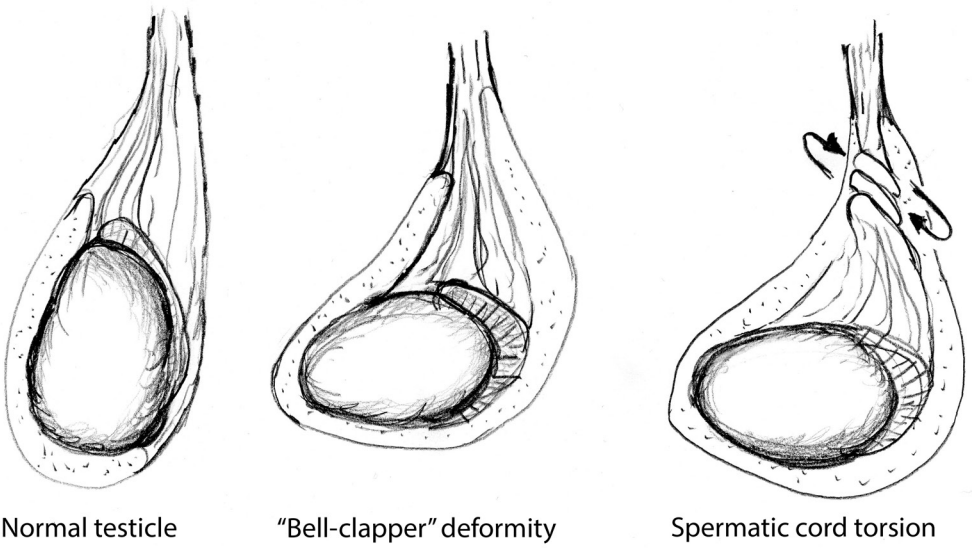


Figure 5. Anatomy of a normal testicle, "bell-clapper" deformity with lack of posterior attachment of testicle and epididymis, and on the right, illustration of spermatic cord torsion.

and Frank 2000) and this contraction may lead to twisting, in which the venous vessels become occluded first, which causes congestion of the testis. Then the artery is obstructed and the testis becomes ischaemic. This will give rise to haemorrhagic necrosis and cell apoptosis with increased neutrofils and oxidative stress (Drlik and Kocvara 2013). The loss of testicular function is directly related to the duration and degree of torsion (Dunne and O'Loughlin 2000). According to animal experiments the Sertoli cells are more vulnerable to ischaemia than the testosterone-producing Leydig cells (Krarup 1978, Baker and Turner 1995).

Since SCT may occur even during sleep (Smith 1955), the tendency to rotate may be due to an additional congenital anomaly in which the cremaster muscle is attached in an abnormal manner (Muschat 1932). Intravaginal torsion is most common in prepubertal and pubertal boys (Pillai and Besner 1998), a fact that strengthens the suggestion that maturational changes cause the structural abnormality, that predisposes certain subjects to SCT (Leape 1979).

The direction of SCT is variable, but it is typically from lateral to medial, i.e. the right testicle rotates clockwise and the left anticlockwise.

2.4.2 Extravaginal torsion

Extravaginal testicular torsion accounts about 10% of SCT cases and is typical among neonates (Pillai and Besner 1998). Here the testis and epididymis rotate together with the tunica vaginalis and the spermatic cord becomes twisted above the tunica vaginalis. Neonatal torsion is not necessarily related to any anatomical abnormality, but it may happen during descent and before the attachment of the testis in the scrotum is finished. Testicular atrophy or vanishing testis may be due to neonatal torsion (Huff et al. 1991). Neonatal torsion may occur prenatally, in which cases it is synonymous with intrauterine or antenatal SCT, perinatally i.e. during birth, or postnatally, after birth (Nandi and Murphy 2011).

2.5 Incidence

There is a bimodal distribution of testicular torsion with peaks in the neonatal and pubertal periods. Only 10% of cases occur during the first year of life and most SCTs are found in pubertal boys (Ringdahl E and Teague 2006). The incidence of testicular torsion below the age of 25 years was estimated to be 1 case per 4000 males in Bristol (Williamson 1976). Hence, one in every 160 young men or boys will develop torsion of the testis (Anderson and Williamson 1988). In the United States the nationwide incidence of SCT in men and boys under 25 years of age is 4.5 cases yearly per 100 000 males (Mansbach et al. 2005). The risk of torsion is nevertheless as high as one in 7.5 in men or boys who have a history of recurrent subacute torsion (Jones 1991). A review of acute scrotum in children under 16 years of age in Chongqing, China, has shown that 1215 patients out of 12804 admissions had acute scrotum and 103 of these had operatively confirmed SCT, including 8 neonatal torsions (Yang et al. 2011). Earlier, a fourth of the children with acute scrotum treated at an emergency department were reported to be SCT cases (Lewis et al. 1995). The incidence of neonatal torsion in Liverpool, United Kingdom, has been reported 6.1 per 100 000 newborns (John et al. 2008).

A new report published recently from Taiwan, where the incidence of testicular torsion is 2.58 per 100 000 person-years (Huang et al. 2013) has shown, that a change in diurnal temperature of 6 °C or greater entails an elevated risk of testicular torsion, the relative risk being 1.8 ($p=0.05$) (Chen et al. 2013). Furthermore, a 10-year nationwide population-based study in Taiwan, has shown that highest incidence of testicular torsion is recorded in the coldest month, January (Chiu et al. 2012). Other climate factors such as humidity, atmospheric pressure, rainfall and total hours of sunshine had no significant influence on SCT rates. In Brazil the incidence of SCT in 2010 was

1.4 per 100 000 men (Korkes et al. 2012), with a significantly higher rate of testicular torsions during the winter (p=0.002).

Familial occurrence of SCT has seldom been reported, Cubillos (2011) observed that familial torsion occurred in about 10% of cases and Shteynshlyuger (2012) achieved the same result in a meta-analysis where up to 10% of patients with SCT had an affected first-degree relative. Also, a high rate of bilateral SCTs was noted in those families. No gene has been identified as responsible for SCT in humans, but it has been found, that the INSL3 hormone and its receptor, RXLF2, induces SCT in "adolescent" mice (Sozubir et al. 2010).

2.6 Clinical features

The typical sign of SCT is severe pain with sudden onset (Kadish et al. 1998, Leape 1979). The pain originates from the scrotum area, spreading to the groin and the lower quadrant of abdomen. Nausea, vomiting and abdominal pain occur frequently, but fever is unusual (Knight and Vassy 1984). Jefferson (1997) found nausea and vomiting to have positive predictive values of 96% and 98%, respectively, in a study of 83 boys with SCT. The pain can sometimes be more gradual, however, which may delay the diagnosis (Melekos et al. 1988). There is commonly a history of antecedent episodes of similar pain and discomfort which have spontaneously resolved. These are signs of incomplete torsion and detorsion (Haynes et al. 1983). The "bell-clapper" deformity, a horizontal orientation of the testis due to the lack of any posterior attachment to the scrotum, allows the testis to twist intravaginally (Jones 1991). The affected testis is normally elevated, and scrotal erythema and oedema are commonly to be found (in 38% of cases), also reactive hydrocele several hours after the first symptoms. The testicle is usually enlarged, indurated and in all cases tender (Kadish et al. 1998). Local palpation is extremely painful, unless necrosis of the testis has already developed. The signs of necrosis are more severe inflammation of the hemiscrotum, with dark and bluish colour of skin (Schul and Keating 1993). Absence of the cremasteric reflex is highly indicative of testicular torsion (Rabinowitz 1984, Kadish et al. 1998) and it was particularly notable in one series of 38 patients with SCT that none of them demonstrated a cremasteric reflex (Caldamone et al. 1984). One typical feature of neonatal SCT is dark, painless scrotal swelling and induration, which may be due to in utero torsion (Barca at al. 1997, Cass et al. 1980). In a recent report by Srinivasan et al. (2011) the absence of any ipsilateral cremasteric reflex, nausea/vomiting and scrotal skin changes were the only consistent factors predictive of SCT to be found by multivariate logistic regression analysis.

2.7 Differential diagnosis

2.7.1 Torsion of the testicular appendages

The appendix testis (hydatid of Morgagni) was first described by Morgagni in 1761, but he believed it to be the cause of adult hydrocele. It is present in about 90% of males and varies from 1 to 10 mm in diameter (Leape 1979). The four testicular appendages are the appendix testis (a remnant of Müllerian duct), the appendix epididymis (a remnant of the Wolffian tubules), the paradidymis (the organ of Giraldès) and the vas aberrans (the organ of Haller). Torsion of a testicular appendage was first clearly recognized by Colt in Aberdeen in 1922. The age range of TAT is from 1 year to young adults, with a peak incidence between 7 and 14 years (Yang et al. 2011, Williamson 1976). It occurs a year or two before SCT, most commonly prepubertally. The appendage enlarges under the influence of human chorionic gonadotropin (HCG) and is prone to twist on its mesenteric stalk (Son and Koff 1985). In many reports it is the most common reason for acute scrotum in childhood (31–58%; Clift and Hutson 1989, Caldamone et al. 1984, Sidler et al. 1997, Yang et al. 2011). Torsion of the appendix of the testis (TAT) produces similar symptoms to those of SCT but they are milder (Macnicol 1974) and their history is accordingly longer. The appendage may be felt as a small, tense, tender bluish lump or nodule on the upper pole of the testis, the "blue dot sign" that is found positive in 14 to 22 % of cases (Knight and Vassy 1984, Melekos et al. 1988). Frequently the whole testis and hemiscrotum will be swollen (in 82.6%), reddish (in 62.1%) and tender (in 94.6%) (Yang et al. 2011), but the finding may sometimes be obscured by secondary hydrocele (Moharib and Krahn 1970). The pain may be severe for a structure of such small size and radiate to the groin or lower abdomen. Systemic symptoms such as nausea, vomiting or fever are extremely rare (Kass and Lundak 1997) and a urine culture is generally negative. Doppler sonography demonstrates normal blood flow in the testicle, but torsion of the appendage cannot always be visualized. Treatment of TAT may be operative or conservative, provided that SCT has been ruled out for certain (Caldamone et al. 1984, Kass and Lundak 1997). Conservative treatment consists of analgesia and rest whereupon the oedema and discomfort should resolve within a week (Schul and Keating 1993).

2.7.2 Epididymitis

Epididymitis is an inflammation or infection of the epididymis, often accompanied by urinary tract infection, and it is seen occasionally in prepubertal boys (Knight and

Vassy 1984). Some studies have shown, however, that ED is more common than had been suspected earlier (Andersson et al. 1989, Fernandez et al. 1997, Gislason et al. 1980, Lewis et al. 1995) and it can count up to 35% of paediatric patients with acute scrotum (Lau et al. 1997). ED is seen in infants and pubertal boys (McAndrew et al. 2002) and young child patients may also have structural abnormalities of the urinary tract (Kass and Lundak 1997, Andersson et al. 1989). Ectopic ureter, hypospadia, imperforated anus, neurogenic bladder or previous catheterization can render subjects prone to episodes of ED. When a boy with anorectal malformation has signs of acute scrotum, there may be vasal anomalies as predisposing factors (Oguzkurt et al. 1998). Most patients with epididymitis are adolescents or adults, however, who usually present with a subacute onset of scrotal swelling and pain. ED may be preceded by urinary tract symptoms like dysuria or urinary frequency and the findings upon physical examination include scrotal oedema, fever, erythema and tenderness. The pain starts gradually from the epididymis, but may spread to the whole testis and inguinal region. In time the pain will increase and hydrocele or orchitis may develop, so that the whole hemiscrotum may mimic the inflammation process of SCT. The pain can be partially relieved by elevating the testis, known as Prehn's sign, but this test is unreliable (Noske et al. 1998). The causes of ED can be bacterial, viral, traumatic or chemical and it can occasionally be associated with systematic disease or it can originate idiopathically (Hermann 1989).

Urinalysis often reveals pyuria or bacteria. A culture should be obtained if ED is suspected. Coliform bacteria are usually found in neonate and prepubertal males and Chlamydia, Ureaplasma urealyticum and Neisseria among sexually active pubertal boys or adult men (Berger 1998, Schul and Keating 1993). Lau et al. (1997) reported, however, that only 10% of their acute ED patients (age range 5 months to 12 years 10 months) had pyuria, so that their recommendation was to treat acute sterile ED in boys without antibiotics if there were no urinary abnormalities to be found. Other laboratory tests are not specific to epididymitis, as leukocytosis, for instance, is seen in 30–50% of patients with ED and SCT as well (Knight and Vassy 1984).

DUS normally shows an increased blood flow in the epididymis and testis as compared with the contralateral testis, and with sensitivity of almost 100% (Middleton et al. 1990), this scanning modality is important for ruling out SCT. Treatment for ED includes antibiotic therapy, if necessary, anti-inflammatory medications and rest. The pain and oedema should resolve within a week and the epididymal induration in a few weeks.

2.7.3 Hernias and hydroceles

A patent processus vaginalis is a common aetiology for scrotal hernias and hydroceles. If there is an omentum or bowel in the processus it is called a hernia, and when it is more narrow, containing only fluid, the result is a hydrocele. These are both common causes of acute scrotal swelling, accounting up to 12% of operations for acute scrotum in one study (Wilson-Storey 1987). Hernias are right-sided in 60% of the cases and bilateral in 10% (Campbell 1998). The risk of incarceration is highest during the first months of life, with 69% occurring by the end of the first year (Nakayama 1989). In addition to scrotal pain there may be nausea and vomiting, and also inguinal and scrotal fullness in the case of an incarcerated inguinal hernia. Fortunately, 90–95% of hernias are reducible, but if a gangrenous bowel loop is present, acute surgical intervention is mandatory (Schul and Keating 1993).

Hydroceles are seen mostly in the infant age group, and more often on the right side (Campbell 1989). Most hydroceles are painless, but some appear suddenly, causing oedema and fullness in the scrotal area and concern for parents. Translumination is useful for the diagnosis of hydrocele. Spontaneous closure and subsequent disappearance of hydrocele is expected during the first years of life, but ligation of the processus is sometimes needed.

2.7.4 Other causes of acute scrotum

Testicular or scrotal trauma can easily be ascertained from a case history. Traumatic lesions include haematoma or contusion, laceration, haematocele and delayed hydrocele. Usually there has been a direct blow to the scrotum. Traumatic testicular torsion is reported to occur in 5 to 12% of all cases of torsion, and mainly as a result of sports injuries (Burgher 1998). The testicle is typically tender and there is a firm scrotal mass, in which transillumination fails. Most scrotal traumas can be treated conservatively, but if there is a laceration of the tunica albuginea, which can be demonstrable by ultrasound, the preferred treatment option is scrotal exploration.

Idiopathic scrotal oedema is characterized by acute scrotal swelling which develops over a short time. It may be bilateral and spread beyond the scrotal sac to the penis, groin or perineum. The scrotum is typically bright pink and mildly tender, but of normal size and texture. This process accounts for up to 5% of acute scrotal presentations and mainly occurs between 5 and 10 years of age (Edelsberg and Surh 1988, Johnston 1979, Qvist 1956). Idiopathic scrotal oedema is considered to be a variant of angioneurotic oedema. The treatment is conservative, with antihistamines for swelling and itching.

Henoch-Schönlein purpura is a vasculitis process that affects the scrotum area in about 10% of cases (Clark and Kramer 1986). This purpura is found in children between the age of 3 and 7. There are typically systemic symptoms and signs such as a rash, colic abdominal pain, arthritis, proteinuria or microscopic haematuria. Rarely are the first symptoms to be found in the scrotum. As in SCT, there may be sudden scrotal pain, nausea, vomiting and redness of the skin.

Acute testicular swelling and pain may be presenting factors in many viral infections, especially mumps, although this is rarely seen these days, because of vaccination programmes. One third of patients with mumps will develop orchitis, which is unilateral in 80% of cases and one third of the orchitis patients will develop testicular atrophy (Beard et al. 1977). The testicle becomes acutely firm, tender and enlarged, and leukocytosis may be present usually followed within a week after parotitis (Herman 1989).

Adolescent boys may have varicoceles, abnormal dilatation of veins, and spermatoceles, cysts of epididymis, which may be confusing, but which can be detected with US (Hörmann et al. 2004).

Tumours, normally in the form of a non-tender unilateral testicular mass, include rhabdomyosarcomas, teratomas, yolk-sac tumours and infiltrating leukaemias (Nistal et al. 1989). Haemorrhage into a testicular neoplasm can mimic an acute scrotum. Patients with a solid mass in the scrotum should be examined thoroughly with a complete blood cell count, assessment of tumour markers and ultrasound or preferably with MRI screening (Damjanov 1989, Mohrs et al. 2012).

Other rare conditions affecting the scrotal area are serious infections such as Fournier's gangrene, which can be life-threatening even in children in 10% of cases (Riviello et al. 1997). This is an anaerobic or polymicrobial infection affecting the scrotum and surrounding perineum. Patients manifest signs of systemic toxicity early in the course of the illness, and there is subcutaneous air to be found locally, which can be examined. Boys with diabetes are more prone to Fournier's gangrene.

Other abdominal infections or acute peritonitis may be present in a case of acute scrotum. If the processus vaginalis is open, the free flow of purulent intra-abdominal fluid fills the scrotum, which is like a window onto the peritoneal cavity in these patients (Friedman and Sheynkin 1995).

2.8 Diagnosis

The diagnosis of SCT is based on a thorough history and physical examination to reveal clinical symptoms and signs and also on differential diagnostics and radiological

imaging. SCT was thought to be a more common reason for acute scrotum in earlier times, because the data were based on surgical findings (Anderson and Giacomantonio 1985, Ben-Chaim et al. 1992, Campobasso et al. 1994, Cass et al. 1980, Clift and Hutson 1989, Fenner et al. 1991, Flanigan et al. 1981, Hastie and Charlton 1990, Hemalatha and Rickwood 1981, Jones 1962, Knight and Vassy 1984, Melekos et al. 1988, Moharib and Krahn 1970), but studies of patient populations attending emergency departments have shown, that SCT is present in less than a quarter of the acute scrotum patients. Anderson, Caldamone, Fernandez and Lewis all report the propotion of SCT cases among their child patients with acute scrotum to be from 19 to 25%. ED was found in 23 to 63% of patients with acute scrotal pain, and TAT in 10% to 46%. This means that it is more essential to be able to pick out the real SCT patients for whom operative treatment is mandatory. Because the clinical features of SCT, TAT and ED overlap, the findings should be considered together with patient history. Sudden, severe pain with a duration of less than 12 hours is typical of SCT cases (Hastie and Charlton 1990), and a history of similar previous episodes more than two weeks apart with spontaneous resolution is also a sign of SCT rather than TAT or ED. Nausea, vomiting and anorexia are common symptoms of SCT, but uncommon in TAT or ED patients (Jefferson et al. 1997, Knight and Vassy 1984, Melekos et al. 1988). Sometimes SCT boys have a history of trauma or recent exercise, while the factors which lead to a diagnosis of ED are fever, a history of gradual pain over 24 hours, dysuria, a history of recent catheterization or of urinary tract infections and some form of genitourinary abnormality (Melekos et al. 1988).

The age of a patient presenting with acute scrotum is important. The incidence of SCT is bimodal, with peaks during the first year of life and in puberty, i.e. boys aged 13–15 years (Anderson and Williamson 1988, Campobasso et al. 1994, Lewis et al. 1995, Williamson 1976), while TAT is most common among prepubertal boys, peaking at 9–13 years of age (Anderson and Williamson 1998, Lewis et al. 1995). There are variable reports on the incidence of ED, but it is most commonly seen in pubertal boys or infant boys (Clift and Hutson 1989, Melekos et al. 1988).

The first physical examination is an essential factor in reaching the right diagnosis and this should in particular include an evaluation of the patient's discomfort and the noting of any local signs that are special to SCT. In addition to erythema and oedema, SCT patients present with an elevated testis of abnormal orientation, a horizontally oriented contralateral testis and absence of the cremasteric reflex (Rabinowitz 1984).

There is no specific laboratory test available for SCT patients, but urinalysis can be helpful in distinguishing ED from SCT. Pyuria is found in 10–50% of boys with ED (Knight and Vassy 1984), but a serum white blood cell count (or CRP) is not useful, since leukocytosis is seen in 30–50% of patients with SCT as well (Melekos et al. 1988).

In conclusion, patients with acute scrotum who arouse a strong suspicion of SCT require urgent surgery (Kass et al. 1993), and those patients with possible SCT should have a DUS evaluation without delay and will need to be operated on as well if decreased or absent blood flow is found or the result is nondiagnostic. If normal or increased blood flow is seen in DUS, conservative treatment for acute scrotum is suitable.

2.9 Radiological imaging

2.9.1 Introduction to imaging methods

Prompt evaluation of every case of acute scrotum is essential in order not to delay the operative treatment of SCT. Children with a swollen, painful scrotum must be evaluated very carefully and with much patience. If the diagnosis is clinically uncertain, as is usually the case, an accurate and immediate imaging method is needed. Earlier this was provided by scintigraphy, but the disanvantages of ionizing radiation, limited availability and poor anatomical imaging of small testicles has left this method chiefly to history (Frush and Sheldon 1998). From the 1980's onwards sonography or ultrasound (US) has gained in popularity because of the superior anatomical detail provided (Babcock 1995). Nowadays, DUS is the gold standard imaging technique for children with acute scrotum (Hörmann et al. 2004). With optimal technical probes and US frequencies combined with experienced and talent radiologist the accuracy of US may reach to 100% (Karmazyn et al. 2005). The availability of US during the night hours can be limited.

In the future the role of magnetic resonance imaging (MRI) in acute scrotal disorders will be clarified (Mohrs et al. 2012), but the potential of MRI is supreme. The availability of MRI is increasing and the use of MRI is becoming more favoured in multiple fields of medicine.

There are also new interesting diagnostic tools like near-infrared spectroscopy (NIRS) with minimal clinical experience so far (Burgu et al. 2013).

2.9.2 Radionuclide imaging

Radionuclide imaging, or scintigraphy, became into use to evaluate acute scrotal symptoms in the 1970's (Riley et al. 1976). Technetium-99m pertechnetate is administered intravenously according to the weight of the patient and both dynamic perfusion and static delayed images are taken. In the normal scintigraphic view the activity is symmetrical in both perfusion and static images, in being well above that

of the surrounding structures in both testicles, but in patients with acute SCT there is decreased perfusion in the dynamic images and photopenia in the static images. In the subacute phase, 6–15 hours from the onset of pain, there is peritesticular reactive hyperaemia. Images show a halo around the photopenic testis. Later, the halo becomes smaller, but the testicle remains non-vital. On the other hand, a similar image can be seen in the case of a hypovascular testicular tumour, a large hydrocele or chronic torsion. Radionuclide imaging can be difficult where paediatric testicles are concerned, however, because of their small size. The disadvantages of this modality include exposure to ionizing radiation, limited availability, poor anatomical detail and the need for an intravenous line and sedatives (Frush and Sheldon 1998). Radionuclide imaging is not used any more for examining acute scrotum in Finland.

2.9.3 Sonography

Sonography, or ultrasound, is the most frequently used imaging modality for evaluating scrotal disorders in children. Its benefits are excellent anatomical and blood flow information and its accessibility and non-invasiveness (Pearl and Hill 2007). Ultrasonography can be performed rapidly without sedatives or intravenous accesses and the scrotum is particularly suitable for sonography, since it is external and there is a contralateral testicle for comparison. Boys and adolescents can be examined in the same manner as adults (McAlister and Sisler 1990). The room and coupling gel has to be warm and the sonography should be performed with a linear, high-frequency (7.0–15MHz) transducer. There are various software applications available, such as harmonic imaging, second harmonic imaging and SonoCT (Hörmann et al. 2004), and the protocol includes small-parts imaging with Doppler settings for detecting low-velocity flow. With power Doppler imaging and stick probe, even the smallest vessels of the testis can be depicted. Transverse, longitudinal and additional views can be obtained if needed. It should be remembered, however, that the homogeneous echotexture of the testicle is more hypoechoic in infants and small children than in older patients (McAlister and Sisler1990).

SCT is characterized by an absence of flow as compared with the normal flow in the contralateral testicle. The early US findings are slightly echogenic hydrocele and slight scrotal wall thickening, but after a few hours, the testicle and epididymis are enlarged and hypoechoic and the spermatic cord is thickened. As the hours pass the echostructure of the testicle changes and becomes heterogeneous due to oedema, haemorrhage, ischaemia and necrosis. A normal echotexture with an absence of intratesticular Doppler flow is predictive of salvage possibilities following SCT (Middleton et al. 1997),

but a heterogeneous parenchymal echotexture indicates non-viability of the testicular tissue in all age groups (Chmelnik et al. 2010). Examination of the spermatic cord is very useful, since it can visualize the spiral aspect of twisted funicular structures. In a multicentre study involving 711 patients at 11 European university hospitals the twist could be detected in 199/208 SCTs and a normal linear cord was observed in all the other acute scrotums (Kalfa et al. 2007). Its sensitivity of 96% and specificity of 99% as recorded at large centres has made high-frequency US the most reliable imaging tool. The intratesticular vessels can be more difficult to identify in small prepubertal testicles, however, making the diagnosis of SCT more demanding (Patriquin et al. 1993, Jequier et al. 1993), but accuracy has been enhanced by using a Doppler ultrasound with high-frequency stick probe. The pitfalls encountered with DUS are connected with partial torsions and spontaneous detorsion. For instance, rotation below 360 degrees with venous obstruction can only be detected by spectral analysis, which shows an increase in the resistive index with the inversion of diastolic flow (Pavlica and Barozzi 2001). Intermittent torsion or detorsion, as manifested clinically in a sudden relief of pain, can be detected by DUS, but instead of hypoperfusion seen in normal SCT, detorsion may present with unilateral hyperemia and hyperperfusion. The overall sensitivity of DUS when used for children is variable, in the range 63–100%, but its specificity is high, 97–100% (Karmazyn et al. 2005).

2.9.4 Magnetic resonance imaging

Excellent anatomic details of scrotum can be achieved with MRI by using surface coils (Mattrey 1991, Schnall 1993). The scrotal evaluation is then performed with axial and coronal T1-weighted and T2-weighted sequences. The scrotum has to be kept warm to avoid cremaster-related motion. Normal testicles are homogeneous in signal intensity, appearing with medium signal intensity, just above that of muscle, on T1-weighted images and with high signal intensity, higher than that of fat, on T2-weighted images. MRI has so far mostly been used to evaluate scrotal mass and in children with suspected cryptorchidism (Schnall 1993), but its accuracy in distinguishing ED from SCT during the subacute phase has been reported to be 100% when searching for a torsion knot and whirlpool pattern and assessing the vascularity of the spermatic cord (Trambert et al. 1990). Dynamic contrast enhanced (CE)-MRI is a new promising modality for diagnosing SCT. This is a perfusion method in which the first pass of the contrast agent bolus through the vasculature of the testicle is detected and the increase analysed on the healthy side for comparison with the affected testicle. Dynamic CE-MRI had a 93% sensitivity and 100 % specificity in a pilot study performed by Terai et al. (2006).

Furthermore, Watanabe et al. (2007) examining 14 patients with SCT, reported sensitivities of 100% for dynamic CE-MRI and 75% for T2-weighted imaging. The disadvantages of MRI are the long imaging time, limited availability, expense and the need for sedatives in the case of young children.

The diagnostic use of MRI is increasing in scrotal lesions (Mohrs et al. 2012). MRI is the most accurate imaging tool for testicular tumours or tumourlike lesions such as congenital, traumatic and inflammatory disorders. The use of MRI in every day practice for characterizing acute scrotal disorders may be in near future (Watanabe et al. 2007), but further larger studies are needed. Precise detection of small testicles requires special coils in order to achieve imaging with good quality. The feasibility of diffusion-weighted (DW) MRI has been tested for clinical use in the detection of SCT (Maki et al. 2011). There are also studies with continuous arterial spin-labeling (ASL) perfusion MRI in use of human testicles (Pretorius and Roberts 2004).

2.9.5 New techniques

Near-infrared spectroscopy is a modality that uses infrared light for continuous, non-invasive monitoring of deep tissue oxygen saturation rather than tissue perfusion. It has been used earlier for monitoring cerebral oxygenation in patients with congenital heart disease (Hirsch et al. 2009) and is ideal for flow conditions, and thus also suitable for detecting SCTs. It has been tested with animal models of SCT for the prompt identification of significantly lower saturation in the affected testicle (Hallacoglu et al. 2009, Aydogdu et al. 2012), but only preliminary pilot studies have been carried out with adults and further with children (DaJusta et al. 2012). Burgu et al. (2013) published a pilot study with 16 adult males presenting with acute scrotum and concluded that NIRS could identify all operatively confirmed SCTs when the testicular oxygen saturation was more than 11.5 units lower on the affected side compared to the contralateral testicle. More studies are needed, but NIRS seems to be a rapid, non-invasive, easy and safe method for the differential diagnosis of SCT and other causes for acute scrotum.

2.10 Treatment

2.10.1 Operative treatment

The treatment of SCT is urgent and, according to the EAU (European Association of Urology) and ESPU (European Society for Paediatric Urology) guidelines, implies surgery within the first 24 hours of the onset of symptoms (Tekgyl 2011). After 24

hours the surgical treatment becomes semi-urgent. Similarly, boys with acute scrotum whose diagnosis is equivocal, i.e. it cannot be ascertained with examination and radiological imaging, still have to be operated on urgently. Testicular salvage depends on early reversal of the vascular obstruction. The scrotum is explored through a midline incision into the raphe, the tunica vaginalis is opened and the testis is exposed and untwisted in a medial to lateral direction in most cases and its viability is assessed. If the testis remains dark it should be wrapped for at least 5 minutes in warm towels soaked in saline (Kass and Lundak 1997). If no subsequent recovery in the colour of the testis is seen, the visceral layer of the tunica vaginalis should be incised and if no bright bleeding can be detected, the testis has to be removed. If detorsion is performed in time, the testicle is anchored to the dartos fascia with two or three non-absorbable sutures, preferably with partial resection of the tunica vaginalis (Bellinger et al. 1989). The contralateral testicle has to be exposed as well and fixation performed in a similar manner to prevent future torsion (Kass and Lundak 1997). Since testicular ischaemia may damage the blood-testis barrier, leading to autoimmunization against the patient's own spermatogonia (Puri et al. 1985), it is not advisable to leave testicles of doubtful viability in the scrotum. This applies to boys over 10 years of age (Mininberg et al. 1993, Urry et al. 1994). It has recently been demonstrated that human sperm quality is preserved following either orchiectomy or orchidopexy, although orchiectomy resulted in better sperm morphology (Arap et al. 2007). Pubertal boys who present with intermittent recurrent testicular pain need orchidopexy in order to avoid SCT with necrosis of the testis. Almost one third of adolescents with SCT have a history of previous intermittent pain (Hutson 2006).

After orchiectomy of a necrotic testicle, a silicon prosthesis can be inserted. A novel surgical approach for placement of the prothesis simultaneously with performing of the orchiectomy has been described by Bush and Bagrodia (2012).

2.10.2 Manual detorsion

If there is a delay in carrying out surgery, a manual attempt at detorsion can be useful (Knight and Vassy 1984). The affected testicle should be rotated outward, from medial to lateral, and if detorsion is achieved, the pain relief should be immediate. Surgical exploration and orchidopexia are still needed (Lewis et al. 1995, Jefferson et al. 1997). There is also one report of 162 patients with SCT, in which the twist was found from medial to lateral in 33% of cases (Sessions et al. 2003).

2.10.3 Treatment of ischaemic reperfusion injury

Prophylactic external cooling before surgery has been recommended for reducing ischaemia-reperfusion injuries (Haj et al. 2007), and other possibilities for alleviating the impact of oxidative stress have also been studied. A hypothesis has been proposed to the effect that testicular compartment syndrome may arise secondarily to detorsion (Kutikov et al. 2008). Since it would be important to lower the pressure in the oedematous testicular tissue enclosed in the firm tunica albuginea, Kutikov made an incision into the tunica albuguinea and inserted a tunica vaginalis patch. Moritoki et al. (2012) showed with a rat model that smaller reductions in intratesticular pressure following SCT and detorsion resulted in disturbances of spermatogenesis.

Several animal experiments have been performed with drugs that reduce the rate of ischaemic reperfusion injury. Rosuvastatin, used for the treatment of hyperlipidaemia, has an anti-inflammatory effect and has been shown to reduce reperfusion injury in brain, intestine and heart tissue, and this was also found to preserve or salvage tissue perfusion after SCT and detorsion (Karakaya et al. 2009). Other compounds with protective effects in animal experiments are darbepoetin alpha, erythropoietin, trimetadizine, ibuprofen and melatonin (Akcora et al. 2007, Yazihan et al. 2007, Unal et al. 2007, Dokmeci et al. 2007, Kanter 2010).

2.11 Prognosis

The duration of ischaemia has the greatest impact on the survival of a testicle following torsion. There are many reports from different clinics with results that differ somewhat, but the trend is clear: if a child patient is operated on within six hours of the onset of symptoms, the success rate is close to 100%, between 6 and 12 hours the rate is 70% and between 12 to 24 hours it falls to 20%. After 24 hours testicular damage is usually irreversible and the necrotic testicle has to be removed so as not to induce immunological processes (Pavlica and Barozzi 2001, Lewis et al. 1995, Jefferson et al. 1997, Sidler et al. 1997). In the United States SCT is reported to have ended in orchiectomy in 34% of cases (Mansbach et al. 2005). In line with the above, Skoglund et al. (1970) described a series of 70 SCT patients with an average age of 9.6 years in which those who were operated on within 5 hours of the onset of symptoms had an 83% salvage rate whereas those operated on within 10 hours had a salvage rate of 70% and thereafter the rate was 20%. Salvage rates for undescended testicles have been reported to be 29–40% (Anderson and Williamson 1988). In a series of 150 boys with acute scrotum described by Caldamone et al. (1984) 38 had SCT and 79% of a subset of these SCT patients (15/19) underwent surgery and orchiopexy on the strength of a clinical diagnosis after

a mean duration of symptoms of 3.8 hours while 47% of the remainder (9/19) were salvaged surgically after diagnosis by means of US, the mean duration of symptoms being 11.3 hours. In a follow-up after a month 13% of the first group (2/15) and 55% of the second group (5/9) had an atrophic testicle.

There are fewer papers dealing with late follow-ups, but Tryfonas et al. (1994) do report on a series of 75 patients with SCT in which most of the testicles were saved, although 11 orchiectomies had to be performed on patients whose symptoms had lasted more than 24 hours. Here 18 late follow-ups were available (after intervals of 1–9 years) and postoperative atrophy greater than 50% was observed in 60% of these cases while in 33% (6 cases) the testicle was totally absent.

Rybkiewicz (2001), examining 37 boys with SCT and 42 healthy controls, found antisperm antibodies in more than half of those with a history of SCT, but in only 17% of the controls. Disturbances in the secretion of LH and/or FSH were observed in 2/3 of the boys or men with SCT and abnormal testosterone in 1/3. These hormonal disorders did not have any influence on virilisation, libido or sexual potency. The theory that attributes antisperm antibodies to a break in the blood-testis barrier is controversial and Anderson (1992), for example, did not find these antibodies after SCT. However, the impairment of the semen after SCT and orchiectomy was remarkable.

Testicular function is often compromised as a consequence of SCT. Based on inhibin B and FSH values measured one month and one year postoperatively, Taskinen et al. (2008) concluded that preserving surgery might be attempted in borderline cases. The true effect on fertility is unknown. Arap et al. (2007) did not find any significant difference in hormonal levels between SCT patients at a late follow up (after 6–10 years) and healthy controls. The sperm quality in terms of motility and morphology was better in patients who were treated with orchiectomy compared with the detorsion group. Antisperm antibody levels were abnormal with a trend for higher levels in the patients who had had SCT, regardless of the testicular fate, but those did not differ statistically significantly from antisperm antibody levels of the normal controls.

3 AIMS OF THE STUDY

1. To compare distribution, symptoms and signs of spermatic cord torsion with those of other conditions causing acute scrotum
2. To investigate the duration of the symptoms of SCT and its influence on testicle salvage
3. To describe the distinctive features of neonatal testicular torsion
4. To clarify the indications for operative and non- operative treatment of acute scrotum
5. To investigate the feasibility of dynamic CE-MRI for the detection of testicular torsion-induced hypoperfusion in an experimental rat model
6. To evaluate the use of dynamic CE-MRI among patients with acute scrotum

4 MATERIALS AND METHODS

4.1 Study I and II

4.1.1 Study patients

Patients who had been treated for acute scrotum at the Hospital for Children and Adolescents in Helsinki between 1977 and 1995 formed the cohort considered in the first two studies. The project was approved by local ethics board. All the patients who had been examined by a paediatric surgeon and operated on were included. The data were collected retrospectively from the patients' records. The data for all the patients less than17 years of age (n=388) were analysed for study I, while study II focused on patients with acute scrotum during the first year of life (n=91). During the period covered by this research all patients with acute scrotum arriving at the hospital were operated on, in order to ensure that the cases of SCT were definitely treated. Clinical signs and symptoms together with the operative findings were collected from the surgical history and medical charts for each patient.

4.1.2 Collected data

Study I presents the age distributions and peak incidences for SCT, ED and TAT. The symptoms and signs of acute scrotum, including pain, tenderness, oedema of the testis, darkness and hardness of the testis and oedema and erythema of the scrotum, were tabulated and abdominal pain, nausea and vomiting, fever and any evidence of the blue dot sign were checked and similarly tabulated. The durations of the symptoms of SCT, ED and TAT in the patients were investigated and similarly tabulated.

For study II the diagnoses of all patients less than one year of age were reviewed together with the durations of signs of SCT, ED and scrotal hernia and physical findings such as a dark, hard testis, swelling, erythema, tenderness and fever were noted. SCT was considered prenatal, if the signs were observed at birth and postnatal, if the scrotum had been normal at birth. Bacterial cultures from urine, tissue fluid or biopsy were recorded for the ED group as also were the results of additional examinations

performed on these patients afterwards including intravenous pyelography, voiding cystography, ultrasonography and cystoscopy. The findings were reviewed and any underlying anatomical anomalies listed.

4.1.3 Surgical methods

The patients had immediately been scheduled for urgent surgery without any attempt at manual detorsion. The operation started with a midline incision into the raphe of the scrotum, and if SCT was found, detorsion was performed. The affected and contralateral testicles were fixed to the dartos fascia with non-absorbable sutures. If detorsion was not followed by instant recovery of the ischaemic testicle, warm towels soaked in saline were wrapped around the testis for five minutes. If there was no further recovery, then tunica albuguinea was incised and in the absence of bright bleeding the testicle was removed. All removed testicles were sent for microscopic examination.

4.2 Study III

4.2.1 Animal model and operation

The protocol for the rat model was approved by Tampere University Animal Care Committee. Adult Sprague-Dawley rats were anaesthetized with fentanyl citrate (0.25mg/500g) and midazolam (0.25mg/500g) and following a midline incision, the testicles were exposed and the gubernaculum divided. The membrane between the testicle and epididymis was divided up to the testicular hilum (Becker and Turner 1995) and SCT was induced by twisting the right testicle either 360 or 720 degrees and fixing it to the dartos fascia with 4-0 polyglactin sutures and the left testicle being fixed without twisting. A continuous 3-0 nylon suture was used to close the incision.

4.2.2 MRI imaging

One hour after the operation the dynamic CE-MRI with gadopentetate dimeglumine and DW-MRI was performed with the rat still under anaesthesia. After transportation to the MRI facility in Tampere University Hospital, the rats were cannulated with a 30 G butterfly needle in the tail vein to administration of the contrast medium for dynamic imaging. After MRI the animals were sacrificed by CO_2 asphyxiation and the laparotomy incision was opened up to verify that the torsion had remained constant during the procedure.

The rats underwent MRI with a conventional 1.5 T scanner and a 3-inch circular surface coil (GE Medical Systems Signa Horizon Echospeed, Milwaukee, WI, USA). The rat was placed prone and headfirst, with its testicles centred on the circular coil. After a coronal T1-weighted spin-echo localizer, an axial T2-weighted fast spin echo series was obtained. The precise parameters of the imaging study are listed in the following Table 1A.

DW-MRI was performed with a single-shot spin echo planar imaging (EPI) sequence. The sequence was sensitized to diffusion by activating the gradients on each of the three principal axes with sensitizing factor b values of 0 and 1000s/mm^2. The other imaging parameters of the DWI sequence are also listed on Table 1A.

A fast spoiled gradient-recalled echo (FSPGR) sequence was used to measure the contrast enhancement of the testicles of the animal. The sequence was started 15 s before manual injection of the contrast media bolus (0.4 ml, 469mg/ml, Magnevist, Schering AG, Germany). A single oblique coronal slice was positioned to cover the central part of both testicles. The parameters of the FSPGR sequence are presented on Table 1A. The time resolution of the dynamic sequence was 1.88s and the data collection time 450 s. For further analysis the DW-MRI and dynamic CE-MRI images were transmitted to a separate workstation (Advantage Windows 4.0, GE Medical Systems, Paris, France).

Table 1A. Parameters of the T2-weighted MR images, DW-MRI and FSPGR.

	T2-weighted axial	DW-MRI axial	FSPGR axial
Time of repetition(TR)	4500 ms	10000 ms	9.6 ms
Time of echo (TE)	90 ms	100 ms	2.1 ms
N of excitations(NEX)	1		
Matrix size	256	128x96	256x192
Field of view	21 cm	22 cm	18 cm
Slice thickness	3 mm	3 mm	5 mm
Intersection gap	0.3 mm		

4.2.3 Data collection and analysis

For DW-MRI apparent diffusion coefficient (ADC) maps were generated with the Functool software (GE Medical Systems, Paris, France). The average of the ADC values was computed from three to five slices by region of interest (ROI) analysis of the central part of the testicle. The central slices were used to minimize the effect of distorsions generated by the single-shot EPI in the edge slices. Dynamic CE curves were generated by positioning the ROI on the testicle and computing the average signal intensity as a

function of time. An initial slope for the CE curve was defined manually. The measured signal intensities were normalized to pre-contrast baseline values at time point zero. The two-way Student's t-test was used for statistical comparison of the values for the right and left testicles.

4.3 Study IV

4.3.1 Patients

Patients for the prospective MRI study were collected from the emergency department of Tampere University Hospital during the years 2001–2005. The protocol was approved by the local ethics board. Young men and boys over 7 years of age who presented with acute scrotum during working hours were asked to join the study. Patients had to be mature enough to cope with MRI without anaesthesia. Altogether 17 patients signed an agreement to participate or in case of younger children the document was signed by a parent.

4.3.2 MRI examinations

In addition to the normal examination protocol of a medical history, physical examination and ultrasound examination, the patients were examined by MRI. An urgent MRI was scheduled so as not to delay the possible operation. If immediate MRI was not available for a patient with acute scrotal problem, he had to be excluded from the study. Neither medication nor anaesthesia was needed. Gadolinium (20ml, 469 mg/ml, Magnevist, Schering AG, Germany) was injected prior to the examination. The visit to the MRI facility lasted 15–30 minutes and the DW and dynamic CE-MRI took an average of five minutes each. Patients with a high suspicion of SCT (nine boys) were then operated on the decision being based on clinical findings and DUS. The MRI results were collected later and compared with the clinical and surgical findings.

The MRI protocol was as described in section 4.2.2. The T2-weighted fast spin echo (FSE) parameters were time of repetition (TR) 4000ms, time of echo (TE) 113ms, echo train length 16, number of excitations (NEX) 4, matrix size 256, field of view 30cm, slice thickness 4 mm and intersection gap 1mm. The DW-MRI parameters were TR 10000 ms, TE 95ms, field of view 30cm, slice thickness 5mm and matrix size was 128x128. The T1-weighted FSPGR parameters were TR 9.6ms, TE 2.1ms, field of view 28cm, matrix size 256x192 and slice thickness 5mm. The time resolution of the

dynamic sequence was 2s and the data collection time 280s. The parameters of T2-weighted, DW- and T1-weighted MRI are listed in Table 1B.

Table 1B. Parameters of the clinical MRI-study with 17 patients. T2-weighted FSE (fast spin echo), DW-MRI and T1-weighted FSPGR.

	T2-weighted FSE	DW-MRI	T1-w FSPGR
Time of repetition(TR)	4000 ms	10000 ms	9.6 ms
Time of echo (TE)	113 ms	95 ms	2.1 ms
Echo train length	16	-	-
N of excitations(NEX)	4	1	1
Matrix size	256	128x128	256x192
Field of view	30 cm	30 cm	28 cm
Slice thickness	4 mm	5 mm	5 mm
Intersection gap	1 mm	0 mm	-

4.3.3 Data analysis

The averages of the ADC values for two to five slices were computed by ROI analysis of the mid-part of the testicle. The dynamic CE curves were obtained by measuring the average signal intensity of the ROI as a function of time. After the MRI examination the patients were either operated on or treated conservatively, according to the clinical and DUS findings. Finally, the MRI findings were compared with the surgical, DUS and clinical diagnoses.

5 RESULTS

5.1 Distribution of patients with acute scrotum

The analysis of 388 patients operated on acute scrotum, as presented in study I, revealed that 100 of them (26%) had SCT. The most usual cause of acute scrotum was TAT (45%) and the next most common findings after SCT were ED (10%), hernia (8%) and hydrocele (6%). Other reasons for acute scrotum (5%) were trauma and haematoma in 7 patients, Henoch-Schönlein vasculitis in three, idiopathic scrotal oedema in two and orchitis in two. One of the boys with orchitis had mumps and the other one epididymo-orchitis of unknown origin. Gangrena epididymis, liponecrosis of the tunica vaginalis, infection of a testicular prosthesis and an undescended testis, a detorsioned testis and testis saltans were each found once (Figure 6).

The distribution of main diagnoses in the infant patients, i.e. less than one year of age, in study II (n=91) was SCT 39%, ED 23%, hernia 24% and hydrocele 10%. Only one TAT was found in this age group (Figure 7).

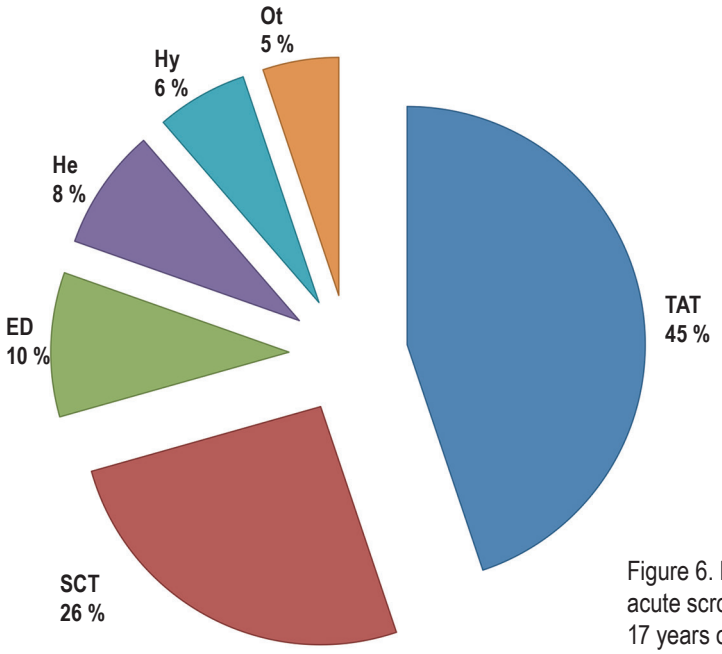


Figure 6. Distribution of reasons for acute scrotum in all patients less than 17 years of age.

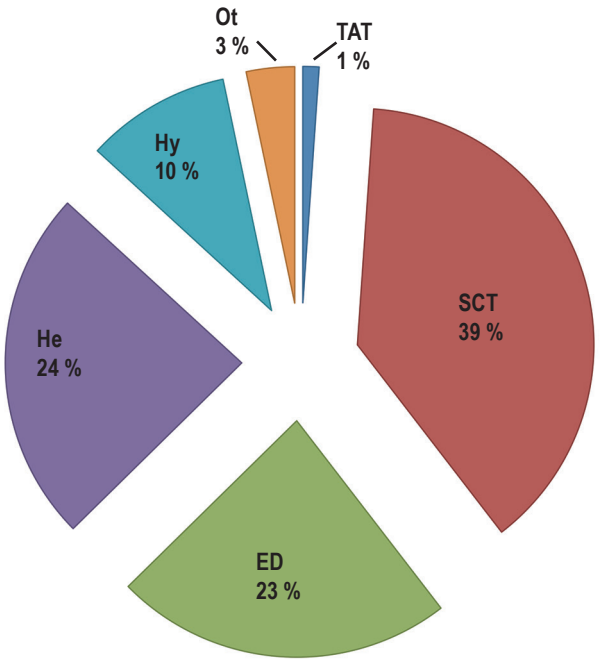


Figure 7. Infant acute scrotum. Distribution of diagnoses behind acute scrotum during the first year of life.

SCT showed two peaks of incidences in study I. SCT was the most common reason for acute scrotum during the first year of life, and the other peak was between the ages of 13 and 16 years. TAT was encountered more frequently in prepubertal or early pubertal patients between the ages of nine and 14 years, but was present in all the age groups after one year of age (Figure 8).

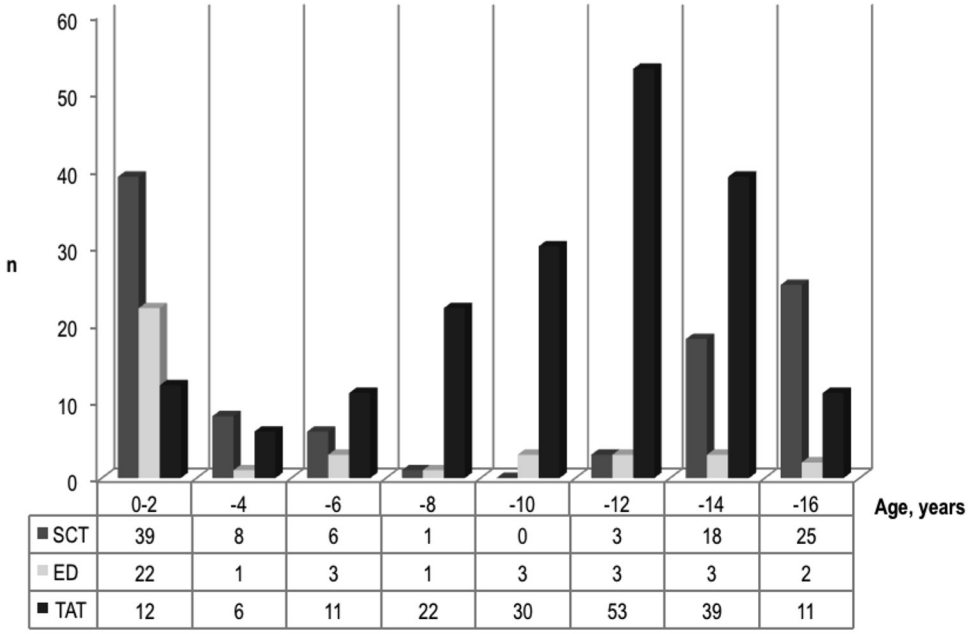
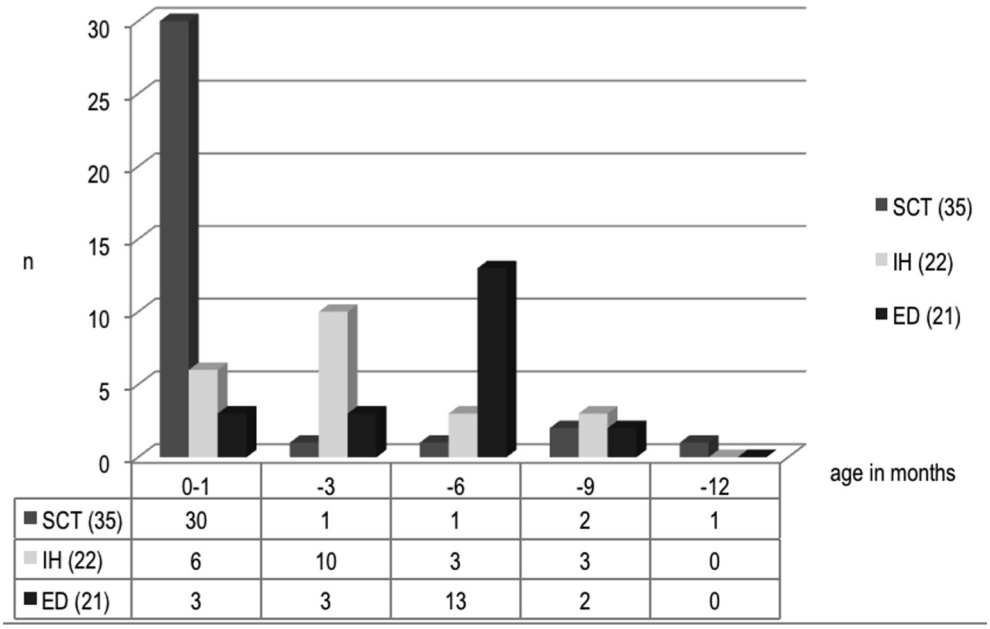


Figure 8. Age distribution (in years) of the three major causes of acute scrotum.

Both ED and SCT occured most frequently in the infant group, more than half of the ED boys being younger than one year of age. ED seemed to be a common diagnosis among three to six month old babies in study II, whereas SCT was found in neonates (Figure 9).



	0-1	-3	-6	-9	-12
SCT (35)	30	1	1	2	1
IH (22)	6	10	3	3	0
ED (21)	3	3	13	2	0

Figure 9. The first year of life. Age distribution of infants with spermatic cord torsion (SCT), inguinal hernia (IH) and epididymitis (ED) in months.

5.2 Symptoms and findings of acute scrotum

The frequencies of symptoms and signs of the three most common causes of acute scrotum, SCT, TAT and ED are presented in Table 2. The acute symptoms of the patients in study I, other than infants, were pain in SCT (88%), TAT (94%) and ED (76%). Swelling of the hemiscrotum was found in 44% of the SCT, in 39% of the TAT cases and in 50% of the ED cases and pain and oedema of the hemiscrotum were the most frequent findings in the subjects with SCT. Pain was absent in 12% of the boys over one year of age. A hard, dark testicle was found only in the SCT group, typically among neonates.

Table 2. Symptoms and signs in acute scrotum caused by spermatic cord torsion (SCT), torsion of testicular appendage (TAT) and epididymitis (ED).

Symptoms and signs	SCT (100) n (%)	TAT (174) n (%)	ED (38) n (%)
Pain, tenderness (all)	68 (68%)	163 (94%)	22 (58%)
Pain (excluding infants)	(88%)	(94%)	(76%)
Oedema of testicle	44 (44%)	68 (39%)	19 (50%)
Dark testicle	21 (21%)	0 (0%)	0 (0%)
Hard testicle	19 (19%)	6 (3%)	3 (8%)
Scrotal oedema	19 (19%)	30 (17%)	5 (13%)
Scrotal erythema	16 (16%)	55 (32%)	14 (37%)
Abdominal pain	7 (7%)	12 (7%)	3 (8%)
Nausea or vomiting	5 (5%)	3 (2%)	1 (3%)
Temperature > 37.5˚C	2 (2%)	5 (3%)	6 (16%)
Blue dot sign	0 (0%)	17 (10%)	0 (0%)

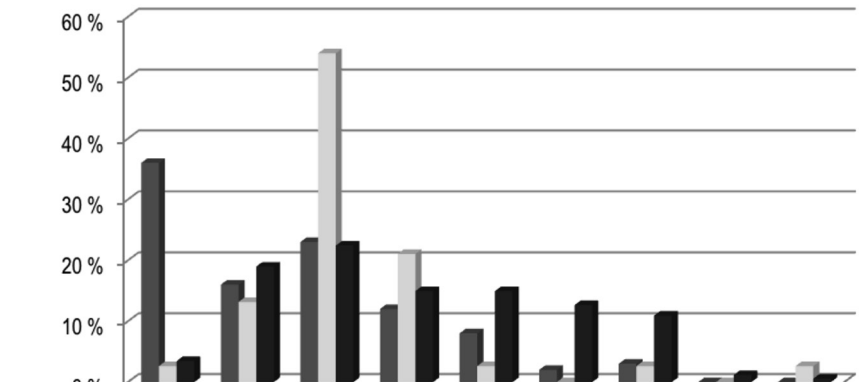
Erythema was frequently found in patients with ED (37%) and TAT (32%), but infrequently in boys suffering from SCT (16%). Abdominal pain was reported by 7 to 8% of the children with SCT, TAT or ED while nausea and vomiting were slightly more common symptoms in the SCT group. A "blue dot sign", which is specific to TAT, was visible in only 17 cases (10% of that group).

A temperature ≥ 37.5˚C was recorded in 2–3% of the torsion patients, but fever was present in 16% of the ED patients. The urine culture was positive in ten patients with ED in the infant group (26%). E.coli, Klebsiella oxytoga, Enterococcus and Streptococcus faecalis were obtained from bacterial cultures. Further examinations of the whole ED group revealed vesicoureteral reflux in two cases, a dysplastic multicystic kidney and a rectourethral fistula.

5.3 Duration of the symptoms

SCT is considered an emergency in paediatric urology (Tekgül 2011) as the duration of ischaemia detracts most from the survival of the twisted testicle. The testicle was salvaged in all the present patients with SCT who were operated on within six hours of the onset of symptoms (36/36), whereas those with a duration of symptoms from six to 12 hours had a 50% salvage rate (8/16) and operations performed more than 12 hours after the onset of the symptoms led to recovery of the testicle in only 4% of cases, those that failed to recover being removed by orchiectomy.

Of the emergency cases that arrived at the ER within six hours of onset, 73% were actually SCTs and altogether 36% of all the SCTs and 3% each of the ED and TAT patients were examined and treated within six hours. Correspondingly, 55% of the patients with ED, 22% of those with TAT and 23% of those with SCT seem to have reached the hospital within 12–24 hours of the onset of symptoms. Most of the boys with TAT (56%) reached the hospital after at least 24 hours of pain and other symptoms (Figure 10).



	0-6 h	-12 h	-24 h	-2 d	-3 d	- 4 d	-7 d	-14 d	more
SCT (100)	36 %	16 %	23 %	12 %	8 %	2 %	3 %	0 %	0 %
ED (38)	3 %	13 %	54 %	21 %	3 %	0 %	3 %	0 %	3 %
TAT (174)	3 %	19 %	22 %	15 %	15 %	13 %	11 %	1 %	1 %

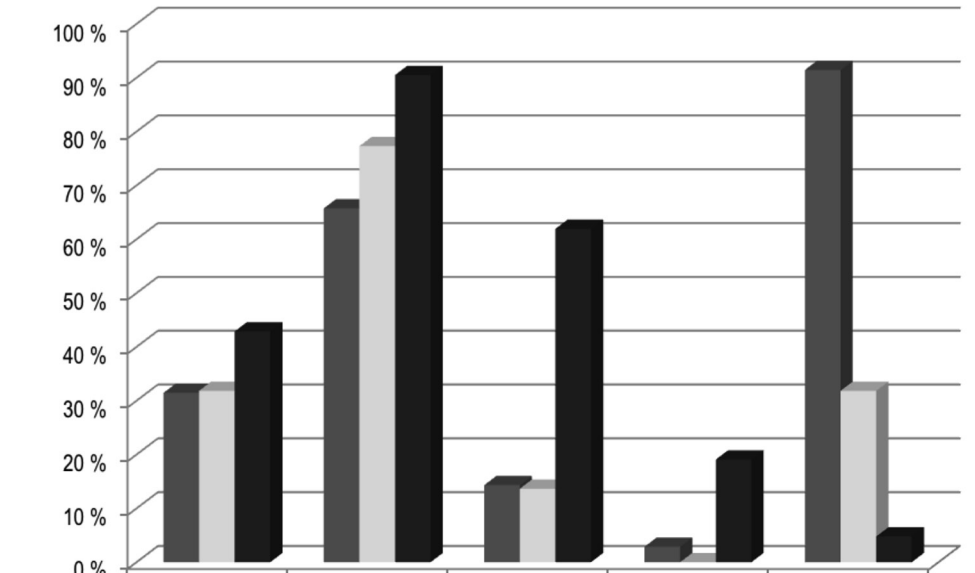
hours and days

Figure 10. The whole cohort. Duration of symptoms in spermatic cord torsion (SCT), epididymitis (ED) and torsion of testicular appendages (TAT) first day in hours and there after in days.

5.4 Infant and neonatal spermatic cord torsion

In infants, SCT was found in 35 out of 91 patients (39%), incarcerated inguinal hernia in 22, ED in 21 and hydrocele in 9. Infrequent diagnoses were scrotal haematoma in two patients, orchitis in one and TAT in one. 30/35 SCTs occurred in the neonatal period, including 15 prenatal or perinatal testicular torsions. Twenty-one SCTs were on the right side and 14 on the left, with no bilateral cases. Of all the neonatal patients with acute scrotum, 77% were suffering from SCT. The incidence of strangulated inguinal hernia was highest from 1 to 3 months of age, and epididymitis was most common diagnosis from 3 to 6 months (13/17, 76%). The incidence of acute scrotum subsided after 6 months, so that only 10 % of the patients were aged from 6 months to one year of age. The incidences of SCT, ED and incarcerated inguinal hernia during the first year of life are depicted in Figure 9.

The signs and symptoms of SCT, ED and incarcerated inguinal hernia are shown in Figure 11. One specific sign of SCT was a dark, bluish, hard testicle (32/35, 91%), but this was also found in patients with strangulated hernias and necrosis of the testicle



	Tenderness	Swelling	Erythema	Fever	Dark and hard testis
SCT (35)	31 %	66 %	14 %	3 %	91 %
IH (22)	32 %	77 %	14 %	0 %	32 %
ED (21)	43 %	90 %	62 %	19 %	5 %

Figure 11. Physical findings in infants with spermatic cord torsion, inguinal hernia and epididymitis.

(7/22, 32%). Erythema and tenderness of the scrotum were found occasionally in SCT infants, while erythema and swelling of the scrotum were the most usual signs of ED.

The infant SCT patients were operated on most urgently, the median time elapsing from recognizing the signs to operation being 12 hours, while in the ED and hernia groups it was 24 hours. Only nine out of the 35 SCT patients (26%) were operated on within six hours of the first symptoms. Four SCT testicles (11.4%) were salvaged, two of which were found immediately after birth. The remaining 31 were removed and histopathological examination verified haemorrhagic infarction or necrosis.

5.5 MRI examination of experimental spermatic cord torsion

A SCT of 360˚caused a clear, consistent decrease in blood flow after one hour of torsion and 720˚ an even more marked perfusion deficit. The ROI values for the apparent diffusion coefficient (ADC) images in the ischaemic and contralateral testes were detected as functions of time and the slope of the enhancement curve was calculated. The maximal slope of contrast enhancement was 0.072%/s in the ischaemic testes versus 0.47%/s in the control testes in the 360˚ group and 0.046%/s versus 0.37%/s, respectively, in the 720˚ group. The dynamic CE-MRI curves and images are seen in Figure 12. The ROIs of the right and left testis are illustrated with white ovals in the top picture. The experimentally induced diminished blood flow to the rats' testes could be measured in both groups, the decrease relative to the contralateral side being 12.4% and 10.8% in the 360˚ and 720˚ SCT group, respectively.

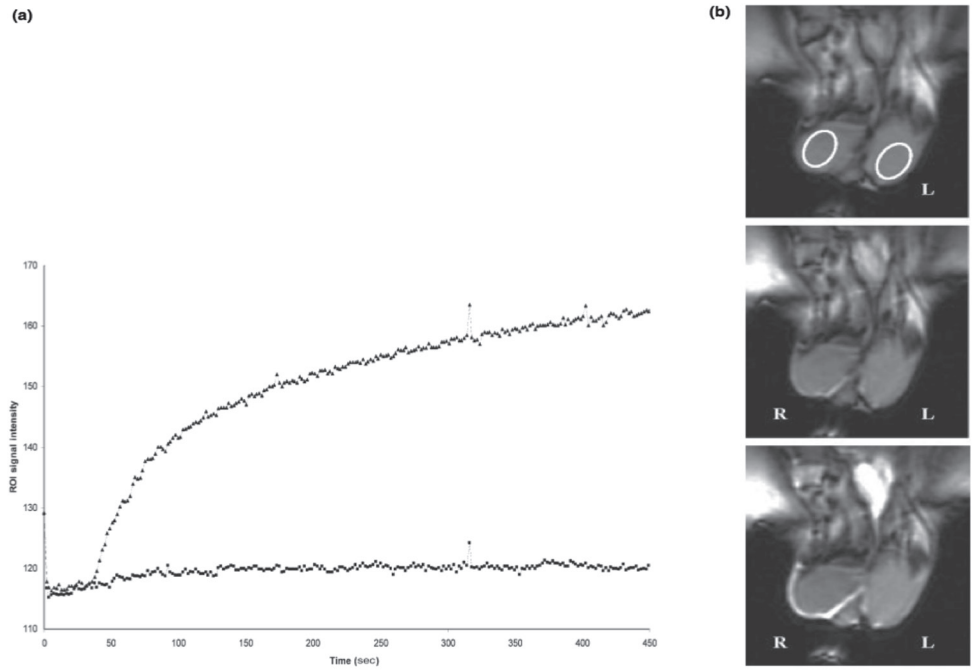


Figure 12. Contrast enhancement curves of the left (▲) and right (■) testicle after contrast bolus injection (a) and series images (from top to bottom) taken 5, 43 and 210 s after the contrast bolus injection (b). Right (R) and left (L) orientation is depicted in the lower corner of each panel (b). The white ovals in the uppermost panel illustrate the region of interest over the left and right testes (b). From Int J Androl 2005; 28:357 with permission.

5.6 MRI of acute scrotum in patients

17 patients with acute scrotum were examined by dynamic CE-MRI and DW-MRI and the results were compared afterwards with the clinical and operative findings. These comprised 3 patients with SCT, 4 with ED, 2 with TAT, 2 with intermittent torsion, one case each of hydrocele, haematoma, idiopathic scrotal oedema and contusion of scrotum and two with testicular pains of unknown aetiology. SCT, ED and TAT were chosen for illustration by means of contrast enhancement curves and T2-weighted images as well as T1-weighted images before and following contrast media, gadolinium. The case of hydrocele is presented as a normal testicle structure finding and enhancement of contrast media in MRI with T2-weighted and pre- and postcontrast T1-weighted images (Figure 13).

The three cases of SCT, were revealed in dynamic CE-MRI by virtue of an almost non-existent gadolinium contrast accumulation on the affected side but rapid contrast

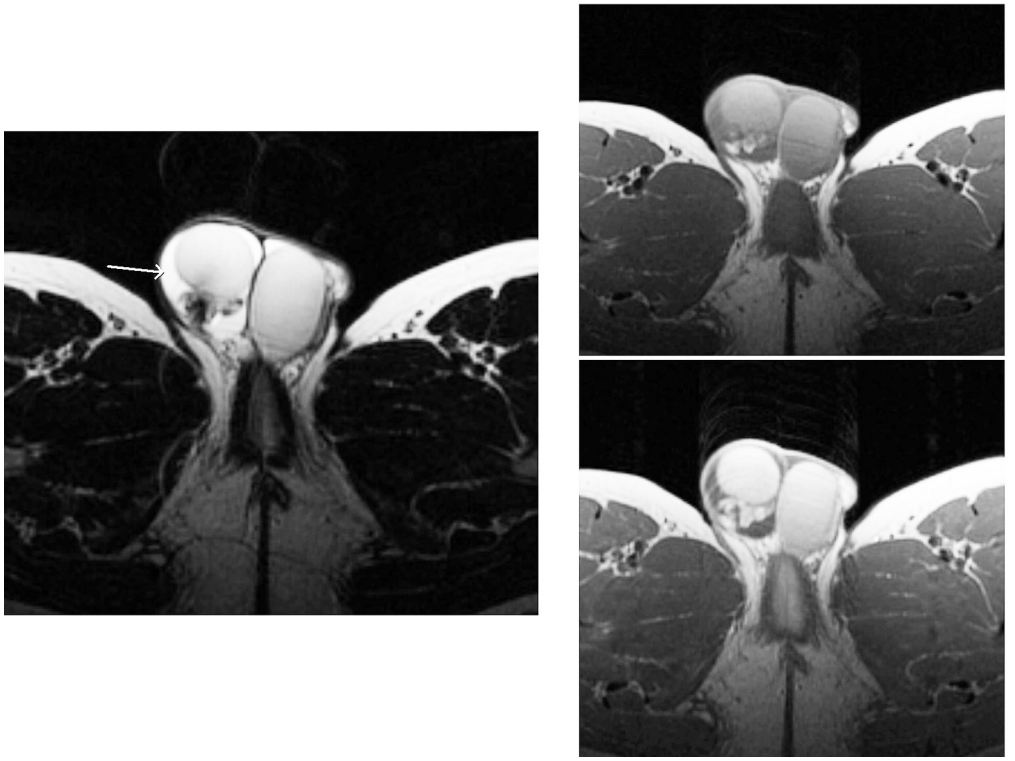
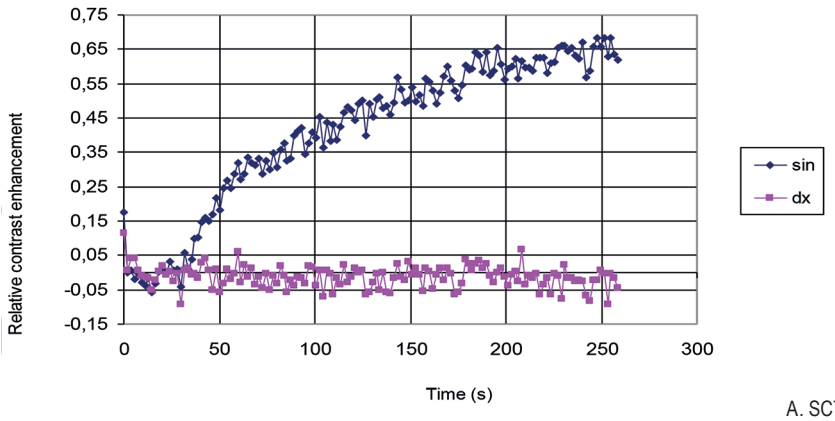


Figure 13. T2-weighted image of testicles of a 18-year-old boy with hydrocele around the right testis (white arrow) on the left image. T1-images before (upper) and following contrast media (lower) on the right side. The normal structure of testicles as well as normal enhancement of contrast media is visualized.

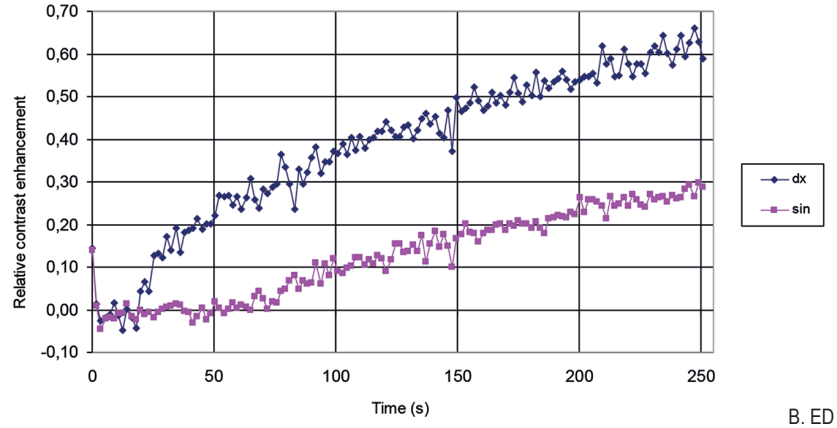
enhancement with a sharp slope on the contralateral side. The dynamic finding is illustrated in Figure 14A, while Figure 15 shows the MRI- images of the same patient, with no contrast uptake in the right testicle. In this case the duration of symptoms had been 48 hours and the right testicle needed to be removed. All the SCTs in this series ended in orchiectomy, because the duration of the symptoms was over 24 hours and the testicles were necrotic.

Six other patients were operated on, the decision being made on the grounds of both clinical and DUS findings. DUS indicated normal testicular circulation in four affected testicles, impaired circulation in one and no blood supply in one testicle. The peroperative findings were two TATs, one hydrocele, one haematoma of the spermatic cord and two twisted testes with spontaneous detorsions. The enhancement curves obtained by MRI were consistent with the operative outcomes.

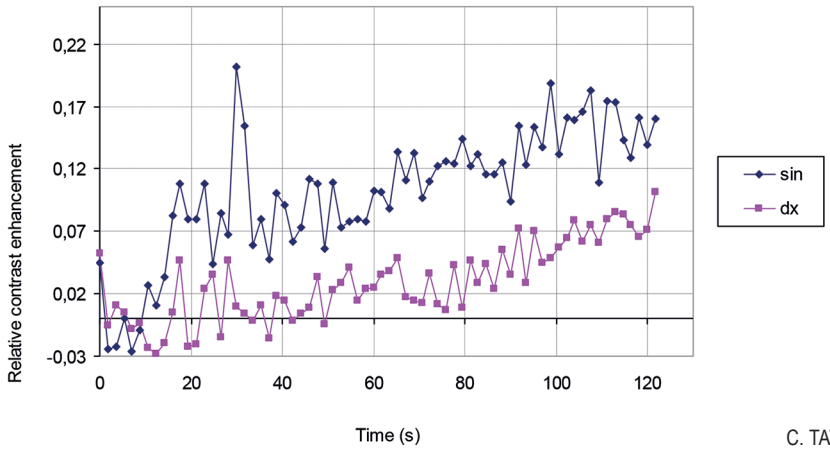
Eight out of the 17 patients were treated conservatively in the light of the clinical findings together with DUS four having epididymitis, two testicular pain of unknown



A. SCT of right (dx) testis



B. ED of right (dx) testis



C. TAT of left (sin) testis

Figure 14. The signal intensities as a function of time measured from the testicles in a patient with A. SCT with flat curve of ischemic right (dx) testis and normal ascending curve of left (sin) testis. B. ED of right (dx) testis. Both curves are ascending, but the slope is higher in the affected side. C. TAT of left (sin) testis. The higher slope is on the left testis due to inflammation of the necrotic appendage and increased circulation.

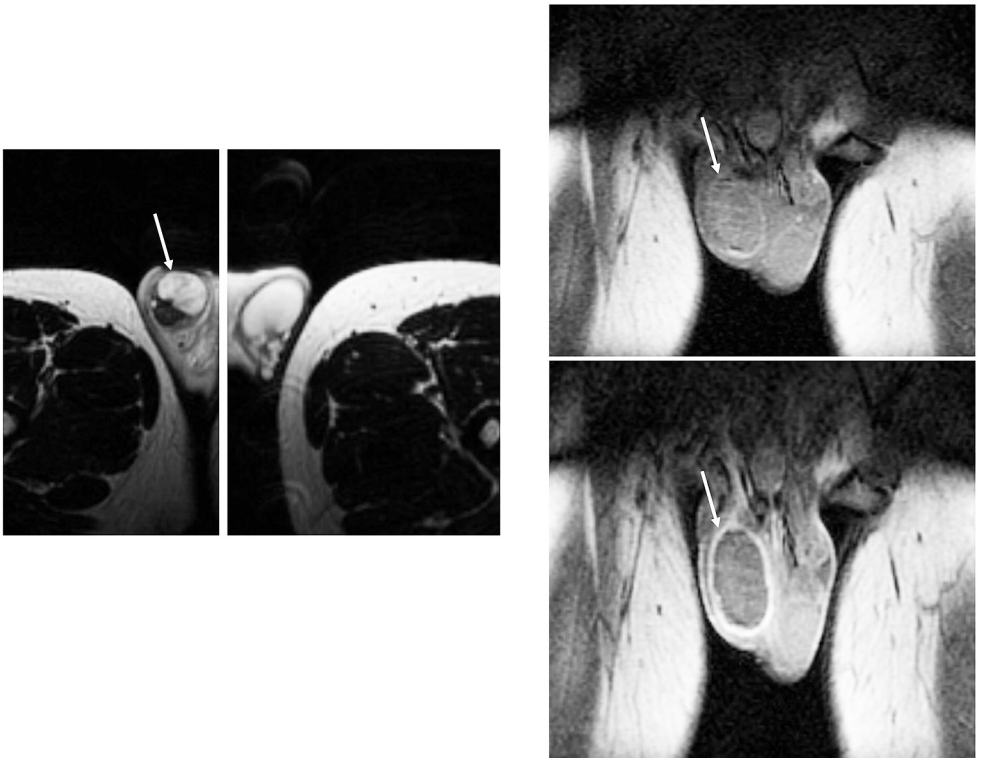


Figure 15. MRI-images of a 15-year-old boy with right sided testicular torsion for 48 hours. T2-weihgted image on the left and T1-weighted images on the right side. In the right bottom T1-image with contrast media the necrotic testis is best demonstrated.

aetiology, one contusion of the testis and one idiopathic scrotal oedema. The slopes of the enhancement curves obtained from the ROI values were all similar in these conservatively treated patients. Dynamic CE-MRI was consistent with DUS and the clinical examination. The contrast accumulation curve of a ten-year-old boy with epididymitis is seen in Figure 14B. There was a history of pain, redness and oedema for two days in the right scrotum area and the right-sided epididymitis involved enhanced circulation, which could be seen with MRI (Figure 16). No atrophy of testis was found at a later follow-up in these eight patients.

TAT was also demonstrated by MRI. A nine-year-old boy had had pain, tenderness and oedema in the left scrotum area for three days. DUS was performed on the first day and testicular circulation was confirmed, as was the clinical diagnosis was ED. Two days later, however, the severe pain and oedema had increased and an exploratory operation was performed, providing evidence of TAT. Increased gadolinium uptake caused by inflammation due to necrosis of the testicular appendage for two days was clearly demonstrated in the contrast media accumulation curve (Figure 14C). Another

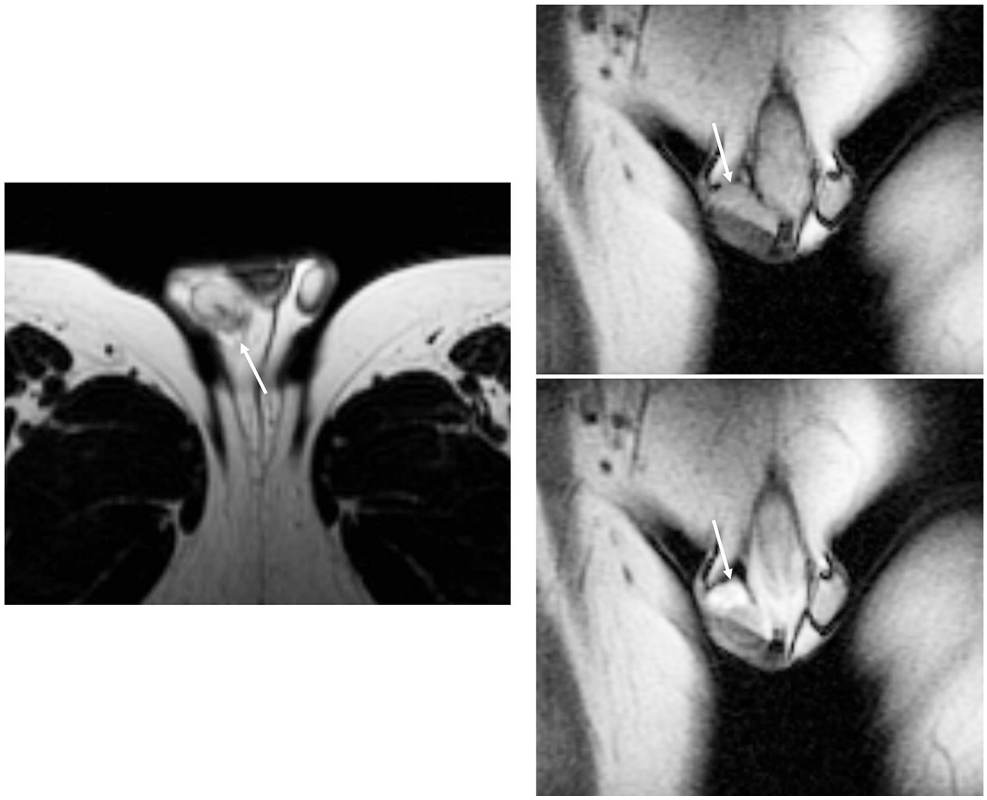


Figure 16. 10-year-old boy with right-sided epididymitis for two days. The swollen epididymis can be presented on the T2-weighted image on the left side. Precontrast T1-weighted image (right top) and postcontrast T1-weighted image (right bottom) illustrates the contrast enhancement of right epididymis (white arrows).

ten-year-old boy with right-sided TAT was operated, because the blood flow of the right testicle could not be ensured by DUS. The MRI findings would have been more demonstrative (Figure 17).

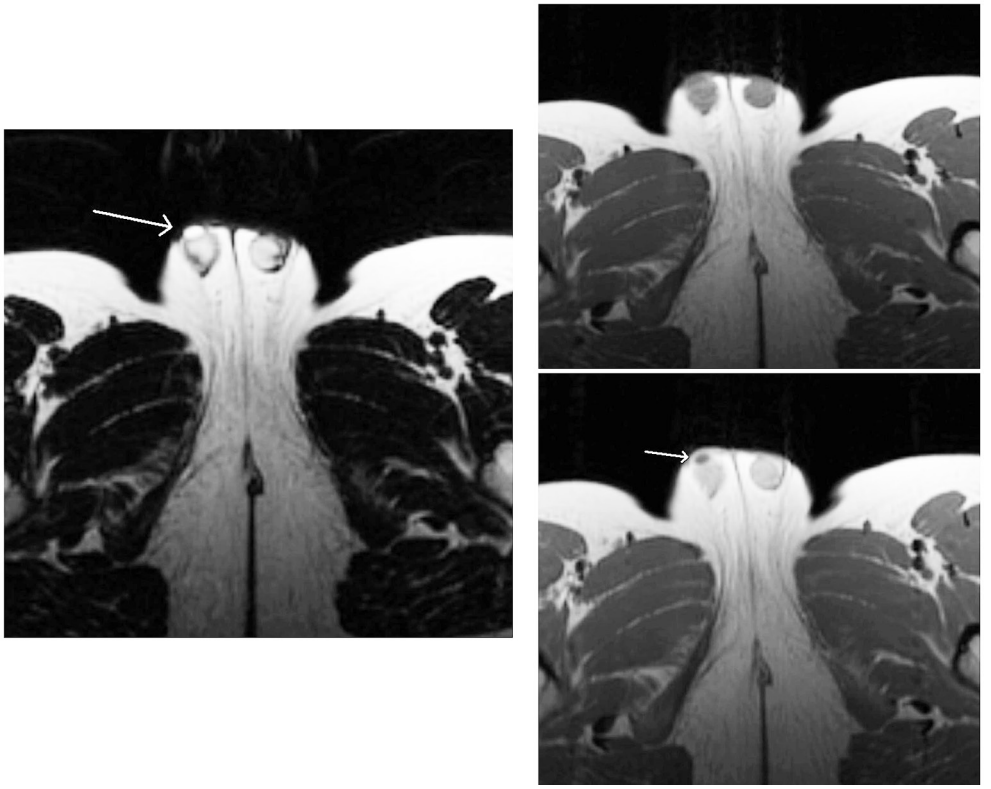


Figure 17. A 10-year-old boy with torsion of right testicular appendage. T2-weighted image on the left picture with white arrow is demonstrative for TAT and T1-weighted image with contrast media (right bottom) shows no contrast enhancement in the appendage.

6 DISCUSSION

6.1 Diagnoses lying behind acute scrotum

The diagnoses of the 388 consecutive patients included in our study were based on surgical findings available in the records of Helsinki University Hospital, which treats over 90% of all acute paediatric patients possibly needing surgery in its catchment area. Thus the degree of patient selection is very low. All the acute scrotum patients coming to the hospital during that time period, 1977–1995, were operated on according to the same clinical protocol, so that the distribution of diagnoses in this cohort is trustworthy.

Acute scrotum is an emergency condition most commonly caused by SCT, TAT or ED. The most damaging of these causes, SCT, has been found previously in smaller series (n=48–238) to underlie 11–25% of all cases of acute scrotum (Anderson and Giacomantonio 1985, Caldamone et al. 1984, Fernandez et al. 1997, Lewis et al. 1995), the most common reason having been either ED (23–63% of cases) or TAT (10–46%), depending on whether the findings are reported from the emergency room or obtained at surgery. It may be difficult to distinguish TAT with inflammation from ED by DUS. Our results regarding the distribution of diagnoses lying behind acute scrotum in childhood are based on surgical findings and point to SCT in 26% of cases and TAT in 45%. These proportions are in consistent with those reported by other clinics. The lower incidence of ED (10%) relative to TAT was based on surgical findings. We thus regard figures obtained here as appropriate for the distribution of acute scrotum cases in a representative Finnish patient series.

The incidence of SCT proved to be bimodal, the first peak appearing during the neonatal period and second in puberty as observed previously (Kadish and Bolte 1998). SCT was a rare cause of acute scrotum in our patients aged between one and 12 years, accounting for only 5,7%, whereas 55% of our patients with ED, which usually appears during the first year of life or among pubertal boys (McAndrew et al. 2002), were below the age of one year. The most obvious cases of pubertal boys with dysuria and ED must have been treated by paediatricians and did not end up requiring surgery. TAT can appear at any time in childhood and adolescence, but its peak incidence is commonly noted in prepubertal boys (Yang et al. 2011). In accordance with this, we found the

peak incidence of TAT to occur from nine to 14 years of age, i.e. in prepubertal and pubertal boys.

The first year of life warrants closer analysis, since examinations are more demanding in that age group and the spectrum of diagnoses is somewhat different from that found in later childhood. It has been seen earlier that SCT is the most common cause of acute scrotum at this age (56–59%), followed by ED (31–44%), while TAT is rare (Clift and Hutson 1989, Chiang et al. 2007, Yang et al. 2011). In our series of 91 surgical patients of this age the causes of acute scrotum were SCT in 39% of cases, ED in 23%, incarcerated inguinal hernia in 24% and hydrocele in 10%. TAT was found only once. Incarcerated inguinal hernia has not been included among the causes of acute scrotums in most other reports. It is also significant that 77% of the infant SCTs in our patient series were found during the first month of life, including both prenatal and postnatal cases, while ED was the most common diagnosis among baby boys aged from three to six months (76%). The frequencies of ED at various stages during the first year of life have not been analysed in previous published works.

6.2 Symptoms and signs

Although it is always emphasized that a good case history and careful clinical investigation are the corner stones of any diagnosis, it is disappointing to see how seriously the signs and symptoms of the various diagnoses relevant to acute scrotum may overlap. Pain, tenderness, oedema around the testicle and scrotum and erythema are found frequently in all three diagnostic groups. According to Yang et al. (2011), the only statistically significant signs pointing to SCT were absence of the cremasteric reflex and an abnormal testicle orientation. Data of the cremasteric sign and the positions of the affected and contralateral testicles were not recorded on the patient charts available for the present purpose, but it can be calculated that 88% of our SCT patients with acute scrotum from Helsinki, excluding infants, complained of pain, as compared with 94% of the TAT patients. The reports by Murphy (2006) and Yang (2011) record pain in 94–95% of SCT patients and in 95–100% of TAT patients. The absence of pain in some SCT patients can be explained by a long history of symptoms, i.e. the testicle had become necrotic over a period of some days and thus the acute pain had abated, while other symptoms had become more prominent and had finally driven the patients to the emergency room. TAT patients more often complained of pain, possibly on account of being at a sensitive age, on the verge of puberty. In the case of ED 58% of our patients complained of pain, which is consistent with the pain prevalence of 65–69% reported by Yang (2011) and Kadish (1998).

Oedema around the testicle or scrotum was found in 63%, 56% and 63% of the boys with SCT, TAT and ED, respectively, the corresponding percentages for swelling given in the recent papers by Murphy (2006) and Yang (2011) being 80–83%, 36–83% and 91–100%. Thus the condition of a patient cannot be judged by oedema of the scrotum, but rather the swelling merely indicates the duration and degree of inflammation in the scrotal area and not the diagnosis.

ED was accompanied by fever in 16% of cases, which is equivalent in figures of 11–19% quoted by Kadish, Mushtaq and Klin. ED caused by viruses does not necessarily affect body temperature. Erythema was most common in the ED group, but only 37% of the records studied here were positive in this respect. Kadish and Yang reported erythema in 67–83% of their ED cases.

Erythema was frequent in the TAT patients, affecting 32% and the blue dot sign was specific to TAT, but was positive only in 10% of cases. The blue dot sign has previously been reported to be positive in 10–23% of patients with TAT (Kadish et al. 1998, Mushtaq et al. 2003, Klin et al. 2001).

Nausea and vomiting are considered to be much more typical symptoms of SCT than of any other cause of acute scrotum (Caldamone et al. 1984, Melekos et al. 1988). These symptoms were rare in our series, but were found in all groups, 5% of the SCT patients were positive for them, 2% of the TAT patients and 3% of the ED patients.

It was shown in study II that a hard or dark testis was a typical sign of SCT in infants, being positive in 91% of our infant group. Chiang et al. (2007) similarly reported a firm, non-tender scrotal mass in 89% of patients younger than three months of age.

6.3 Duration of the symptoms

It may be difficult to evaluate patients with acute scrotum by reference to clinical signs and symptoms, but a thorough history indicating the duration of the symptoms may be of help. Three quarters of those, who sought medical help within six hours of the onset of the symptoms had SCT, 12% had TAT and only 2% had ED. Comparable figures have not been reported earlier. Ischaemic pain caused by SCT seems to bring sufferers to hospital earlier than other conditions.

The timing of ischaemia has the greatest impact on the survival of a testicle under torsion. It has been established earlier that if a patient is operated on within six hours of the onset of symptoms the success rate is close to 100%, whereas between six and 12 hours the rate is 70% and between 12 to 24 hours it falls to 20%. (Pavlica and Barozzi 2001, Lewis et al. 1995, Jefferson et al. 1997, Sidler et al. 1997). In the present patient series all the testicles operated on within six hours of the onset of symptoms were

salvaged, but only half of those in the time range from 6 to 12 hours and only 4% after 12 hours. Our findings are consistent with previous ones, as the slight differences in salvage rates may be due to imprecise histories in some studies. The lack of any late follow-up information is a weakness in all the relevant literature.

To summarize, our findings indicate that patients arriving at an emergency department within six hours of the onset of symptoms should have immediate exploratory surgery, whereupon there is a high probability of saving the testicle. After that time period further examinations with imaging modalities are needed to select the right patients for surgery.

6.4 Neonatal testicular torsion

Neonatal SCT is mostly extravaginal and accounts about 10% of all torsions (Pillai and Besner 1998). Neonatal torsion occurs after birth in 25% of cases, with a bilateral frequency of 11–21% (Yerkes et al. 2005). In the present series of SCT patients 35% were less than one year of age and 30% were neonatal. It was also calculated that 77% of neonatal acute scrotums were caused by SCT. The question of whether neonatal acute scrotum needs urgent surgical exploration, semi-urgent surgery or none at all has remained highly controversial (Yerkes et al. 2005, Sorsensen et al. 2003, Pinto et al. 1997, Das and Singer 1990). Yerkes et al. (2005) suggested urgent exploration, because of the high probability of bilateral cases and Sorensen et al. (2003) recommended it having found a salvage rate from 40 to 50% among neonatal torsion cases. Likewise, Pinto et al. (1997) reporting on the outcome for those neonatal testicles in their series that had been operated on within six hours of the onset of symptoms (2/10), noted that they were well preserved after one year of follow-up and therefore also preferred emergency surgery. Das and Singer (1990), on the other hand, reported that 72% of neonatal SCTs develop prenatally and thus concluded that the likelihood of finding a viable testis was extremely remote. In survey of paediatric surgeons and urologists in the UK and Ireland conducted by Rhodes et al. (2011) only 11 surgeons (10%) had ever found a viable neonatal testis. In the present group of patients 4/35 testes (11.4%) were salvaged by operating on them within six hours and two of these were prenatal or perinatal. In a follow-up from six to 12 months afterwards the salvaged testicles proved to be well preserved.

The salvage rate in a systemic literature review by Nandi and Murphy (2011), covering 284 neonatal torsions was 8.96%, increasing to 21.7% with prompt exploration. There were even three prenatal SCTs that were salvaged (Nandi and Murphy 2011). The authors consequently advocated either semi-urgent or urgent exploration. This would

be consistent with our observations, that neonatal SCTs are worth exploration within six hours from the onset of symptoms and with consideration up to 24 hours. At least orchiopexy to the contralateral testicle should be performed. DUS is suggested preoperatively. Neonates are a special group of patients, whose risks with anaesthesia has to be considered seriously while making a decision on operative treatment.

6.5 Developing imaging techniques

SCT affects the young male population, in that it represents a significant risk of testicular loss and has an uncertain impact on fertility. Research into SCT should thus focus in its aetiology and on the need for a rapid diagnosis in order to minimize testicular injury and improve salvage rates. Scintigraphy is unable to depict anatomical details, it exposures subjects to ionizing radiation and it requires intravenous line and even sedatives, when children are being examined. Since traditional ultrasound is dependent on the radiologist's experience, new quantitative diagnostic tools have been developed: contrast-enhanced ultrasound (CEUS), perfusion computer tomography (PCT), dynamic CE-MRI and near-infrared spectroscopy (Drlik and Kocvara 2012). Perfusion MRI without contrast media can be performed with ASL technique (Wong 2014). Our interest was in developing the feasibility of dynamic CE-MRI for detecting diminished perfusion in a twisted testicle, first with a rat model and subsequently in a pilot human study.

Earlier animal experiments have shown a 720° torsion to cause severe testicular damage (Turner et al. 1997) and we similarly found that both 720° torsion and 360° incomplete torsion caused significant distinguishable perfusion changes in the affected testicle as compared with the contralateral testicle. More variability in the contrast enhancement pattern was seen during incomplete torsion, however. Where previous protocols have used a blood-pool contrast agent (Costabile et al. 1993) and continuous arterial spin-labelling perfusion MRI (Pretorius and Roberts 2004) in animal and human studies, our goal was to use gadolinium as a contrast agent in combination with T1-weighted imaging. Thus it was the gadolinium uptake into tissues that was being measured rather than the first pass perfusion through the testicular vasculature. Our results demonstrated that this protocol is simpler than the previous ones and enables perfusion differences to be observed visually on a calculated enhancement curve and to be easily interpreted by a clinician.

Watanabe et al. (2000) were the first to use a similar MRI protocol for detecting testicular perfusion in patients with SCT, in whom they found a diminished gadolinium uptake. To investigate this further, we tested perfusion in a rat model with

incomplete torsion and were able to show, that various degrees of torsion reflected in the gadolinium uptake. Thus our results suggest that patients with incomplete testicular torsion can also be identified with dynamic CE-MRI.

DW-MRI has been in clinical use for detecting ischaemia in certain tissues, especially in neuroradiology and cases of cerebral ischaemia, where ADC values can be measured for the ischaemic tissue. It has been shown earlier by means of a rat model (Kangasniemi et al. 2001) that ischaemia caused by the complete cessation of arterial perfusion can be detected with DW-MRI in testicles, as elsewhere. In the present work we were able to measure diminishing ADC values in the testicles even though the value differences induced by ischaemia for only one hour were small. DW-MRI would be valuable in clinical use, however, because it is able to detect ischaemia in a testicle in which torsion has resolved itself spontaneously. The time course of the ADC changes and DW characteristics should be studied further in order to DW-MRI to be used in a clinical context for detecting cases of acute scrotum and SCT. New studies with an animal model have been published recently that confirm the feasibility of DW-MRI as a diagnostic tool for detecting SCT (Maki et al. 2011).

6.6 MRI for the clinical detection of SCT

MRI has previously been used mainly for imaging testicular tumours, because of its excellent resolution with regard to the scrotal contents and its use in cases of acute scrotum has only been looked into in recent years. The accuracy of MRI for distinguishing ED from the subacute phase of SCT was 100% when searching for a torsion knot and whirlpool pattern and assessing the vascularity of the spermatic cord (Trambert et al. 1990). It is important, however, to evaluate whether the testicular blood flow in an acute scrotum is normal, impaired or increased in order to choose the right treatment modality. Watanabe et al. (2000) showed the feasibility of dynamic CE-MRI for detecting various scrotal disorders in a series of 42 patients (age range 4–80 years, mean age 33) and Terai et al. (2006) reported a sensitivity of 93% and a specificity of 100% for the use of T2-weighted images and dynamic CE-MRI for diagnosing SCT in a group of 39 patients (median age 13 years). The chief limitation was the inability to rule out intermittent torsion. The same group later tested MRI as an emergency modality with a series of 14 SCT patients (Watanabe et al. 2007) again achieving the best accuracy with a combination of dynamic CE and T2-weighted MR images. The results of our pilot dynamic CE-MRI study involving 17 boys and young men with acute scrotum were equally encouraging. The accuracy of the enhancement curves for evaluating testicular blood flow was 100%, with ED and TAT giving steeper

slopes for the curves whereas SCT gave only flat, consistent base-line signal relative to the values for the contralateral testicle. The T2-weighted images were not as accurate when evaluated alone.

The limited availability and high cost of MRI are factors that detract from its value at present, but in cases involving anaesthetic or surgical risks such as unclear conditions with regard to skin problems, trauma or possible infection inside the scrotum, CE-MRI could assist in deciding whether to resort to surgery. The need for anaesthesia with young children is the weakness of MRI, but neonatal SCT could be verified with MRI without full anaesthesia. MRI is objective and has the greatest diagnostic potential, so that it could be used in the future to eliminate unnecessary operations and to quantify the ischaemia affecting a testicle. The availability and technical development of MRI is nevertheless increasing in the future and MRI could be used more frequently for evaluating cases of acute scrotum. The disadvantage of CE-MRI is the use of gadolinium, which rarely may induce side-effects. Although rare, but severe side-effect such as nefrogenic fibrosis has been described (Nardone et al. 2014). DW imaging of acute scrotum with testicular ADC measurements can allow for the detection of SCT without any use of contrast media.

In conclusion, although DUS is the current gold standard for the imaging of acute scrotum, MRI has some particular advantages. It would be possible with a combination of T1-weighted images DW-MRI and dynamic CE-MRI not only to distinguish SCT from other conditions, but also to evaluate the degree of ischaemia, in other words to help the surgeon to decide whether to choose orchiopexy or orchiectomy.

6.7 Suggestion for management of acute scrotum

Based on the results of this research and review of the literature the treatment of acute scrotum depends on clinical findings and their duration combined with DUS findings. If there is a strong suspect of SCT after thorough clinical history and physical examination and DUS is not instantly available, urgent surgery is suggested. Strong suspect should cross surgeon´s mind when there is a patient with painful scrotum and acute history of less than six hours, the patient is neonate or pubertal and the cremasteric sign is missing. If there is any uncertainty of the etiology of an acute scrotum, DUS is strongly recommended. In the future, the imaging modality might be MRI or possibly NIRS. The decreased or absent blood flow finding in an affected testicle leads to urgent surgery, if the symptoms have lasted less than 24 hours. Manual detorsion can be attempted preoperatively.

With a longer history the operative treatment is semi-urgent. Normal or increased blood flow detected by DUS in the affected testicle compared with the unaffected side leads to conservative treatment. Suspicion of SCT is the only reason for urgent surgery concerning acute scrotum, operative treatment of TAT is optional (Figure 18).

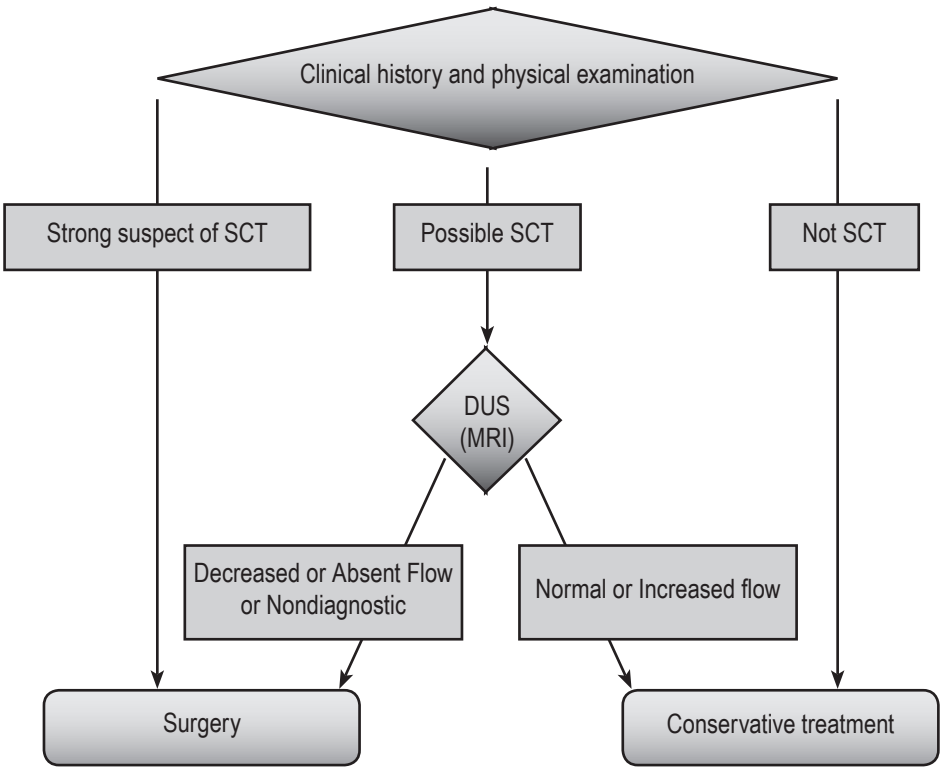


Figure 18. Algorithm for management of acute scrotum.

6.8 Limitations of the study

The cohort of this research involved retrospective analysis of patients with acute scrotum over a period of almost twenty years. There is always some inaccuracy in data collection and deficiency of some details, when the study is done retrospectively. The standard use of DUS was not available those years, which gives a historic point of view it this research. The pilot MRI study was difficult to accomplish since the availability of MRI had to be ensured in each case. The number of patients is very limited and four patients of the group were adults. The visit to the MRI facility had to pass without delay and MRIs were extremely strained by normally scheduled patients.

7 SUMMARY

This thesis is based on an analysis of 388 consecutive paediatric or adolescent patients who were admitted to the Hospital for Children and Adolescents in Helsinki during the years 1977–1995 because of symptoms of acute scrotum. According to the clinical practise of the time, they were all operated on. The distribution of principal diagnoses was SCT 26%, TAT 45%, ED 10 %, hernia 8% and hydrocele 6% while the other causes of acute scrotum (5%) were trauma and haematoma (7 cases), Henoch-Schönlein vasculitis (3), idiopathic scrotal oedema (2), orchitis (2) and a few solitary cases. The distribution of diagnoses during the first year of life was SCT 39%, ED 23%, hernia 24% and hydrocele 10%. The peak incidences of SCT occurred during the first month of life and around puberty, whereas TAT was encountered more frequently in prepubertal or early pubertal patients, between the ages of nine and 14 years. ED was most common in infants aged from three to six months.

The typical sign of SCT, severe pain with sudden onset, was found in 88% the of patients from one to 16 years of age. Three quarters of the boys who arrived at the hospital urgently and who were operated on within six hours of the onset of symptoms had SCT. Other clinical features of SCT in this review were tenderness (68%), oedema of the testicle and scrotum (63%), erythema (19%) and nausea and vomiting with abdominal pain (12%). A hard or dark testicle was found in 91% of the neonatal SCT cases. A symptom specific for ED was fever (16%) and there is also a possibility of underlying anatomical anomalies in infants with ED. Vesicourethral reflux was found in two subjects, and a multicystic dysplastic kidney and a rectourethral fistula in one each. ED was caused by bacteria in 26% of cases, all below the age of one year. Coliform bacteria were found in some of the infants. One sign that was specific to TAT was the "blue dot sign", which was positive in 10% of cases.

The duration of ischaemia is the major factor affecting the survival of a twisted testicle. In the present series the testicle was salvaged in all the cases of SCT which were operated on within six hours of the onset of symptoms (36/36), half of those in which the symptoms had lasted six to 12 hours but only 4% of those in which surgery took place more than 12 hours after the onset of symptoms. The testicles that failed to recover were removed. The overall salvage rate for the SCT cases was 48%. Altogether

36% of all the SCT cases in the series, 3% of the ED cases and 3% of the TAT cases were examined and treated within six hours.

During the first year of life, SCT was found in 35 out of the 91 (39%) patients brought to the hospital, incarcerated inguinal hernia in 22, ED in 21 and hydrocele in 9. TAT was found only once. A dark or hard testis was frequently detected in the SCT neonates, but erythema and tenderness were found infrequently. 30 out of the 39 (77%) patients seen during the neonatal period had SCT, including 15 prenatal or perinatal cases. Four testicles (11.4%) could be salvaged by emergency operative treatment.

The blood perfusion of the testicle is the crucial factor when evaluating cases of acute scrotum and SCT. Magnetic resonance imaging (MRI) is very accurate in terms of anatomical details, and combined with dynamic contrast enhancement values it has been reported to achieve a sensitivity of 93% and a specificity of 100%. The accuracy of dynamic CE-MRI in our pilot study of 17 emergency patients with a scrotal disorder was 100%. We were also able to show with a rat model that reduced contrast medium uptake was observable in both 720° SCT and 360° incomplete torsion cases implying that dynamic CE-MRI might also be able to identifying incomplete testicular torsions. Diffusion-weighted MRI, which has primarily been used for detecting cerebral ischemia, yielded slightly reduced values for an ischaemic testicle after one hour of ischemia indicating that DW-MRI is also a promising tool for evaluating the degree of ischaemia caused by SCT and detecting intermittent torsion. The results of dynamic CE-MRI can be presented in the form of curves which are easily interpretable by a surgeon. Further investigations into these diagnostic modalities will be needed in the future.

8 CONCLUSIONS

SCT was mostly seen among neonates and in puberty, ED is most frequent at the age of six months and puberty and TAT, which is the most common reason for acute scrotum, has its peak incidence just before puberty. One quarter of all the acute scrotum cases were caused by SCT, but this was the most common cause during the first year of life.

The symptoms of acute scrotum caused by SCT, TAT and ED overlap, but severe pain seems to bring patients with SCT to the emergency room at an earlier juncture. Three quarters of the patients with acute scrotum who sought medical help within six hours of the onset of symptoms had SCT.

The overall testicle salvage rate in cases of SCT was 48%. When detorsion was performed with in six hours all the testicles could be saved, but if ischaemia had lasted for six to 12 hours only half were saved and beyond this time only 4% of the testicles operated on recovered.

A distinct feature of neonatal SCT was a dark, hard testicle. Given urgent operative treatment, 11.4% of the neonatal SCT testicles could be salvaged.

Our results suggest that an immediate operation should be seriously considered for a patient with sudden onset of symptoms and with arrival at the hospital within six hours. All unclear cases with history of less than 24 hours should be examined further with DUS or another modern imaging modality before possible urgent operation.

Better imaging tools are being developed to enable more accurate diagnosis. Dynamic CE-MRI is a feasible modality for detecting hypoperfusion induced by SCT.

Dynamic CE-MRI succeeded in providing reliable data of ischaemia in the testicle in a clinical trial and may thus be helpful when selecting patients with acute scrotum for urgent surgery.

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11 ORIGINAL PUBLICATIONS

Scandinavian Journal of Surgery 96: 1–000, 2007

A 19-YEAR REVIEW OF PAEDIATRIC PATIENTS WITH ACUTE SCROTUM

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ABSTRACT

Background and Aims: **The aim of the study was to compare incidence, symptoms and signs of spermatic cord torsion to those of other conditions causing acute scrotum.**

Material and Methods: **Records of 388 consecutive boys under 17 years of age treated for acute scrotum at The Hospital for Children and Adolescents in Helsinki in 1977–1995 were reviewed. During the period studied all patients with acute scrotum underwent urgent surgery to ensure accurate diagnosis and treatment. The duration and characteristics of the symptoms, clinical findings prior to operation and the age of the patients were registered.**

Results: **Scrotal explorations revealed 100 cases (26%) of spermatic cord torsion (SCT), 174 cases (45%) of torsion of the testicular appendage (AT), 38 cases (10%) of epididymitis (ED), 32 cases (8%) of incarcerated inquinal hernias and 44 (11%) other conditions. During the first year of life SCT was the most common cause of acute scrotum, another peak incidence being in adolescence. Almost half of the boys with AT were nine to 12 years of age (median 11). Except for infants, the patients´ acute symptoms were pain (SCT 88%, AT 94%, ED 76%). Swelling in the hemiscrotum was found in 44% of SCT, in 39% of AT and in 88% of ED cases. Epididymitis was also accompanied by erythema (37%) , but infrequently with fever (in 16%). Erythema was found also in AT (32%), but the "blue dot sign" was found positive in only 17 (10%) of the boys with AT. Three quarters of the boys who were operated on within six hours from onset of symptoms had testicle torsion. All testicles were saved when detorsion was performed within six hours, but salvage was possible in only half of the cases when symptoms had lasted more than six but less than 12 hours.**

Conclusions: **The high probability of SCT among those admitted to an emergency department within six hours from the onset of the symptoms justifies immediate surgical exploration.**

Key words: Acute scrotum; spermatic cord torsion; epididymitis; torsion of testicular appendage

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INTRODUCTION

The incidence of spermatic cord torsions (SCT) among subjects with acute scrotum varies from 18% to 45% depending on the age of the patients, the type and location of the hospital and the method of diagnosis (1). The diagnosis of acute scrotum in addition to clinical examination is confirmed mostly by doppler ultrasound (DUS). A few decades ago all patients with acute scrotum underwent urgent surgery in order to treat all SCTs as soon as possible. This generally accepted approach was also adopted in the Hospital for Children and Adolescents in Helsinki. As definite diagnoses relating to acute scrotum were confirmed by exploration in 1977–1995, we undertook a review of all cases from that time period to establish the incidence as well as clinical picture of SCT and compare the findings to those in other conditions causing acute scrotum.

MATERIAL AND METHODS

We retrospectively reviewed the records of patients less than 17 years of age suffering from acute scrotum in the Hospital for Children and Adolescends during the period 1977–1995. Those who were examined by a paediatric surgeon and operated on were included. The diagnosis was made clinically and confirmed by a scrotal exploration. As doppler ultrasound (DUS) was used for diagnosis only during last few years, the findings by this diagnostic method were not presented.

The information reviewed included age of patient, duration of pain before operation and a history of fever and vomiting. The findings recorded upon physical examination were tenderness, erythema or oedema of the scrotum and testes, translumination and a "blue dot sign". In the ED group review was made of results of urinanalyses (before antibiotic treatment was started) and further investigations to exclude anatomical disorders. When SCT was found, the testicle was derotated. If the testis remained dark it was wrapped with warm saline soaked towels for at least for five minutes. Subsequently, if no recovery in the colour of the testicle was seen, testicular capsule was incised. When no bright bleeding was detected, the testicle was removed and the contralateral testicle was fixed to the dartos fascia. If there appeared to be secondary infection in a necrotic testis the contralateral fixation was postponed for a few weeks, or fixation was done concomitant with application of a silicone prosthesis.

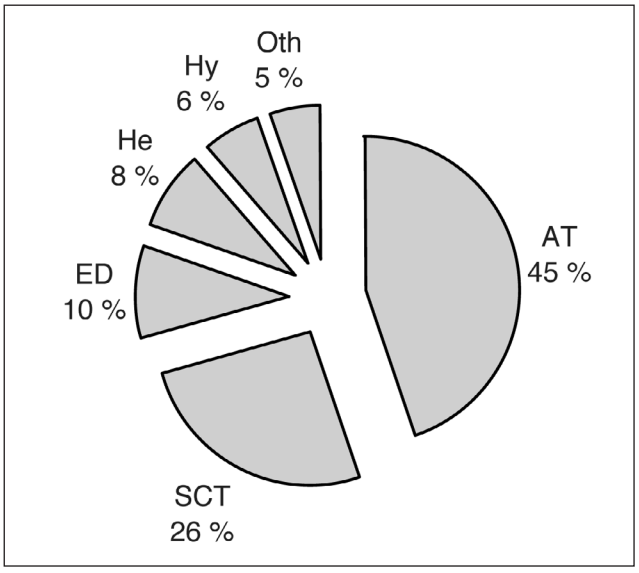


Fig. 1. Distribution of reasons for acute scrotum in patients under 17 years of age.

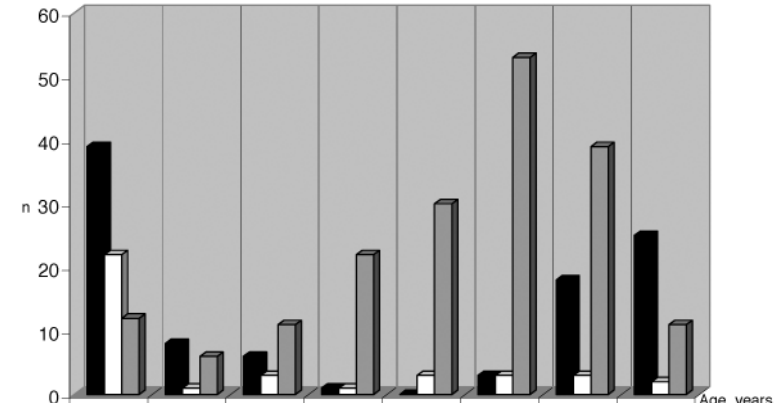
RESULTS

A total of 388 patients were included the study and operated on, confirming the following diagnoses: AT in 174 (44,8%), SCT in 100 (25,8%), ED in 38 (9,8%), incarcerated inguinal hernia in 32 (8,2%), hydrocele in 24 (6,2%) and other reasons in 20 (5,2%) boys (Fig. 1). The other reasons for acute scrotum were idiopathic scrotal oedema in two, epididymo-orchitis and orchitis parotica in two, one gangrena epididymis, one infection of a testicular prothesis, one retention and incarceration of a testis, one testis saltans, hematoma scroti in three, one twisting (rotating) testis, Henoch-Schönlein vasculitis in three, contusion or trauma in four and one liponecrosis of the tunica vaginalis.

Two peak incidences of SCT were found, one during the first year of life, the other between ages of 13 and 16 years (Fig. 2). Torsion of the testicular appendage was encountered more frequently in boys between ages of nine and 12 years. More than a half of the boys with ED were below the age of one year. Later in childhood and adolescence ED was seldom diagnosed, without any variation in incidence. The four most frequently made diagnoses during the first year of life were SCT, incarcerated inquinal hernia, ED and hydrocele (Fig. 3).

The duration of the symptoms at examination was less than six hours in 36% of patients with SCT and in 3% with ED as well as with AT (Fig. 4). Thus, patients with ED (55%) and AT (22%) and SCT (23%) seem to have reached the hospital within 12–24 hours from onset of symptoms. However, children reached the hospital after 24 hours from onset of symptoms were mostly with AT (56%) and less in groups SCT (25%) or ED (27%).

Pain and oedema of the hemiscrotum were the most common findings in the subjects suffering from SCT (Table 1). Pain was absent in 12 % of children more than one year of age. Hard and dark testis was found only in the SCT group, typically among neonates. This finding was mostly (in 68%) made during the first 24 hours from the onset of the symptoms. Ninety-four per cent of patients with AT presented with testicular pain, 56% with scrotal or testicular oedema. Redness was frequently found in cases with ED (37%) and AT (32%). 7 to 8% of boys complained of abdominal pain in each three groups of SCT, AT and ED. "A blue dot sign" was specific for AT and was visible in only 17 cases (10 % of this group). Ten of these were found within six to 24 hours from the first symptoms.



	0-2	-4	-6	-8	-10	-12	-14	-16
SCT	39	8	6	1	0	3	18	25
ED	22	1	3	1	3	3	3	2
AT	12	6	11	22	30	53	39	11

Fig. 2. Age distribution of the three major causes of acute scrotum.

Patients with ED also complained of pain (58%) and often presented with testicle oedema (50%) and redness (37%). Temperatures > 37,5 degrees Celsius were noted in six boys suffering from ED (16% of the group).

In cases of ED postoperative urine culture was positive in ten patients (26%, all below the age of one year). E.coli was cultered in five, Klebsiella in two, Enterococcus in two cases. Information on one culture was missing. Bacterial growth was also checked in a sample taken peroperatively from the epididymis of these patients. In four cases the culture was positive: Enterococcus (twice), Hemophilus influenzae and Staphylococcus epidermidis were found.

Further investigations were undertaken in ED group of patients as follows: intravenous pyelography (10), voiding cystography (10) and ultrasonography (9) to exclude any disorders causing ED in young boys. These examinations revealed vesicoureteral reflux (gradus II) in two subjects and a multicystic dysplastic kidney in one. In cystoscopy, performed in six

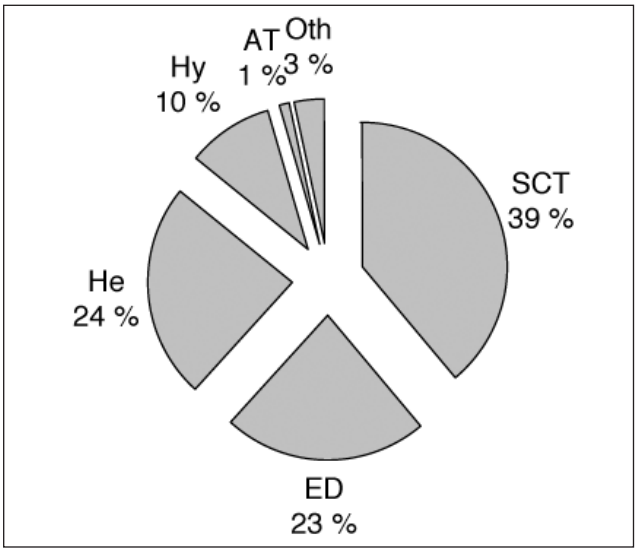
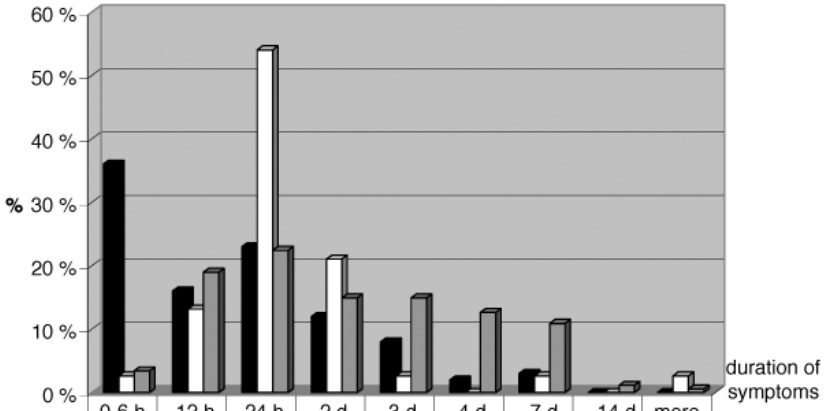


Fig. 3. Distribution of diagnoses of acute scrotum during the first



	0-6 h	-12 h	-24 h	-2 d	-3 d	-4 d	- 7 d	- 14 d	more
SCT (100)	36 %	16 %	23 %	12 %	8 %	2 %	3 %	0 %	0 %
ED (38)	3 %	13 %	54 %	21 %	3 %	0 %	3 %	0 %	3 %
AT (174)	3 %	19 %	22 %	15 %	15 %	13 %	11 %	1 %	1 %

Fig. 4. Duration of symptoms in spermatic cord torsion (SCT), epididymitis (ED) and torsion of testicular appendages (AT).

TABLE 1

Symptoms and signs in acute scrotum caused by spermatic cord torsion (SCT), torsion of testicular appendage (AT) and epididymitis (ED).

Symptoms and signs	SCT n = 100		AT n = 174		ED n = 38	
Pain, tenderness	68	68 %	163	94 %	22	58 %
Oedema of testis	44	44 %	68	39 %	19	50 %
Dark testis	21	21 %	–	–	–	–
Hard testis	19	19 %	6	3 %	3	8 %
Scrotal oedema	19	19 %	30	17 %	5	13 %
Scrotal erythema	16	16 %	55	32 %	14	37 %
Abdominal pain	7	7 %	12	7 %	3	8 %
Nausea or vomiting	5	5 %	3	2 %	1	3 %
Temperature > 37,5° C	2	2 %	5	3 %	6	16 %
Blue dot sign	–	–	17	10 %	–	–

cases, a rectourethral fistula was seen in a patient with VATER association.

All SCT patient operated within six hours from onset (35%) were salvaged whereas of those operated within six to 12 hours (16%) only half (8) recovered and those operated within 12–24 hours only 4% recovered.

DISCUSSION

The management of acute scrotum might be more challenging today than a decade ago, when urgent surgical exploration was the "method of choice" to investigate and treat almost any acutely swollen or painful scrotum. This old approach was also our policy in Helsinki before 1996. The hospital treats over 90% of all acute paediatric patients in the area; the degree of selection of patients is very low. However, a quarter of the patients in this study (26%) had SCT, which constitutes an absolute indication for surgery. Epididymitis was found in 10 % and AT in 45% of the cases. Anderson and Giacomantonio (2) found SCT in 23% of their 48 patients below the age of 15 years. Caldamone and associates (3) reported a similar 25% incidence of SCT in their 150 patients, also including young men (age range 0–21 years). These figures are consistent with our own. Other studies has shown varying distributions of diagnoses associated with acute scrotum: Lewis and Bukowski (4) found SCT in 16%, AT in 46% and ED in 35% of 238 patients below the age of 19 years. Kadish and associates (5) reported a high incidence of ED (71%), but low incidences of SCT (14%) and AT (14%) in their study of 90 patients (0–18 years). The diagnoses in that study, however, were based mainly on clinical or ultrasound findings and only some of the patients had been operated. Earlier series, including our own, are based on surgical findings and more recent studies on findings in the emergency room, which explains some of the variation in incidences. The higher incidences of ED may be explained by diagnostic difficulties in distinguishing ED from AT by ultrasonography. A necrotic appendix gradually causes inflammation in the surrounding tissues, mimicking ED.

The age distribution in different diagnostic groups in our series was similar to that in earlier studies (6, 7). During the first year of life SCT was the most common cause of acute scrotum, but between age of one and 12 years SCT was rare. In the present material only 22 cases (5,7%) of SCT were diagnosed in that age group. In early puberty the prevalence of SCT again increased.

Except for scrotal pain as such, clinical status and a history were of questionable value in decision-making. Although pain was a leading symptom in SCT, it was complained of by 88% of boys more than one year of age.When examining children it is important to recognize that absence of pain does not exclude possibility of SCT in a swollen scrotum. Some studies (5, 8), however, have found a tender testicle in 100% of patients with SCT. Appendiceal torsion was the most common cause of acute scrotum in the present series. The peak incidence of the condition was found between the ages of ten and 13 years; which is consistent with findings elsewhere (4). Sudden scrotal pain caused by AT was probably of lesser degree than pain caused by SCT, because three quarters of the patients with acute scrotum who sought medical help within six hours of the onset of the symptoms had SCT, 12% of them had AT and only 2% had ED. No such findings have previously reported. Although operative treatment of AT is not imperative, it is acceptable, since morbidity is diminished compared to conservative treatment with anti-inflammatory analgesics and rest. Our study also showed that all testicles with torsion were salvaged when the blood supply was restored within six hours. Similar frequencies of salvage have reported in other studies (9). Based on these findings we strongly recommend urgent surgical exploration in all patients whose severe scrotal symptoms have lasted less than six hours. It is as important to the primary medical care system as to the surgery unit to realize that acute scrotum is still an emergency.

In this study patients with ED were mainly (55%) below the age of one year. Only 16% of them were brought to the hospital within 12 hours from the beginning of any signs or symptoms. In such cases scrotal exploration should be avoided. It is stated that ED in young patients is caused mainly by bacterial infections, but in older subjects by viral infections (10). In our study bacteria cultures were studied. Although the culture was found positive in ten postoperative

urine samples and in four samples taken from the surface of the epididymidis, none of the patients had same bacteria in urine and in the epididymis sample. Thus ED can be related to urine tract infection or sometimes it is haematogenic in origin. Lau and associates (11) found 10% of ED (age range from five months to 12 years and ten months) patients to have pyuria and four out of five bacterial growth in urine sample: E. coli in three cases and Proteus mirabilis in one. Only a few abnormal urinary tract findings were recorded in boys with ED.

The use of US as a tool in deciding on a diagnosis has probably dramaticly influenced the choice of treatment in acute scrotum. Kass and associates 1993 (12) concluded that Doppler ultrasound should be applied in all cases of acute scrotum, and the method is still useful.However, it should be borne in mind that US may be different in accuracy in different hands . The subject is still controversial; Murphy and associates 2006 (13) concluded that early scrotal exploration of all cases with testicular pain ensures maximal testicular salvage. US seems to be especially useful when there is already a delay in seeking for medical help and no hope of salvage of the testis.

New examination methods are coming available. Magnetic resonance imaging (MRI) can be useful, when ultrasound findings are inconclusive and futher evaluation is required (14). Terai and associates 2006 (15) found that MRI is a highly accurate imaging modality for the diagnosis of testicular torsion, but further prospective studies will be needed.

According to this study those patients who entered hospital within six hours from the onset of symptoms were likely to have SCT. A decision for conservative treatment based on US findings is thus warned in these early patients, especially since recovery is best during the first six hours.

In conclusion, SCT was found here in a quarter of patients with acute scrotum. Ischaemic pain caused by SCT seems to bring sufferers to hospital earlier than other conditions. Patients with acute scrotum other than SCT tend to reach the hospital only after a delay. All patients attending hospital within six hours from the onset of the symptoms should be immediately operated. If the blood supply was restored in six hours all testicles with torsion were salvaged, but if the ischaemia had lasted six to 12 hours only half could be saved.

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TITLE PAGE

ACUTE SCROTUM DURING THE FIRST YEAR OF LIFE

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Running head: Infant Acute Scrotum

ABSTRACT

Objective
The aim of the study was to evaluate the age distribution of spermatic cord torsion (SCT) compared to other causes of acute scrotum during the first year of life and to describe distinctive features in each causative group in order to clarify the dilemma between operative and nonoperative treatment of acute scrotum.

Material and Methods
Ninety-one neonates (44) and infants (47) were operated on for acute scrotum and the definitive diagnoses for the testicles thus confirmed. The duration of the symptoms and the physical findings were recorded. The histopathology of the removed testicles was studied and bacterial cultures from patients with epididymitis (ED) were obtained.

Results
Thirty-five (39%) boys had SCT. Incarcerated inguinal hernia (IH) and epididymitis were found in 22 (24%) and 21 (23%) patients, respectively. Torsion of testicular appendage (TAT) was only seen once. A dark and hard testicle was detected in 91% of the SCT patients, erythema and tenderness were found infrequently. During the neonatal period 30 of 39 (77%) patients had SCT including 15 cases in which torsion had occurred prenatally. Only four testicles with SCT were salvaged.

Conclusions
The cause of acute scrotum during the first month of life was mostly SCT, while ED was seen more frequently between the age of 3 and 6 months. A dark and hard testicle was a common finding in SCT patients while swelling and erythema were typical of ED. Four testicles (11.4 %) with SCT were operatively salvaged.

KEY WORDS: acute scrotum, spermatic cord torsion, infant

INTRODUCTION

"Acute scrotum" is a rather common problem needing urgent action in a paediatric surgery emergency department. The most common causes in children less than 18 years of age are torsion of a testicular appendage (TAT) in 10 to 46%, spermatic cord torsion (SCT) in 11 to 31% and epididymitis (ED) in 10 to 71% of emergency department patients [1,2,3]. Inguinal hernia (IH), acute hydrocele, orchitis, Henoch-Schönlein purpura, idiopathic scrotal oedema, varicocele, tumour, abscess and leukaemic infiltration to the scrotum infrequently mimic the symptoms of SCT.

However, studies of acute scrotum during the first year of life are rare. The spectrum of diagnoses in this age group is somewhat different: SCT is the most common (39–59%), followed by ED (23–31%) and TAT (1–9%) [4,5,6,7].

The incidence of causative factors in acute scrotum is often based on imaging findings of the scrotum with ultrasonography. In this retrospective study all consecutive patients with acute scrotum were operated on and the diagnoses thus confirmed. Our main interest was to compare the frequency of SCT with that of other causes of acute scrotum in boys less than one year of age treated in a university hospital covering population of one million people.

By definition in acute scrotum there is sudden pain and swelling in the hemiscrotum, indicating possibly inflammation or ischaemia. However, the historical features and findings on physical examination of babies differ from those of older patients, who are more able to express their symptoms [7]. In this study our second aim was to explore possible differences in physical findings between various diagnoses that would possibly help when deciding whether or not to operate on an acute scrotum of an infant or a neonate male. [8,9,10,11,12,13].

MATERIAL AND METHODS

In this study the medical records of all males under one year of age who entered the Hospital for Children and Adolescents (Helsinki University Hospital) between 1977 and 1995 because of acute scrotum were reviewed. All the patients were operated on. Clinical findings such as temperature, tenderness, oedema, redness or erythema, darkness and hardness of the scrotum, duration of the symptoms and final cause of the acute scrotum after exploration were recorded. The scrotum was considered acute if there had been clinical presentation characterized by a change in colour and rapid oedema and possibly pain or tenderness of the scrotum or there was a suspicion of SCT or incarcerated inguinal hernia. Large hydroceles with a clear transillumination sign were not considered as "acute scrotum" and were not operated or included in the study. Patients with obvious urinary tract infections and acute scrotum were included.
The duration of symptoms before the surgical approach was obtained from the charts. In cases of SCT the testicle was first derotated and if the colour and blood circulation recovered it was fixed in place with non-absorbable sutures. The contralateral testicle was also observed and fixed to the scrotal septum with non-absorbable sutures simultaneously. If the derotated testis did not recover within 5 minutes, when wrapped in warm saline-soaked towels, it was removed and the contralateral testicle was fixed. All removed testicles were sent for microscopic examination.

Diagnostic criteria for acute epididymitis were three or more of the following clinical findings: gradual onset of pain, fever, abnormal urine sediment, tenderness and induration of the epididymis, recent catheterization or history of genitourinary abnormality [1]. For patients with epididymitis radiological imaging was arranged to determine the underlying anatomical anomalies; sonography of the urinary tract as well as voiding cystourethrogram (VCUG) and in rare cases urography were carried out after the acute inflammatory period. Bacterial cultures were obtained either from urinalysis or biopsies of the epididymis or samples of tissue fluid taken perioperatively. The urinalysis was obtained by douple urine samples or by a punction of a bladder.

RESULTS

Thirty-five (39%) of the 91 boys aged less than one year old who were operated on for acute scrotum actually had SCT. Thirty of these were neonatal, of which 15 were perinatal or prenatal. Twenty-one were on the right side and 14 on the left side. There were no bilateral cases. Incarcerated inguinal hernia was found in 22 (24%), epididymitis in 21 (23%) and sudden hydrocele in 9 (10%) subjects. Other findings (4%) were one TAT, two scrotal haematomas and one orchitis due to mumps. These results are shown in Table 1. The incidence of SCT, IH and ED by age in months is demonstrated in Figure 1.

The duration of the symptoms in SCT, IH and ED is presented in hours and days in Figure 2. The median duration of the symptoms preoperatively in SCT was 12 hours (range 0–24) in 29 out of 35 boys. There were three neonates with a prenatal torsion, whose symptoms had been lasted from 2 to 6 days before surgical intervention. Surgery was delayed in another three babies (4, 8 and 10

months of age), due to parental ignorance. In patients who suffered from epididymitis the median preoperative presentation of symptoms was 12 to 24 hours. The duration of symptoms of inguinal hernia was more diverse, but the median was one day.

Only nine out of 35 (26%) testicular torsion patients were operated within 6 hours of the first symptoms. A dark, bluish and hard testis seemed to be specific for SCT (32/35, 91%), but this finding was also positive in patients with strangulated hernias and necrosis of testicle (7/22, 32%). Four testicles (11.4 %) were salvaged, two of which were considered prenatal or perinatal with abnormal scrotal finding detected at birth. Thirty-one testicles were found to be clinically necrotic and were removed. Histopathological examination revealed that all removed testicles had haemorrhagic infarction or necrosis.

The physical findings of SCT, IH and ED patients are presented in Figure 3.

Incarcerated inguinal hernia was found in 24% of infant boys with acute scrotum. Of these, 73% (16/22) were less than 3 months of age; 48% (10/22) were aged from 1 to 3 months. The typical sign was oedema of the scrotum extending to the inguinal area. Six testicles were found to be necrotic and were removed during the operation. The histopathological finding was necrosis haemorrhagica of the testis. One dark testicle was left behind and at the 5-month follow-up it had recovered.

Epididymitis was found in 23% of the operated patients. Epididymitis was the most common diagnosis among boys aged from 3 to 6 months (13/17, 76%). The typical symptom of epididymitis was erythema of the scrotum, which was rare among other boys. The epididymis or the whole scrotum was swollen in 19/21 patients and painful in 9/21. Body temperature exceeded 37.5 degrees Celsius in 4/21 patients. Fever was only observed in the ED group of patients. ED was diagnosed at operation if the epididymis was inflammated and the testicular appendages were normal. Nine patients had a positive bacterial culture in either urine or tissue fluid samples. Urinalysis was positive in seven cases: *E. coli* growth was seen in urine culture in four cases and no growth was found in three samples. Bacterial growth was obtained from biopsies of the infected epididymis or tissue fluid of nine patients (with negative urinalysis verified in three patients): *E. coli* (six cases), *Enterococcus* (four cases), and *Streptococcus feacalis* and *Klebsiella oxytoga* (one case each). The bacteria found in infant patients with epididymitis are listed in Table 2.
Deferred investigations in the boys with epididymitis consisted of voiding cystourethrogram, sonography, cystoscopy and urography in rare cases. These investigations found no physical abnormalities, other than that two boys were associated with grade two vesicoureteral reflux and one with a rectourethral fistula and VACTERL association.

Hydrocele was found in nine (10%) of the studied patients. Eight of these were younger than 6 months of age. Seven patients had had acutely enlarged scrotum for less than 24 hours. Oedema of the scrotum, tenderness and positive transillumination was detected in eight, five and one patient respectively.

Torsion of testicular appendage was found in only one patient, who was 2 months old. The hemiscrotum was red, swollen, dark and tender.

DISCUSSION

There are multiple studies on acute scrotum in childhood, but none of the previously published papers have focused on the first year of life. Our data are very reliable, because all acute scrotums reviewed in this study were explored by operation. There are diagnostic difficulties among babies with acute scrotum, and patients are unable to express pain, which may delay treatment. Ultrasound has its limitations on small testicles. MRI would be more accurate, but its availability is limited under emergency situations since patients need to be anaesthetized [5]. Since the duration of the symptoms during the first year of life is difficult to estimate, whether or not to operate on acute scrotum immediately remains under debate.

SCT is the most common cause of acute scrotum during the first year of life [3,4,6] and especially during the neonatal period. In our study 77% of all neonatal patients with acute scrotum suffered from SCT. The incidence of strangulated inguinal hernia was highest from 1 to 3 months of age and epididymitis was most frequent from 3 to 6 months. In a study by Chiang et al (2007) of 16 infant patients the incidence of SCT and ED was reported as 8 versus 2 during the first month of life and 1 versus 5 in infants less than 3 months of age, respectively [7]. Our study shows that the incidence of acute scrotum subsides between 6 months and 1 year of age since only 10% of the study patients belonged to this age group. This has not been reported previously.

In our series of ED patients (21) diagnostic criteria were fulfilled and supported with operative findings. In further studies abnormalities were found in three patients (14%), which is less than in other reports with up to 26% of anomalies [14]. However, urodynamic studies were not performed in our series of infants. Nine of 21 patients with ED (43%) had a positive bacterial culture, when the sample was taken peroperatively. Two of them had a sepsis. In the study by Santillanes et al (2011) bacteria was found only in 4% of ED patients aged from two months to 17 years [15].
In infancy ED can be caused by ascending urinary infection with retrograde flow of urine into the seminal vesicles and vas or by bloodstream infection [7]. We agree that all infant patients with ED should have renal ultrasound and VCUG investigations, because of the possibility of underlying anomalies [17].

It is remarkable that only one (1%) TAT was detected in our relatively large study group whereas in earlier studies on paediatric patients with acute scrotum TAT has been found in 26–74% of cases [6,14,17]. However, our study is the only one concentrating on the first year of life whereas previous reports covered the whole childhood.
The high rate of strangulated hernias (24%) in our patients is explained by the fact that in most other studies hernias were simply excluded [4,17]. Today, the standard use of ultrasound provides more information preoperatively. However, strangulated inguinal hernia may cause considerable morbidity not only for the bowel, but also to the ipsilateral testicle. In 6 of our 22 cases the violated testicle had to be removed because of necrosis, which was later histologically confirmed.

The possibility of SCT among neonates as a cause of acute scrotum is remarkable.
An acute scrotum during the first year of life may be caused by SCT, ED, strangulated hernia, hydrocele, haematoma, TAT or orchitis. Physical findings may be overlapping, but a dark bluish scrotum is mostly found with SCT, whereas a reddish hemiscrotum combined with fever indicates ED. Epididymitis in infants is frequently caused by bacteria.

Although it is clear that not all infants with acute scrotum require urgent exploration, it remains advisable to explore suspected SCTs, especially if there has been a normal testicle soon after birth. Surprisingly, two testicles of prenatal or perinatal SCTs were salvaged in our study. When the time

from pain onset to surgery is less than 6 hours the testis can be salvaged [17,18]. In our study four out of 35 testes were salvaged and they were all explored within 6 hours of the notice of symptoms. Whether the ultimate time limit is 24 or 48 hours remains controversial, consisting entities of twisting testes and degree of the torsion.

Whether the neonatal acute scrotum needs to be surgically explored urgently, semi-urgently or not at all remains controversial [2,9,11,13,17,19]. All four salvaged testicles with SCT were operated within 6 hours of the assumed onset of symptoms. All other affected testicles had to be removed. In a clinical follow-up 6 to 12 months later the salvaged testicles of our study patients were found to be in good shape. In a systematic literature review by Nandi and Murphy in 2011, consisting of 284 neonatal torsions, the salvage rate was 8.96%, increasing to 21.7% with prompt exploration [13]. Even three prenatal SCTs were salvaged. They advocated either semi-emergent or urgent exploration. This is consistent with our findings. On the other hand, John et al. (2007) and Kaye et al. (2008) postulated that prenatal torsions were never salvageable with series of 24 and 16 neonates respectively [20,21]. In Rhodes´survey of paediatric surgeons and urologists in the UK and Ireland in 2011 only 11 (10%) surgeons had ever found a viable neonatal testis with SCT [12]. In their retrospective study in 1997, Pinto et al. reported the outcome of testicles one year after neonatal SCT [22]. Only two out of ten salvaged testicles were normal. These were explored within 6 hours of discovery. They concluded that exploration is safe and should be performed in an emergency to increase the rate of testicular salvage.

For a clinician there are now valuable tools available in the imaging field. Colour Doppler ultrasound has helped remarkably in decision-making among young children with acute scrotum [17,19,23,24]. Even so, each neonate and infant patient with an acute scrotum should be investigated thoroughly with an accurate history and clinical findings, and the benefit of surgery should be considered individually for each age group and patient. Indeed, a patient with symptoms of long duration and fever or urinary infection should not be operated, except there is evidence of abscess.

Conclusions: SCT was found in 39% of all acute scrotums during the first year of life and in 77% during the first month of life. Among baby boys aged from 3 to 6 months ED was the most common diagnosis (13/17, 76%). A dark and hard testicle was a common finding in SCT patients while swelling and erythema of the scrotum was the most usual sign of ED. Patients with SCT were operated most urgently, the median duration of the symptoms being approximately 12 hours, while in the IH and ED groups it was 24 hours. A total of 11.4 % of the testis torsions were salvaged by emergency surgery.

Declaration of interest: the authors report no conflicts of interest. The authors alone are responsible for the content and writing the paper.

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LEGENDS TO FIGURES

Table 1. Relative aetiology of infant acute scrotum.

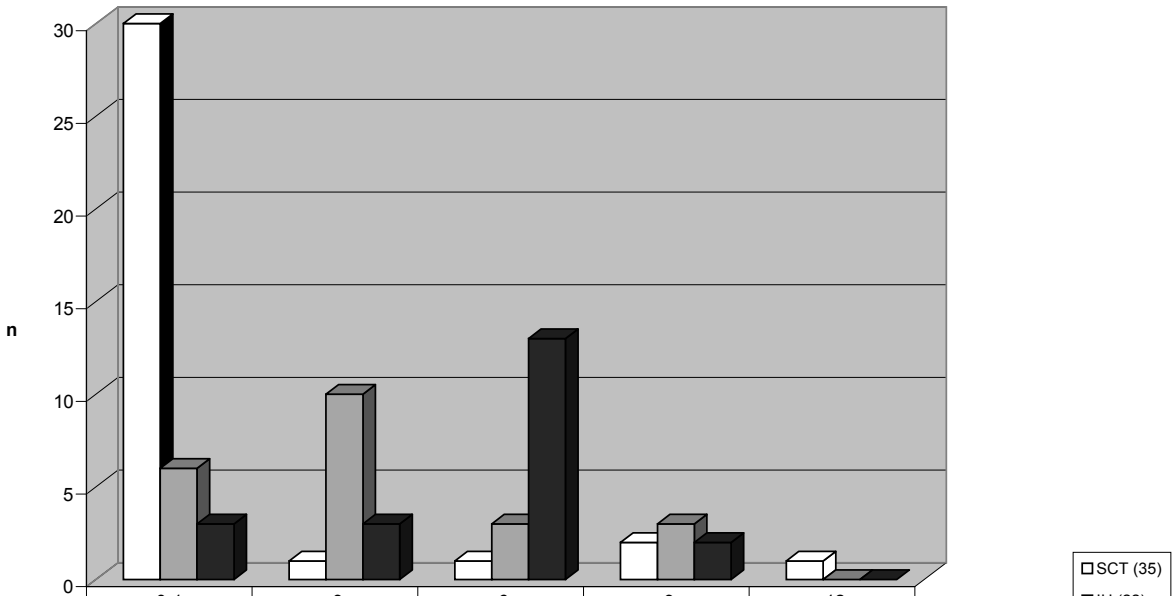
Table 2. Bacteria cultured in infant patients with ED.

Figure 1. The age distribution of infant SCT, IH and ED in months.

Figure 2. The duration of symptoms in infant SCT, IH and ED.

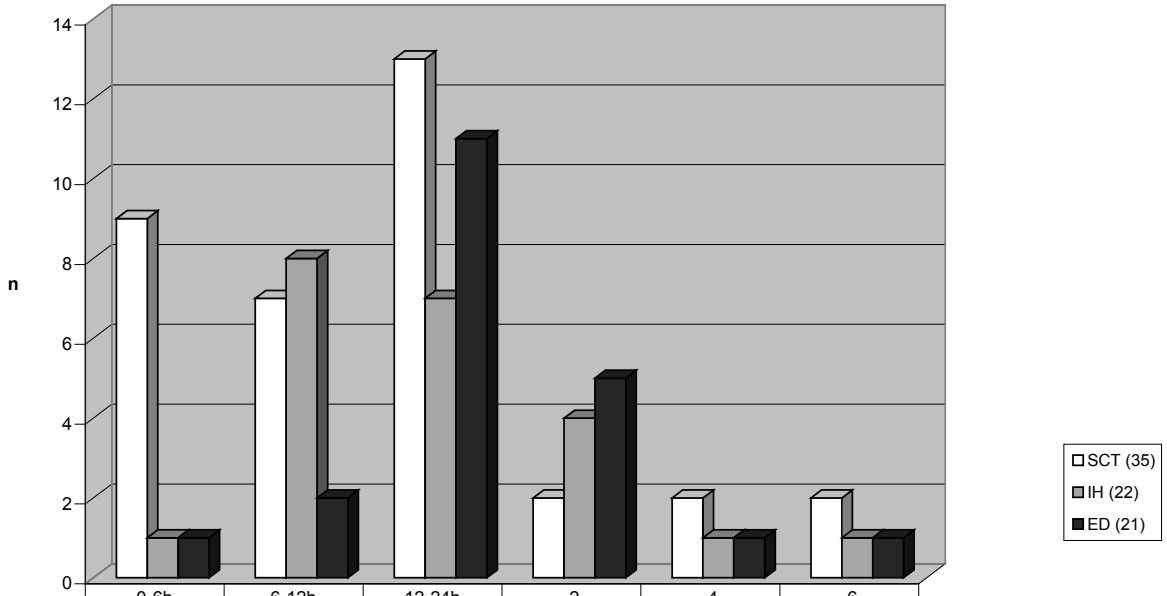
Figure 3. Physical findings of infant SCT, IH and ED.

Figure 1.

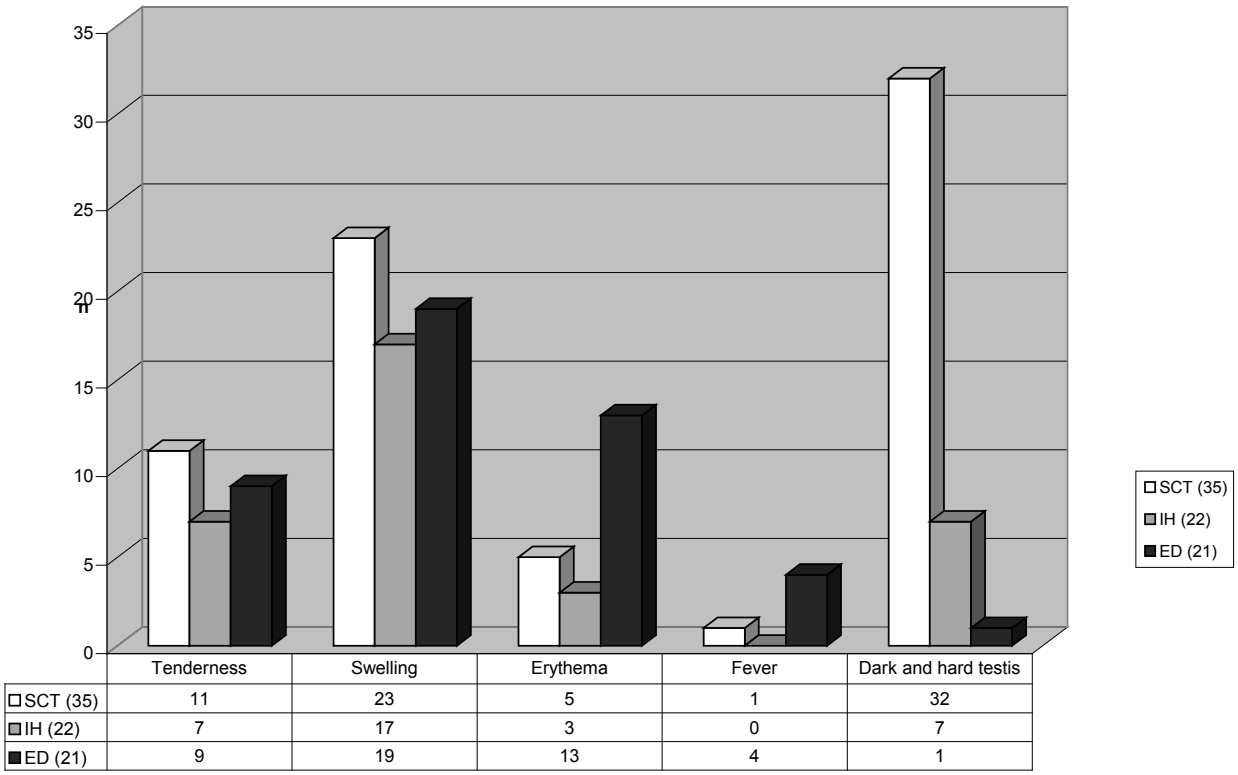


	0-1	-3	-6	-9	-12
SCT (35)	30	1	1	2	1
IH (22)	6	10	3	3	0
ED (21)	3	3	13	2	0

Figure 2.



	0-6h	6-12h	12-24h	-2	-4	-6
SCT (35)	9	7	13	2	2	2
IH (22)	1	8	7	4	1	1
ED (21)	1	2	11	5	1	1



	Tenderness	Swelling	Erythema	Fever	Dark and hard testis
SCT (35)	11	23	5	1	32
IH (22)	7	17	3	0	7
ED (21)	9	19	13	4	1

Figure 3.

Table 1. Relative Aetiology of Infant Acute Scrotum

Diagnosis	**No of Patients**	**Percentage**
Torsion of spermatic cord	35	39
Incarcerated inguinal hernia	22	24
Epididymitis	21	23
Hydrocele	9	10
Scrotal Hematoma	2	2
Orchitis	1	1
Torsion of testicular appendage	1	1
Total	91	100

Table 2. Bacteria cultured in infant patients with ED.

Bacteria	**Number**
E.coli	10
Enterococcus	4
Streptococcus feacalis	1
Klebsiella oxytoca	1

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Magnetic resonance imaging of experimental testicular torsion

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Summary

We investigated the feasibility of contrast enhanced (CE)-dynamic magnetic resonance imaging (MRI) for the detection of testicular torsion induced hypoperfusion in an experimental rat model. Adult Sprague–Dawley rats were subjected to unilateral testicular torsion of 360 or 720 degrees. After 1 h, the tail veins of the anaesthetized rats were cannulated and T2 -, diffusion-weighted and T1-weighted CE-dynamic MRI were subsequently performed by a 1.5 T MRI scanner. On apparent diffusion coefficient (ADC) images, the region of interest values of the ischaemic and control testes was compared. From CE-dynamic MR images, the maximal slopes of contrast enhancement were calculated and compared. In testicular torsion of 360 degrees, the maximal slope of contrast enhancement was 0.072%/s vs. 0.47%/s in the contralateral control testis ($p < 0.001$). A torsion of 720 degrees diminished the slope of contrast enhancement to 0.046%/s vs. 0.37%/s in the contralateral testis ($p < 0.001$). Diminished blood flow during torsion also followed in decreased ADC values in both 360 degrees (12.4% decrease; $p < 0.05$) and 720 degrees (10.8% decrease; $p < 0.001$) of torsion. Torsion of the testis causes ipsilateral hypoperfusion and decreased gadolinium uptake in a rat model that can be easily detected and quantified by CE-dynamic MRI. In diffusion-weighted MRI images, acute hypoperfusion results in a slight decrease of ADC values. Our results suggest that CE-dynamic MRI in combination with diffusion-weighted MRI can be used to detect compromised blood flow due to acute testicular torsion.

Keywords: acute scrotum, magnetic resonance imaging, testicular torsion

Introduction

Colour Doppler ultrasound (US) is widely considered to be the imaging modality of choice to detect acute testicular torsion. Although the sensitivity and specificity of colour Doppler US can exceed 90% in ideal conditions (Baker *et al.*, 2000), the reliability of the examination is highly dependent on the operator's skill and the patient's characteristics (Steinhardt *et al.*, 1993). Therefore, in a clinical setting, surgical exploration is often warranted because compromised perfusion cannot be conclusively ruled out by US.

Several pharmacological agents have been demonstrated to have a protective effect against the reperfusion injury caused by torsion–detorsion (Visser & Heyns, 2003). However, the most important factor determining testicular damage is the duration of ischaemia (Dunne & O'Loughlin, 2000). In order to minimize the time to correct diagnosis and treatment, a reliable and objective imaging modality would be helpful.

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Doppler US is in its best in detecting the absence of blood flow, but not in all cases is the blood flow totally occluded during testicular torsion (Costabile *et al.*, 1994). Early in torsion, some arterial flow may persist which may be confusing. Likewise, torsion may resolve spontaneously, under which conditions Doppler US may appear normal although the tissue is still ischaemic. An optimal imaging modality would therefore be able to measure the blood flow quantitatively and also ideally detect secondary changes in the ischaemic tissues. Potentially magnetic resonance imaging (MRI) techniques could be used to solve these technical problems. Contrast enhanced (CE)-dynamic MRI using blood-pool contrast agent, diffusion-weighted MRI and continuous arterial spin-labelling perfusion MRI have been tested in animal models and humans to evaluate the usefulness of different MRI protocols in determining testicular blood flow (Costabile *et al.*, 1993; Watanabe *et al.*, 2000; Kangasniemi *et al.*, 2001; Pretorius & Roberts, 2004). In the present study, we employed CE-dynamic MRI using gadopentetate dimeglumine, which is the standard clinically used contrast agent, and diffusion-weighted MRI in an experimental rat model. Our goal was to characterize a quantitative MRI protocol that would be suited for the measurement of testicular perfusion and also the detection of ischaemic tissue changes.

Materials and methods

Animals and surgical procedure

Adult 4-month-old Sprague–Dawley rats were used in this investigation. The Tampere University Animal Care Committee approved the experiments. Prior to operation, the animals were anaesthetized with fentanyl citrate at a dose of 0.25 mg/500 g and midazolam at a dose of 0.25 mg/500 g animal weight. During the operation, testes were exposed through a midline incision and the gubernaculum was divided. The membrane between testis and epididymis was divided up to the testicular hilum (Becker & Turner, 1995). The right testis was rotated either 360 or 720 degrees and fixed by joining the gubernaculum stump to the dartos with a 4–0 polyglactin suture. The left testis was treated in a similar fashion, except the testis was not rotated. The laparotomy was closed with a continuous 3–0 nylon suture. The animals were subsequently transferred to the MRI facility, the tail veins cannulated with a 30 G butterfly needle and the MRI performed at 1 h post-torsion with the animal still under anaesthesia. After the MRI, the animals were killed by CO_2 asphyxiation and the laparotomy incision was opened to confirm the torsion had remained during the imaging procedure.

MRI

MRI was performed with a conventional 1.5 T scanner (GE Medical Systems Signa Horizon Echospeed, Milwaukee, WI, USA) using a 3–inch circular surface coil. The animal was placed prone with testicles centred on the circular coil. After coronal T1-weighted spin–echo localizer an axial T2-weighted fast spin–echo series (time of repitition (TR) 4500 ms, time of echo (TE) 90 ms, NEX 1) was obtained with echo train length of 16. The matrix size was 256, field of view 21 cm, slice thickness 3 mm and intersection gap 0.3 mm. Diffusion-weighted imaging (DWI) was performed with single shot-spin echo planar imaging (EPI) sequence. The sequence was sensitized to diffusion by activating the gradients in each of the three principal axes with sensitizing factor b values of 0 and 1000 s/mm^2. The other imaging parameters of the DWI sequence were TR 10 000 ms, TE 100 ms, field of view 22 cm, slice thickness 3 mm and matrix size 128 × 96. Fast spoiled gradient-recalled echo (FSPGR) sequence was used to measure the contrast enhancement of the testicles. The sequence was started 15 s before the contrast bolus (0.4 mL, 469 mg/mL, Magnevist, Schering AG, Germany) was manually injected. A single oblique coronal slice was positioned to cover the central part of both the testicles. The parameters of the FSPGR sequence were TR 9.6 ms, TE 2.1 ms, field of view 18 cm, matrix size 256 × 192 and slice thickness 5 mm. The time resolution of the dynamic sequence was 1.88 s and data collection time 450 s. Diffusion-weighted and dynamic CE images were transmitted to a separate workstation (Advantage Windows 4.0, GE Medical Systems, Paris, France) for further analysis.

Data collection and analysis

Apparent diffusion coefficient (ADC) maps were generated with a commercially available Functool software (GE Medical Systems, Paris, France). The average of the ADC values was computed from three to five slices by region of interest (ROI) analysis of the central part of the testicles. The central slices were used to minimize the effect of distortions generated by the single shot EPI to the edge slices. Dynamic contrast enhancement curves were generated by positioning the ROI on the testis and computing the average signal intensity as a function of time. A sample of the contrast enhancement curve is shown in Fig. 1(a). An initial slope of the contrast enhancement curve was defined manually. The measured signal intensities were normalized to pre-contrast baseline values at time point zero. The two-way Student's t-test was used to compare statistically the values of the right and left testes.

Results

A testicular torsion of 360 degrees caused a clear and consistent decrease of blood flow at 1-h post-torsion. The maximal slope of contrast enhancement was 0.072%/s vs. 0.47%/s in the contralateral control testis ($p < 0.001$) indicating a nearly complete cessation of blood flow (Table 1a). A torsion of 720 degrees diminished further the slope of control enhancement to 0.046%/s vs. 0.37/s in the

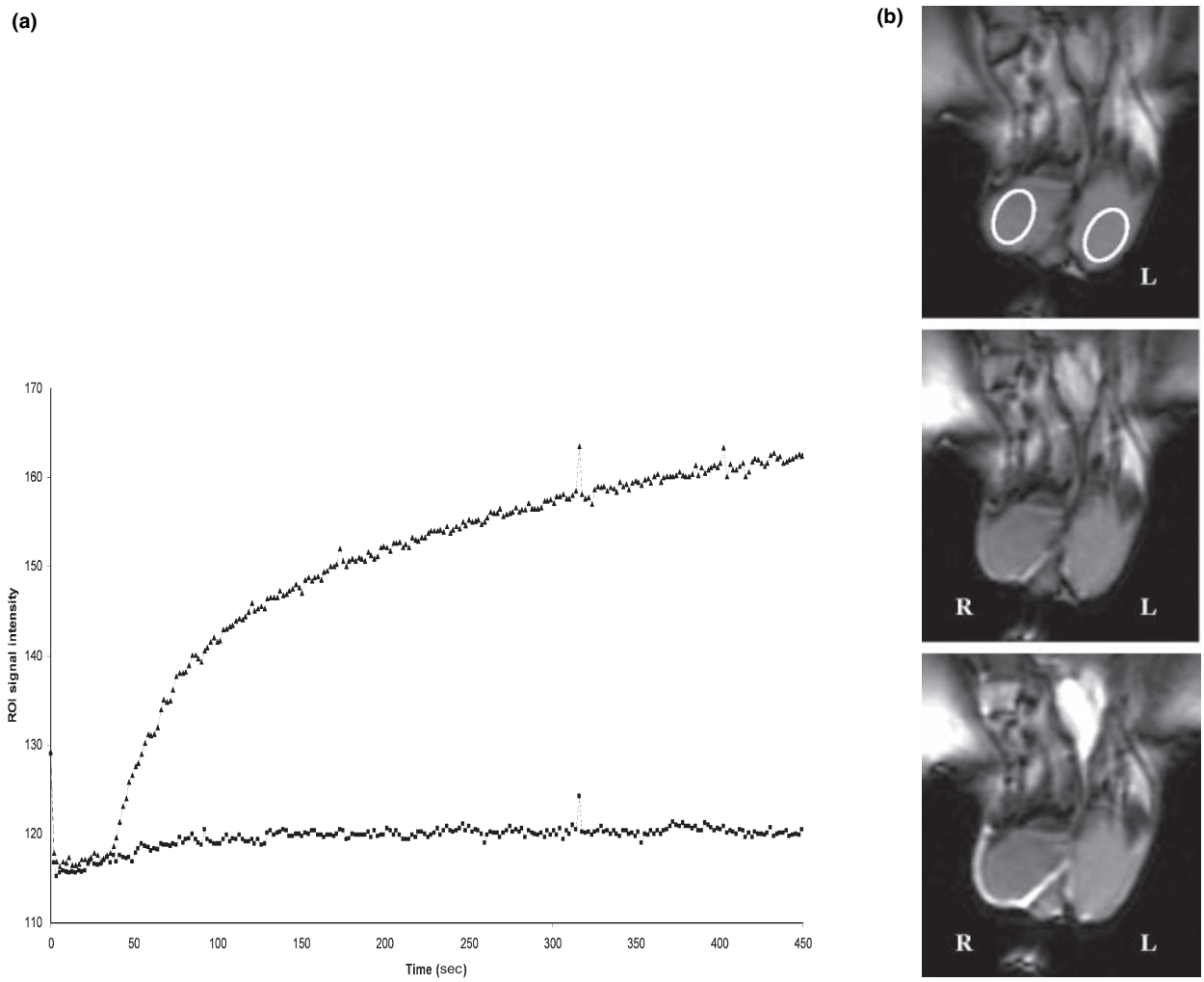

Figure 1. Contrast enhancement curves of the left (▲) and right (■) testicle after contrast bolus injection (a) and series images (from top to bottom) taken 5, 43 and 210 s after the contrast bolus injection (b). Right (R) and left (L) orientation is depicted in the lower corner of each panel (b). The white ovals in the uppermost panel illustrate the region of interest over the left and right testes (b).

contralateral testis ($p < 0.001$). Figure 1a depicts a typical dynamic contrast enhancement MRI scan demonstrating an almost non-existent contrast accumulation during a 720-degree testis and a rapid contrast enhancement on the contralateral side. Figure 1b depicts a series of MRI scans demonstrating the visual difference in contrast enhancement during a 720-degree testicular torsion.

Diminished blood flow during torsion followed the decreased ADC values in both 360 degrees (12.4% decrease; $p < 0.05$) and 720 degrees (10.8% decrease; $p < 0.001$) of torsion indicating measurable ischaemia-induced tissue changes after 1 h of torsion (Table 1b).

Discussion

The present investigation demonstrated the feasibility of CE-dynamic MRI in the detection of compromised testicular perfusion. In previous animal studies a transient 720-degree torsion has been demonstrated to cause severe testicular damage (Turner *et al.*, 1997). In a study by Costabile *et al.* (1994), a variability of perfusion was seen after a 720-degree testicular torsion. However, our data showed that this degree of torsion reproducibly causes a nearly complete cessation of testicular circulation. A slightly different operative procedure in these studies may account for this difference. We also studied the effect of 360-degree testicular torsion in the dynamic contrast enhancement to test if an incomplete torsion could be distinguished by this method. Our data demonstrated that the incomplete torsion of 360 degrees also causes a significantly compromised tissue perfusion that was easily detected. However, during incomplete torsion, more variability is seen in the contrast enhancement pattern.

Prior to this investigation, perfusion MRI using a blood-pool contrast agent (Costabile *et al.*, 1993) and continuous arterial spin-labelling perfusion MRI (Pretorius & Roberts,

Table 1. (a) Maximal slope of contrast enhancement in contrast enhanced (CE)-dynamic magnetic resonance (MR) images in right and left testis and (b) apparent diffusion coefficient (ADC) in right and left testis

Degree of torsion	CE-dynamic MRI, right testis, mean ± SD (%/s)	CE-dynamic MRI, left testis, mean ± SD (%/s)	*t*-test[a]; *p*-value	
(a)				
360	0.47 ± 0.04	0.072 ± 0.030	<0.001	$n = 4$
720	0.37 ± 0.18	0.046 ± 0.0033	<0.001	$n = 5$
	ADC, right testis, mean ± SD (10^{-5} mm^2/s)	ADC, left testis, mean ± SD (10^{-5} mm^2/s)	*t*-test[b]; *p*-value	
(b)				
360	7.67 ± 0.096	6.72 ± 0.76	<0.05	$n = 4$
720	7.64 ± 0.24	6.82 ± 0.26	<0.001	$n = 5$

[a]Comparison between the maximal slope of contrast enhancement of right and left testis; [b]Comparison between the ADC of right and left testis.

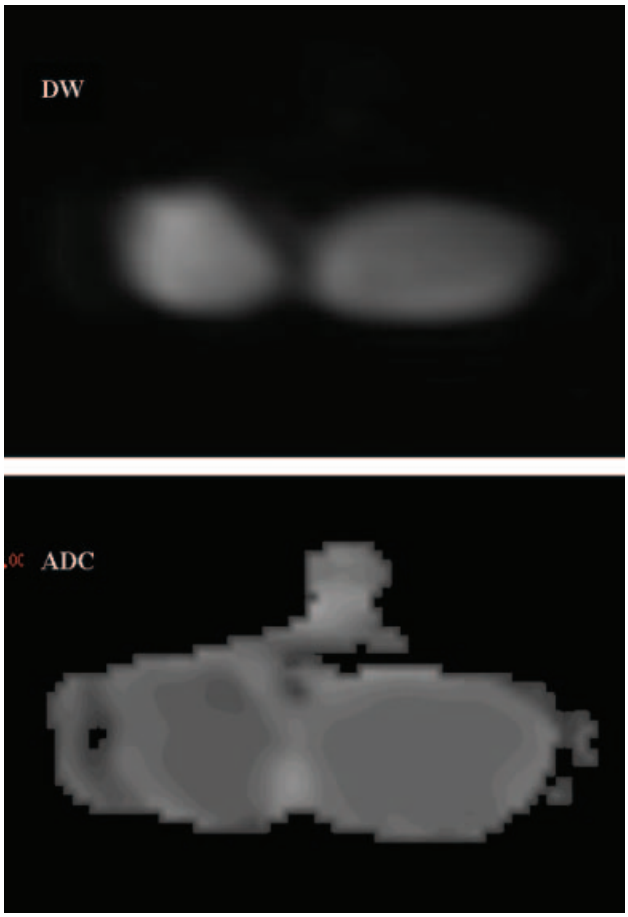

Figure 2. A representative diffusion-weighted MR image (DW) and an apparent diffusion coefficient (ADC) map of the testes.

2004) have been tested in an animal model and human in order to evaluate the usefulness of different MRI protocols in determining testicular blood flow. With CE-dynamic MRI used in our study, the contrast agent uptake into tissues was measured instead of evaluating the first pass perfusion through the testicular vasculature. The CE-dynamic MRI for testis can be performed using gadolinium as contrast agent and a simple dynamic T1-weighted imaging sequence. Also, no sophisticated post-processing software was necessary for the evaluation of the results. The difference in gadolinium uptake may even be visually observed when compared to contralateral testis (Fig. 1b).

Watanabe *et al.* (2000) utilized an MRI protocol similar to ours in humans for determining testicular perfusion during different pathological conditions. They found a decreased gadolinium uptake into the testes of torsion patients. Our goal was to further investigate in an experimental model, whether various degrees of torsion reflect the gadolinium uptake values measured from CE-dynamic MR images. Our results suggest that in patients having an incomplete testicular torsion, CE-dynamic MRI may show a decreased gadolinium uptake.

The primary clinical application of the DWI has so far been in the early detection of the cerebral ischaemia. In animal models the restricted diffusion of the brain tissue has been noticed in approximately 10 min, usually reaching a minimum ADC value at 8–32 h and the measured ADCs stayed at least few days below those of normal tissue. In testicles we have previously demonstrated an altered DW MRI signal caused by complete cessation of the perfusion after ligation of the testicular artery (Kangasniemi *et al.*, 2001). Similarly in this study, the decreased perfusion in torsion resulted in tissue ischaemia, which could similarly be detected by diffusion-weighted MRI. The utilization of this technique was clinically potentially useful, because in a case of spontaneously resolved torsion, measurable ischaemic tissue changes could be detected with this technique. However, the change in the ADC value in the ischaemic testes was relatively small at 1 h after the cessation of testicular blood flow. To refine the DWI as a clinical tool in selecting patients for emergency orchidopexy, the time course of the ADC changes and the DW characteristics of the irreversible testicular ischaemia should be further studied. A small change in the ADC value, such as seen in this study, may suggest that no irreversible testicular damage has occurred and a possibility of salvage of twisted testis by emergency manual detorsion and orchidopexy.

Conclusion

We demonstrated two simple MRI techniques for the evaluation of testicular torsion in rat model:

diffusion-weighted MRI and CE-dynamic MRI. Both techniques are available in clinical 1.5 T MR scanners with vendor pulse sequences and software.

Acknowledgement

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MAGNETIC RESONANCE IMAGING OF ACUTE SCROTUM

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ABSTRACT

Background and Aims: **The aim of the pilot study was to evaluate the feasibility of dynamic contrast enhanced (CE)-magnetic resonance imaging (MRI) in the detection of testicular ischemia and its ability to differentiate testicle torsion from other causes of acute scrotum.**

Material and Methods: **Seventeen boys or young men with an acute scrotum were included in the prospective study during the time period from October 2001 to December 2005. The median age of the patients was 16,4 (7–44) years. The duration of the symptoms preceding the MRI study varied from six hours to 30 days. The study protocol included physical examination by a surgeon, laboratory tests and Doppler ultrasound (DUS) and finally testicles were imaged by using a 1,5 T MRI scanner; T1-weighted and diffusion weighted images were produced. The gadolinium uptake, reported as the region of interest (ROI) perfusion values and presented as curves, was compared between the affected and contralateral testicle. In testicles with normal blood circulation the ROI values increased during the imaging time. Nine patients were operated on, because the spermatic cord torsion could not be excluded by clinical or DUS findings.**

Results and Conclusions: **All the normal testicles gave increasing ROI values meanwhile all three testicles with torsion gave constantly low values referring to no perfusion. Other causes of acute scrotum, such as epididymitis and torsion of testicular appendage seemed to be related with normal perfusion. Dynamic CE-MRI seems to show reliably ischemia of testicle and thus it may be helpful in selecting patients with acute scrotum for urgent operation.**

Key words: Acute scrotum; epididymitis; magnetic resonance imaging; spermatic cord torsion ; torsion of testicular appendage; dynamic CE-MRI

INTRODUCTION

The diagnosis of testicle torsion is still challenging. Physical history, clinical examination and ultrasound (DUS) are valuable in the evaluation of the patient (1, 2). Still, only fourth of the patients actually need emergency surgery (3). Although colour DUS can exceed 90% in sensitivity and specificity, its reliability varies depending on the experience of the radiologist (4). Findings on early torsions of spermatic cord as well as on twisting testicles may be confusing.

Dynamic contrast enhanced (CE)-magnetic resonance imaging (MRI) is a promising new modality for detecting acute scrotal problems and in distinguish-

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ing testicular and extratesticular disorders (5). Cheng and associates (6) found in their animal studies that relative blood volume measurements by MRI using a special blood pool marker should improve the diagnosis of testicular torsion in the acute setting. Watanabe et al. (7) examined 14 patients with testicle torsion with a dynamic CE-MRI and found 100% sensitivity in cases of complete torsion. The study did not include any other testicle conditions causing acute scrotum.

We tested an MRI based imaging modality to measure the testicle blood flow quantitatively in order to evaluate its ability to differentiate testicle torsion from other causes of acute scrotum. We employed CE-dynamic MRI using gadopentetate dimeglumine and diffusion-weighted MRI, which has previously been characterized with a rat model (8, 9). Time-signal intensity curves were created for affected and contralateral testicles. Finally, the diagnoses based on clinical, DUS and surgical findings were compared with the MRI findings.

MATERIAL AND METHODS

PATIENTS

The research protocol was approved by the local ethical board. Young men and boys older than seven years with acute scrotum were asked to join this prospective study during the time period from October 2001 to December 2005. 17 patients were willing to participate. The median age of the patients was 16,4 years (range 7 to 44). Eleven patients were under 18 years. The right and left testicle were affected in ten and seven cases, respectively. The onset of the scrotal pain varied from six hours to 30 days (mean four days).

The patients went through physical examination by a surgeon, laboratory tests (blood cell count, CRP and urine sample) and DUS study by a radiologist. As soon as possible, the patients were scheduled for urgent dynamic CE-MRI. Gadolinium was given prior to the examination. Neither medication or anaesthesia was needed. A dynamic MRI study lasted 5 minutes and the total time of the visit in the MRI-unit varied from 15 to 30 minutes, which did not delay the treatment of the patients. Those patients (n = 9) with a high suspicion of testicular torsion were operated on; decision was based on the evaluation of clinical findings and DUS.

MR IMAGING

Magnetic resonance imaging was performed with a conventional 1.5 T scanner (GE Medical Systems Signa Horizon Echospeed, Milwaukee, WI, USA) using a general purpose flexible surface coil. The patient was placed supine with testicles centred on the flexible coil. After coronal T1-weighted gradient-echo localizer an axial T2-weighted fast spin-echo series was obtained with echo train length of 18. TR (time of repetition) was 4000 ms, TE (time of echo) 113 ms and NEX (number of excitations) four. Matrix size was 256, field of view 30 cm, and slice thickness 4 mm, intersection gap 1 mm. Diffusion-weighted (DW) imaging was performed with single shot spin-echo EPI (echo planar imaging) sequence. The sequence was sensitized to diffusion by activating the gradients in each of the three principal axes with sensitizing factor b values of 0 and 1000 s/mm^2. The other imaging parameters of the DWI sequence were TR 10000 ms, TE 95 ms, field of view 30 cm, slice thickness 5 mm, and matrix size 128 x 128. Fast spoiled gradient-recalled echo (FSPGR) sequence was used to measure the contrast enhancement of the testicles. The sequence was started 15 s before the contrast bolus (20 ml, 469 mg/ml, Magnevist, Schering AG, Germany) was manually injected. A single oblique coronal slice was positioned to cover the central part of the both testicles. The parameters of the FSPGR sequence were TR 10 ms, TE 3 ms, field of view 28 cm, matrix size 256 x 192, and slice thickness 5 mm. The time resolution of the dynamic sequence was 2 s and data collection time 280 s. DW and dynamic CE-images were transmitted to a separate workstation (Advantage Windows 4.0, GE Medical Systems, Paris, France) for further analysis.

DATA COLLECTION AND ANALYSIS

Apparent diffusion coefficient (ADC) maps were generated with a commercially available Functool-software (GE Medical Systems, Paris, France). The average of the ADC values were computed from two to five slices by region of interest (ROI) analysis of the central part of the testicles. The central slices were used to minimize the effect of distortions generated by the single shot echo planar imaging to the edge slices. Dynamic contrast enhancement curves were generated by positioning the ROI on the testis and computing the average signal intensity as a function of time. Finally, the diagnoses based on clinical, Doppler ultrasonic and surgical findings and were compared with the MRI findings.

RESULTS

The conventional T1 and T2 images could not detect pathology and thus were not diagnostic. But contrast enhancement in MRI could be analyzed accurately in all patients. Three patients had a torsion of spermatic cord, which could also be demonstrated with MRI. Figure 1A shows an almost non-existent gadolinium contrast accumulation on the affected right side and rapid contrast enhancement on the contralateral side. The patient had had symptoms for two days, thus the right testis was necrotic and had to be excised and left testis detached to the scrotal fascia. Unfortunately, in all cases the affected testis was already in necrosis and could not be salvaged. MRI diagnosis was accurate in all of these cases. Also DUS showed no circulation in these testicles. Figure 1B shows T1 image of torsion of right testis.

There were six other patients who were operated on because of acute scrotum. Decision was made both on clinical and DUS findings. In these patients the DUS showed normal testicular circulation in 4 affected testicles, impaired circulation in one testicle and no blood supply in one case. Peroperative findings were two torsions of appendix testis, two twisted testes with spontaneous detorsions, one hydrocele and one haematoma of spermatic cord. The enhancement curves with MRI were consistent with operative outcomes. Eight of the 17 patients in the study were treated non operatively based on clinical findings and DUS and their diagnosis was confirmed without exploration: four had epididymitis, two testicular pain of unknown aetiology, one contusion of testis and one idiopathic scrotal oedema (table 1). In this group,

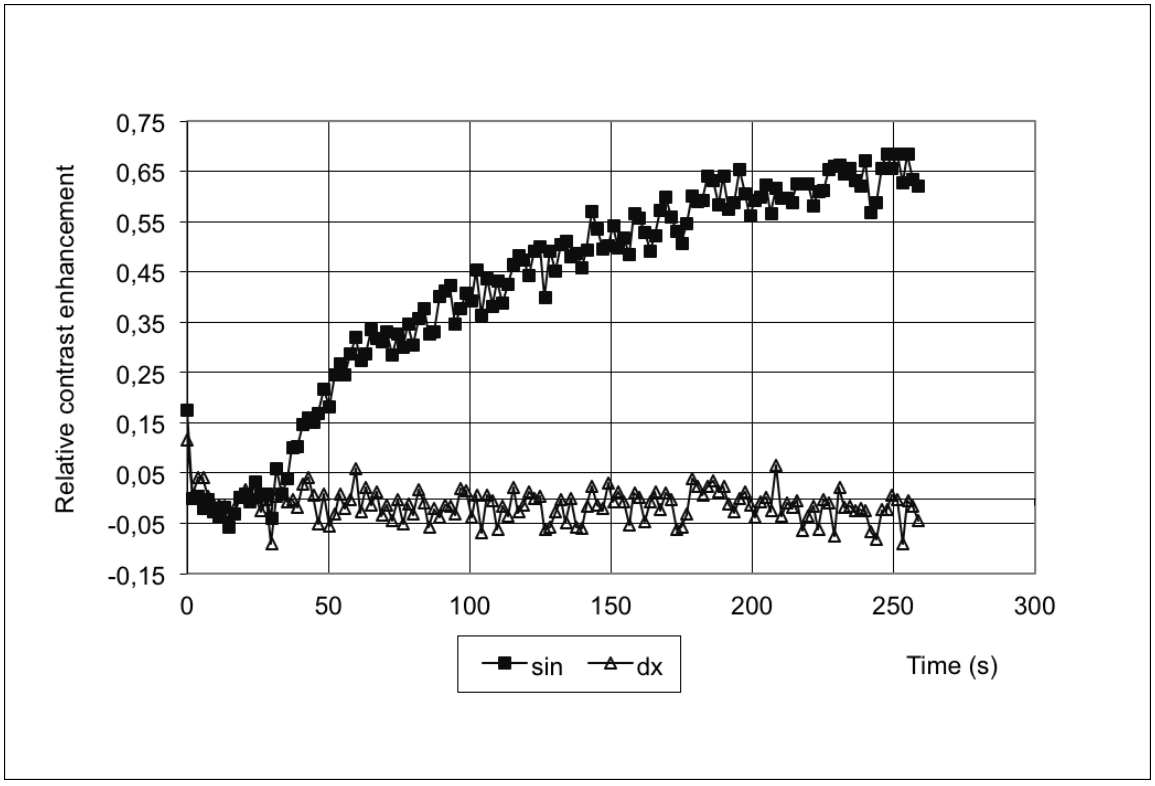

Fig. 1A. The signal intensities as a function of time measured from testicles of a patient with a torsion of the spermatic cord. A flat curve is obtained from the signals of the ischemic right testicle (dx) and an ascending curve from the normal left testicle (sin).

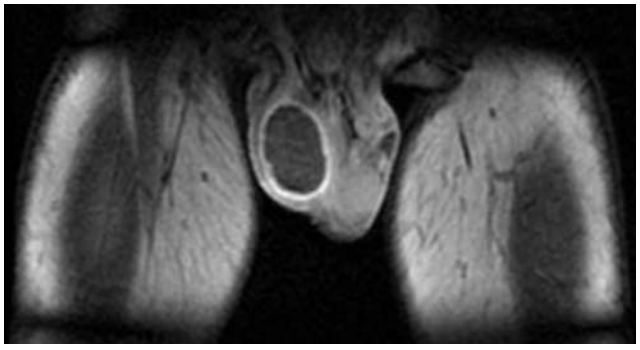

Fig. 1B. Dynamic contrast enhanced MRI image of testicles of a patient with right-sided torsion of the spermatic cord. Uptake of the gadolinium in the affected testicle is missing.

TABLE 1

Patients with acute scrotum and diagnoses.

Diagnosis	N = number of patients (17)
Torsion of testis	3
Torsion of testicular appendage	2
Epididymitis	4
Intermittent torsion	2
Hydrocele	1
Haematoma	1
Idiopathic scrotal oedema	1
Contusion of scrotum	1
Testicular pain	2

MRI findings were consistent with clinical history and physical examination; also the affected side had a good gadolinium contrast accumulation.

A representative contrast accumulation curve of a ten year old with epididymitis can be seen on figure 2A. There had been pain, redness and oedema for two days in right scrotum area without trauma and the boy was treated conservatively. Figure 2A demonstrates hyperaemia, increased testicular hyperperfusion of the affected (right) side. Figure 2B shows T1 image of epididymitis of right testis.

There was a trend towards restriction of water diffusion as measured by ADC values, but the disparity was not statistically significant.

The torsion of testicular appendage was also demonstrated by MRI. A nine year old boy had had pain, tenderness and oedema in the left scrotum area for three days. Doppler ultrasound was performed on the first day and circulation of the testis was assured; epididymal region was enhanced leading to a clinical diagnosis of epididymitis. However, two days afterwards because of severe oedema and pain, an operation and exploration was performed. Torsion of testicular appendage was found and treated (figure 3A). As with the case of epididymitis (figure 2A), torsion of testicular appendage leads to hyperperfusion of the affected side. Figure 3B demonstrates T1 image of torsion of left testicular appendage.

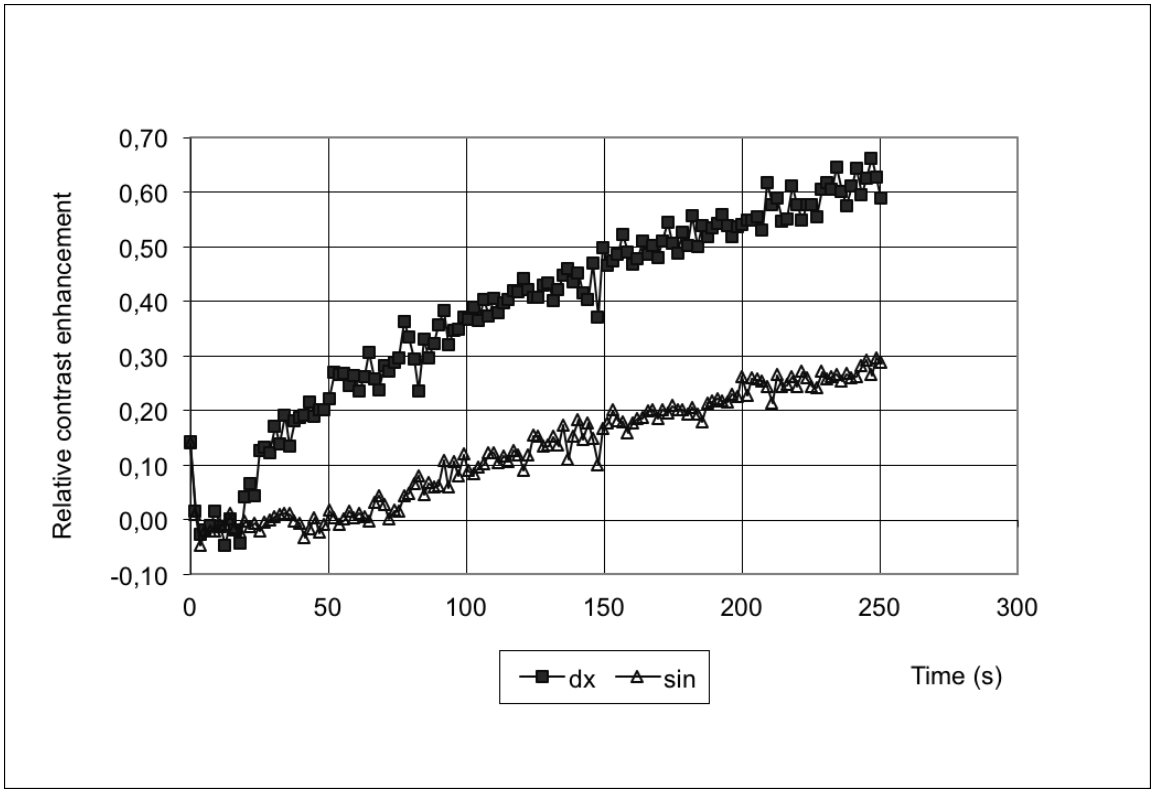

Fig. 2A. The signal intensities as a function of time measured from testicles of a patient with a right-sided epididymitis. Both curves are ascending, but due to increased circulation the slope is higher in the affected (dx) than in the left side (sin).

DISCUSSION

Acute scrotum is not an unusual clinical diagnosis among young boys and men. Approximately one in 4000 males will have testicular torsion by the age of 25, mostly between 12 and 18 years of age (10). MRI is a highly specific and sensitive imaging modality for evaluation of scrotal pain (11). Testicular torsion could be found by distinguishing the whirlpool pattern and the knot in spermatic cord. When MRI is performed with contrast enhancement, also ischemia caused by torsion of a testicle can be detected. Our research group has earlier successfully shown that diffusion weighted CE-MRI is 100% sensitive in diagnosing testicular ischemia in rats (8,9). This study was conducted to test the same method as a diagnostic tool in humans with acute scrotal pain. We have adjusted parameters suitable for dynamic MRI in a clinical material.

In the present study, young men and boys with acute scrotal pain were evaluated with dynamic CE-MRI in addition to a routine physical and ultrasonographic examination. Testicular ischemia was found in three patients with testicular torsion by comparing the ROI values between the testicles; a testicle with a normal blood supply showed an increasing signal intensity after iv-gadolinium injection, while an ischemic testicle gave only base-line consistent signal. The ROI values are displayed as a curve showing the average signal intensity as a function of time. A clinician with no specific knowledge on MRI can easily see the difference between a flat ROI curve of a testicle with torsion and an ascendant normal curve of the contralateral testicle. To our knowledge this is the first study that demonstrates a clear lack of dynamic contrast enhancement in testis torsion patients. Fur-

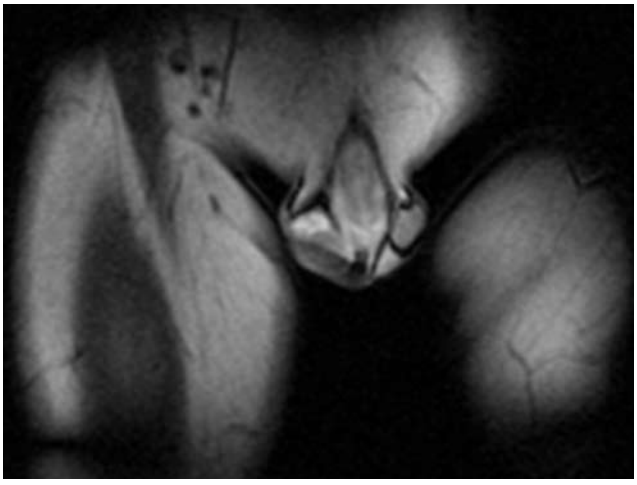

Fig. 2B. Dynamic contrast enhanced MRI image of testicles of a patient with right-sided epididymitis. Uptake of the gadolinium in the right epididymis is enhanced, but the testicles themselves show equal signal intensity.

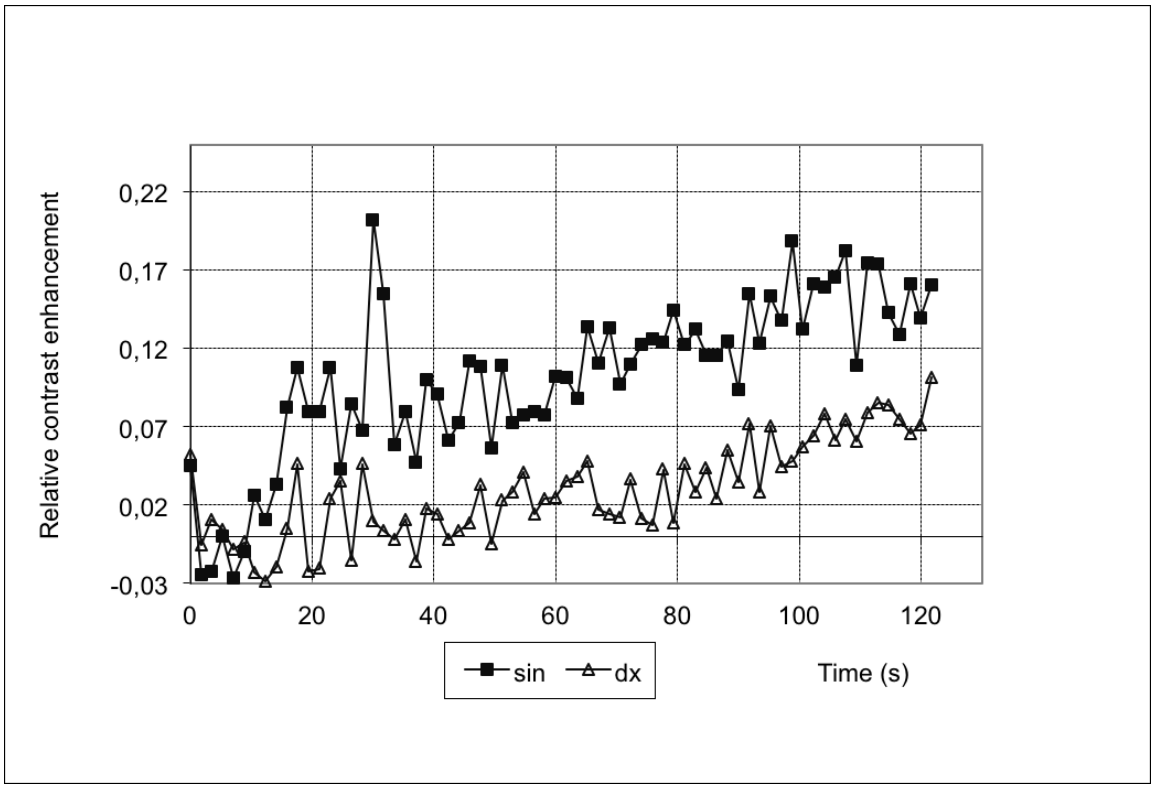

Fig. 3A. The signal intensities as a function of time measured from testicles of a patient with a left-sided torsion of testicular appendage. Both curves are ascending, but due to inflammation of the necrotic appendage the increased circulation is shown as higher slope in the left side (sin) than in the normal right side (dx).

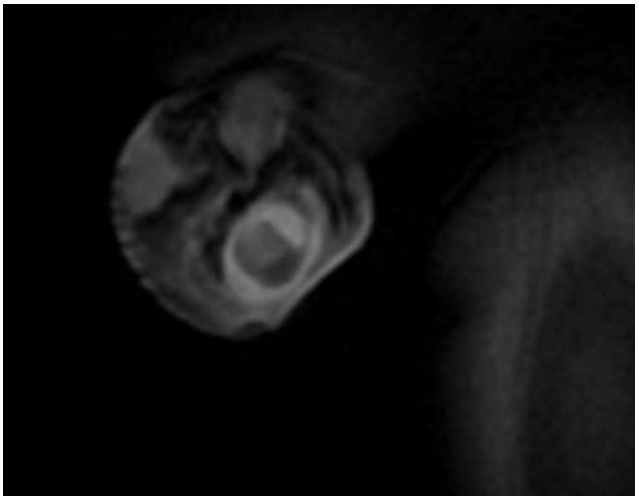

Fig. 3B. Dynamic contrast enhanced MRI image of testicles of a patient with left-sided torsion of the testicular appendage. Uptake of the gadolinium is enhanced around the left testicle. The testicles themselves show equal signal intensity.

thermore other common reasons for acute scrotum were also investigated with MRI: scrotum with epididymitis or torsion of appendage testis manifested by hyperperfusion when compared to the contralateral side. This phenomenon, however, might be caused by inflammation and increased circulation in structures around the testicle which is difficult to outline from ROI.

Although DUS is widely used for finding disorders in circulation it is reliable only in 90 % of cases with acute scrotum (4). Terai et al (12) concluded that MRI could not rule out intermittent torsion and the specificity of MRI was less than 100%, underlining the importance of good clinical examination. The MRI used was T2-weighted images with gadolinium injections. Our findings were equal; detorsion could not be distinguished.

Dynamic CE-MRI has been shown to have a better contribution to diagnostics. Watanabe (7) found sensitivity of 100% for dynamic CE-MRI and 75% for T2-weighted imaging with complete testicular torsion. In our study dynamic CE-MRI showed no enhancement of affected side with cases of testicular torsion and necrosis. There were six other patients who were operated on because of acute scrotum. In these patients the DUS and the dynamic CE-MRI showed normal testicular circulation in four testicles, but based on clinical findings a clinician made a decision for scrotal exploration. In two patients testicular circulation seemed to be poor by DUS but normal by dynamic CE-MRI. One of the patients had spontaneous detorsion of the twisted testicle between the examinations, but the other one had epidymitis. So, in this study accuracies of DUS and dynamic CE-MRI were 94% and 100%.

The Diffusion-weighted images are widely used in neuroimaging, especially in detecting acute ischemia. Otherwise there is scarce documentation of the effect of ischemia on parenchyma organs and we neither found out considerable results.

Although MRI could be a valuable diagnostic tool in avoiding unnecessary surgery, its utilization has limitations. Availability of an urgent MRI study by an experienced radiologist may be difficult and younger patients need sometimes anaesthesia for MRI, which makes MRI less preferable compared to DUS (13). In this study, DUS revealed ischemia in all three testicles with torsion but in six patients a torsion couldn't be excluded in certain by DUS and these patients were operated on.

The challenge of distinguishing true testicular torsions from other causes of acute scrotum still remains. As soon as the patient with acute scrotal pain arrives at the surgical unit, careful history, good physical examination and clinical evaluation together with DUS is still a golden standard. In some cases, however, when there is a bias between clinical and DUS findings or especially when the exploration of the scrotum is not desirable e.g. because of poor skin condition, trauma or possible infection inside the scrotum, a diffusion weighted CE-MRI could assist in making decision of operation. The poor availability of MRI decreases its present value in clinical practise; but in selected cases its outstanding accuracy makes it an interesting addition to the present diagnostic armamentarium.

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