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Original Article

Long time follow-up for patients with testicular torsion: new findings

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Abstract: Background: Testicular torsion is the major urologic emergency. If not treated promptly, this condition can result in testicular necrosis or long-term functional impairment. At present, there are few paper about long time follow-up of these patients. The primary objective of our study is to report the long-term clinical-instrumental data (mean follow-up 12 years) of patients treated for testicular torsion. Methods: We considered patients treated for testicular torsion during the period between 1997 and 2017. Inclusion and exclusion criteria were created. Patients were contacted by phone between December 2021 and January 2022. Each patient underwent clinical and ultrasonographic evaluation, and in addition, some subjects were offered additional tests (hormonal assays and semen analysis). Results: During the study period, 22 patients were treated for testicular torsion. From the ultrasonographic study, it was found that the volume of the affected testis is reduced and it is associated with microcalcifications and heterogeneous echogenicity. Morphovolumetric recovery seems to be more related to age of onset than to the degree of torsion. Conclusions: Based on our results we can state that affected testes, if preserved, grow less and have altered ultrasonographic morphology. Clinically, the age of onset of torsion seems more important than the degree of torsion.

Keywords: Fertility, follow-up, pediatric, testes, torsion

Introduction

Testicular torsion (TT) may result in altered blood supply and possible secondary transient or permanent ischaemic damage [1].

The annual incidence of this condition has been reported to be 3.8 cases per 100,000 males younger than 18 years [2].

The identification of the aetiological factors underlying testicular torsion is not easy. However, a number of genetic and environmental factors, a positive history of previous trauma, the abnormal conformation of the tunica and the presence of an increased cremasteric reflex have been reported to be predisposing factors [1, 3]. Finally, it should be mentioned that cryptorchid testicle and oscillating testicle are also risk factors [4].

Various studies report the existence of a time window of 4-8 hours, after which significant damage occurs. Although most patients present with different symptoms and timing, it is recommended to perform exploratory surgery as soon as possible if testicular torsion is suspected [5]; Urgent surgical treatment is now the gold standard for both definitive diagnosis and management of the condition [1, 6].

Currently there are only a few studies in the literature, concentrated in the last 20 years, concerning the long-term evaluation of testicular torsion outcomes, especially on testicular function and quality of tissue. These paper reported

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different outcomes about testicular function, but really no data about the quality of tissue and parenchyma are reported.

The aim of our study is to investigate gonadal quality in patients with a history of testicular torsion from childhood to adolescence. Analysing the data obtained from long time follow-up, we could find clinical and instrumental evidence associated with a probable alteration of fertile potential in order to avoid infertility.

Material and methods

Study population

We considered patients treated for testicular torsion at our Hospital. To obtain a long-term follow-up of at least 5 years after surgery, patients treated from 1996 to 2017 were considered. All patients had to be over 18 years of age at the time of selection; subjects treated before 1997 (due to lack of searchable operating records) and subjects treated after 2017 (thus with lower follow-up) were excluded from the study.

The research was approved by the IRB of the Pediatric Fertility Lab under number 2021/PFL6, oral and written consent was obtained by each patients or parents. Ethical approval was obtained under number CESC 2021-TORSION.

All medical charts of the Pediatric Surgery Unit since 1997 were consulted, searching for the surgical diagnosis of 'testicular torsion'. For more recent data, after 2013, the electronic ORMAWEB surgical register was consulted by entering the coding of testicular torsion (ICD-9 code 608.20-608.21-608.22) as the disease search code.

We defined criteria for inclusion and exclusion from the study before consulting the surgical reports.

Inclusion criteria: Surgery for single- or bilateral testicular torsion; Torsion was defined as twisted testes more than 180° detected during surgery; Patients currently alive and contactable by telephone; Patients who both accepted the telephone contact and performed the proposed clinical follow-up visit.

We considered as exclusion criteria: Incomplete data; Patients who have undergone other surgeries prior to testicular torsion or afterwards, excluding only re-torsion (crucial for epidemiological data); Patients diagnosed with testicular torsion pre-operatively but not confirmed at surgery.

Preliminary contact

All patient data were obtained via the GECOS operating system after approval by the Medical Directorate. The patients were contacted by telephone between December 2021 and January 2022, by the same surgeon, and the purpose of the study and the intention to perform an andrological check-up were explained and the date of the appointment agreed upon.

Andrological examination

During the examination, additional specific questions were asked about andrological health, including the quality of the erection, any problems with ejaculation, testicular pain, or lower urinary tract symptoms (L.U.T.S.-Low urinary tract symptoms).

During the objective examination, scrotal skin, penile shaft, urethral meatus, preputial frenulum and gonad volume were checked. All visit were done by an experienced surgeon.

All patients underwent scrotal ultrasound with measurement of the volume of the gonads, evaluation of the quality of the parenchyma (accurately reporting the presence of diffuse or focal alterations), presence of lesions, presence of microcalcifications (quantifying their entity and number and classifying them as mild if in the presence of 5-10 hyperechogenic spots per scan moderate, in the presence of 10-20 hyperechogenic spots per scan; severe or 'starry sky', in the presence of >20 hyperechogenic spots per scan [7]), morphology of the epididymis and possible presence of varicocele. All the ultrasound were performed by the same radiologist skilled in pediatric and adolescent andrology [7, 8].

A Siemens Sonoline Elegra Ultrasound Imaging System (Siemens AG, Munich, Germany) with a 7.5 MHz linear probe was used for the ultrasound scan. Testicular volume was calculated

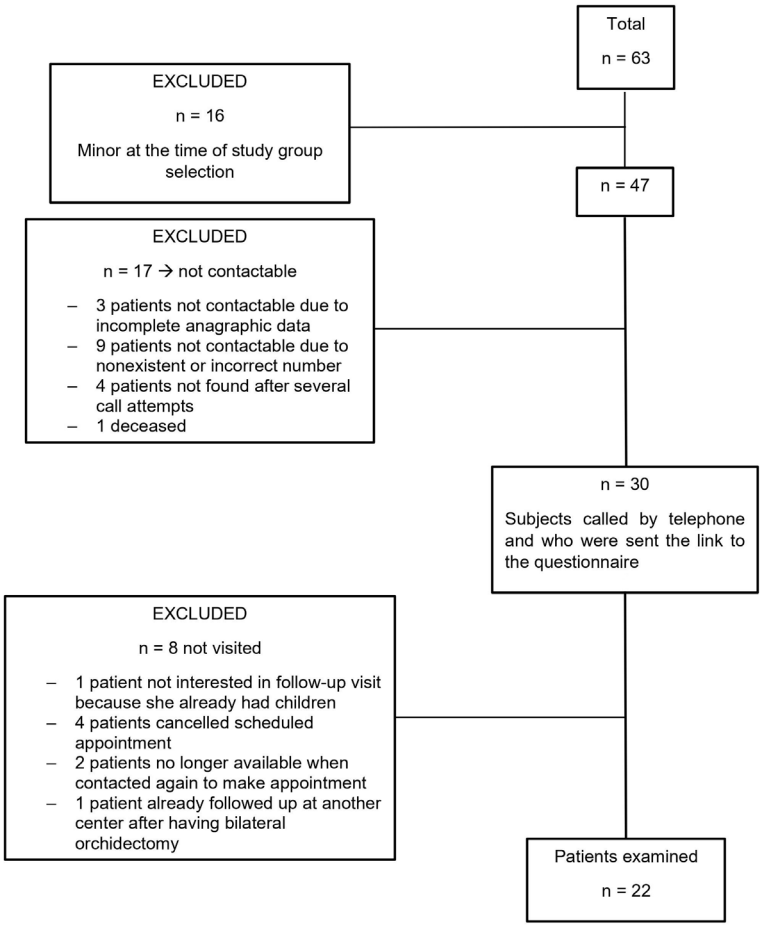

Figure 1. Patients selection: inclusion and exclusion criteria for the study. Long time follow-up.

using Lambert's formula Vol (ml) = 0.71 × L × W × H [9].

Proposed follow-up

All patients were offered seminal fluid analysis, a test that could be performed under an agreement with the Centre for Medically Assisted Procreation of the Azienda Ospedaliera Universitaria Integrata of Verona.

Upon completion, it was also offered to perform a haematochemical sampling to measure the hormone balance (FSH, LH, Testosterone).

The results were then compared with clinical and ultrasound data.

Statistical analysis

Student's t-test (two-tailed) and chi-square test were conducted. Data about right and left testes, recovery, volume and number of microcalcifications were assessed by the Mann-Whitney test. Differences between the right and left testicles were evaluated by the paired t-test for ultraousnd parameters and the Wilcoxon matched-pairs signed-rank test for their volume, grade of torsion, number of microcalcifications and age at surgery. The correlations between the ultrasound results and the sperm parameters, were evaluated by Spearman's test. All statistical analyses were performed using SPSS (v.15.0) software. A $P<0.05$ was considered as significant.

Results

*Study population (**Figure 1**)*

From November 1997 to October 2021, 63 patients underwent surgery for confirmed testicular torsion. Of these, 16 were excluded because they were less than 18 years at the time of selection (born in 2004 or later), resulting in a total of 47 patients aged between 18 and 36 years.

Patients contacted by telephone were offered the possibility of an andrological check-up, investigating their interest into it and then contacting them again to make an appointment. Between December 2021 and February 2022, we visited a total of 22 patients in the andrology outpatient clinic.

According to the surgical reports, the treated patients had an age at surgery of 10.8±4.4 years (1 day-15 years). The follow-up visit took place at an average distance of 12.1±4.9 years after surgery (5 years-24 years).

*Evaluation and ultrasound parameters (**Table 1**)*

An important finding to report is that there was no correlation between age at surgery and gonad preservation ($P>0.05$).

Through the ultrasound study, it was found that during the follow-up the volume of the twisted testis was lower than the volume of the healthy testis (contralateral), 14.3±10.6 ml vs 23.9±6.4 ml respectively (P<0.05); with respect to the detection of microcalcifications (12/22 patients) no statistical difference was found in relation to the volume of the pathological gonads, however a pathological testis volume of less than 15 ml was associated with a higher number of microcalcifications (>10) (P<0.05) (**Figures 2**, **3**).

Regarding the parenchyma quality and echogenicity, no statistical differences were found with respect to volume (P>0.05). Interestingly, there was no difference between the volume of the 'healthy' testis if operated before or after puberty (22.7±5.7 ml vs 23.8±5.8 ml) (P>0.05), but this difference was significant for the pathological gonads 19.1±7.1 ml vs 22.7±4.5 ml. The operated testis, therefore, recovered less volume if operated before puberty (P<0.05).

Analysing the ultrasound results further, no statistical difference was noted between those who had homogeneity of parenchyma between healthy and operated testis (21.1±7.3 ml vs 23.1±5.9 ml) but there was a statistical difference in volume in subjects with different homogeneity between the two gonads (15.9±8 ml vs 24.2±5.6 ml) (P<0.05). This mean that it is essential to perform ultrasound not only to evaluate volume but also quality of tissue.

Considering instead monorchid patients in comparison with patients with two gonads (surgically treated but with derotated testes), it was possible to show a statistical difference between the volume of the "healthy/non torsed testes" testis but only in the prepubertal operated patient (<12 years at surgery) (30.7±7.5 ml vs 22.1±6.1 ml) (P<0.05). It was also possible to show a difference in the volume of the "healthy" testicle if the operation took place before or after puberty and in relation to the presence of a contralateral pathological testicle; thus, the healthy testicle of the monorchid patient operated pre-pubescent grows more than the healthy/non torsed testicle of the patient operated pre-pubescent but with preserved pathological testicle (P<0.05).

A fundamental aspect is the ultrasound evaluation in relation to the degree of torsion at surgery; from the analysis of the data it was possible to show that there is no relationship between degree of torsion and gonad loss (480±270 degrees vs 320±298 degrees) (P>0.05). However, if we consider the gonad volume in the long term, using the volume of 15 ml as cut-off for andrological normality associated with probable normospermia, a difference in torsion of 307.5±105 degrees vs 349.1±322 degrees was noted between those with a volume < or > of 15 ml (P<0.05) (data to be commented on in the discussion).

Finally, the presence of microcalcifications was not shown to correlate with the degrees of torsion (P>0.05); the degree of torsion also did not correlate with the quality of the testicular parenchyma (P>0.05).

Proposed andrological follow-up

During follow-up 14 subjects had a blood sample exam (14/22); analysing the hormonal values, we can report a statistical difference only on the FSH level in relation to the testicular volume of the pathological gonad < or >15 ml: 6.3±2.0 vs 4.9±1.3 (P<0.05). However, it should be noted that the average FSH level in the entire study population was higher than the healthy general population (data in the Pediatric Fertility Lab database), albeit within the normal range, thus demonstrating that unilateral testicular pathology can alter gonadotropin levels. With respect to the remaining hormones tested, no statistical correlation could be shown.

At the time of the study 10 patients (2 monorchid patient) performed semen analysis and no major alterations were reported (W.H.O. 2021 criteria); among these patients it was possible to show that there was a difference in quality (motility, morphology, and sperm count) between monorchid patients and patients with 2 gonads. Only total sperm count and motility were higher in younger patients (less than 25 years) (**Table 2**).

Discussion

Testicular torsion represents the major emergency in urology. The resulting impairment of the testicular blood supply is associated with reversible or irreversible parenchymal damage related to both the extent of torsion and the time of torsion [1-9].

Table 1. Patients data and characteristics

Gonad preservation
• No correlation with age at surgery (P>0.05)
Volume
• Twisted testis < healthy testis (14.3±10.6 ml vs 23.9±6.4 ml respectively (P<0.05)
• No difference between healthy testis if operated before or after puberty (22.7±5.7 ml vs 23.8±5.8 ml) (P>0.05)
BUT
significant difference for the pathological gonads (19.1±7.1 ml vs 22.7±4.5 ml) (P<0.05)
• If homogeneity of parenchyma, no statistical difference between healthy and operated testis (21.1±7.3 ml vs 23.1±5.9 ml) (P>0.05)
BUT
statistical difference in subjects with different homogeneity between the two gonads (15.9±8 ml vs 24.2±5.6 ml) (P<0.05)
• Monorchid vs two gonads:
-Prepubertal operated patients → difference between the volume of the "healthy" (30.7±7.5 ml vs 22.1±6.1 ml) (P<0.05)
-Healthy testicle in monorchid patient operated pre-pubescent > patient operated pre-pubescent but with preserved pathological testicle (P<0.05)
Microcalcifications
• 12/22 patients (55%)
• No correlation with volume of pathological testis (P>0.05)
BUT
pathological testis volume of less than 15 ml was associated with a higher number of microcalcifications (>10) (P<0.05)
Degree of torsion
• No relationship with gonad loss (480±270 degrees vs 320±298 degrees) (P>0.05)
BUT
Difference in torsion of 307.5±105 degrees vs 349.1±322 degrees between those with a volume < or > of 15 ml (P<0.05)
• No correlation with the presence of microcalcifications (P>0.05)
• No correlation with the quality of the testicular parenchyma (P>0.05)

Figure 2. Testicular volume of the affected testes: long time follow-up after 12 yrs. Final effect of torsion with small testicular volume and abnormal parenchyma.

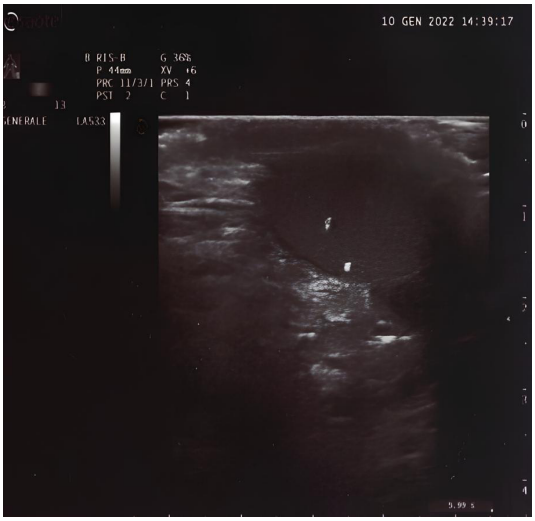

Figure 3. Microcalcifications on the treated testes: at 10 yrs follow-up from surgery, the affected testes is small with calcifications, and it reflects the abnormal function.

As far as management is concerned, it is recommended to attempt manual detorsion of the testis in all patients whenever possible (the main limitation being the intense scrotal pain reported by the patient) [6, 10]. It should be emphasised, however, that successful detorsion (defined on the basis of physical examination and pain regression) does not exclude the need for surgery and that the prolonged waiting time for surgery has been shown to be associated with a consistent alteration of the blood supply in any case [11].

However, the literature is still controversial both on the parameters to be used to perform orchidectomy and on the clinical and biological evolution of a preserved hypofunctioning or atrophic testis; long-term follow-ups are therefore crucial [12, 13].

According to the EAU guidelines, patients with previous testicular torsion require follow-up to monitor the development of complications [6].

Testicular ultrasound for at least 18 months after torsion is recommended with also hormonal tests [12].

Long-term ultrasound assessment

Cost et al. reported a higher rate of orchidectomy in subjects younger than 9 years of age compared to those older than 10 years, and the study by Barada et al. found that subjects younger than 18 years of age tend to present to the specialist later, resulting in a higher risk of gonadal loss. In contrast, other authors report a higher number of subjects undergoing orchidectomy with increasing age [14].

One finding in the literature deserves attention in relation to testicular volume, the type of surgery and the period in which it took place: according to Zhang et al., the pregnancy rate appears to be higher in patients operated on during childhood than in adolescence. In patients with pre-pubertal torsion, no significant differences in pregnancy rate or time to conception are reported between orchiectomised and non-orchiectomised patients. In contrast, among patients operated on in adolescence, those who have had orchiectomy have a significantly longer time to conception than those in whom the gonad was preserved. In general, these studies have shown that preservation of the testis results in a higher pregnancy rate. However, even in the case of orchiectomy, the fertility rate is very close to that of healthy couples (approximately 84% in orchiectomised patients versus 85% in healthy couples) [15].

Among our study results, it was found that there was a significant difference in the volume

Table 2. Seminal data

PATIENTS			
• 10 patients: 2 monorchid patients-8 patients with 2 testes (W.H.O. 2021 criteria)			
Seminal data	Group 2 testes	Monorchid	*p* value
• Volume	mL (mean) 1.5-5 (2.8)	1.5-3.6 (3.1)	>0.05
Motility	42%-68% (54.04%)	45%-66% (62.73%)	<0.05
Morphology	4%-8% (4.8%)	4%-7% (5.9%)	<0.05
• Sperm count	21-182 × 6 10^6 (mean 58.85 6 10^6)	19-250 × 6 10^6 (73.81 6 10^6)	<0.05
Microcalcifications			
• No differences between number and semen quality			
Degree of torsion: No correlation between semen quality and grade of torsion			

of the twisted testis if operated on before or after puberty, with less recovery in the pre-pubertal patient. In contrast, there was no difference in healthy testicle volume between patients operated on before or after puberty. This would seem to be in disagreement with what other authors have observed regarding pregnancy rate/conception time (higher in the case of pre-pubertal torsion), if we consider the relationship between testicular volume and spermiogenesis. Furthermore, as discussed above, our results suggest that, in pre-pubertal patients, there is a statistically significant difference in healthy testis volume between monorchids and gonad-preserved patients: the monorchid has a larger healthy testis volume. It must be commented that in andrology, the pregnancy rate for testicular pathology is always difficult and controversial to prove.

Some authors report also that an abnormal development of the affected testis after detorsion. The smaller volume of the affected testis compared to the healthy one and compared to controls are, according to these authors, independent of the duration and type of torsion [16].

Our results, similarly to these observations, show that there is a statistically significant volumetric difference between the smaller detached testis and the healthy testis; however, this difference was observed in patients with an ultrasound-impaired testis, whereas it is not significant in the case of subjects with a homogenous testis. This means that a testicle with altered parenchyma tends to recover less than a testicle with an ultrasound uninjured parenchyma, which is comparable in size to the contralateral testicle, and therefore that, if intervention is successful before there is actual parenchymal damage, then the gonad has a normal development.

However, contrary to what has been observed by other authors, we have shown that the presence of a testicular volume >15 mL (using 15 volume as the cut-off for andrological normality) generally correlates with a higher degree of torsion, which could be explained in relation to the fact that a higher number of torsion turns probably corresponds to more pain and thus to faster treatment.

Further on, an interesting finding emerged from our study, which has not been reported by others in the literature, namely that the testis of a monorchid patient operated on in the pre-puberal period grows more than the healthy testis of the patient operated on in the pre-pubertal period but with a preserved pathological testis; this could be due to the fact that the preservation of a functionally impaired gonad can alter the hormonal axis affecting the growth of the healthy contralateral testis.

A review of the literature reveals some disagreement as to whether or not the degree of torsion is a predictive factor for testicular loss [12]. Dias et al. in their study found a clear correlation between this finding and gonad loss [17]. In contrast, according to other studies, the number of turns would not be a predictor of testicular viability [18, 19].

From our study, it emerged that there was no link between the rate of orchiectomy and the severity of torsion.

Moreover, it has been reported in medical literature that during ultrasound follow-up for tes-

ticular torsion (mean time 3 years) there was ultrasound inhomogeneity of the affected testis in more than 30% of cases. Also, this field did not correlate with the type of torsion (complete or incomplete) and its duration [16].

Our results also show no correlation between ultrasound quality of the parenchyma and the degree of torsion. The only data that we cannot refute is the correlation with the duration of torsion (data not available due to lack of it in the surgical record).

An important issue inherent to testicular torsion and long-term parenchymal damage is the presence of testicular microcalcifications (MT). Testicular microcalcifications are incidental ultrasound findings, and in andrological patients, along with inhomogeneities of the testicular parenchyma on ultrasounds, are frequent findings affecting almost 9% of subjects [20, 21]. Several studies have reported a correlation between testicular microcalcifications, especially in clusters, and the risk of developing testicular carcinoma. However, the results are ambiguous: on the one hand, Wang et al. reported a 12-fold higher incidence of testicular cancer in MT subjects than in non-MT subjects and in the general population; on the other hand, studies based on follow-up programmes, such as that of DeCastro et al., reported a very low incidence of cancer in patients followed long-term (specifically in the study cited above, after 64 months of observation, only 1 patient developed testicular cancer). Moreover, there is still open debate about the association between MT and male infertility, and subfertility itself is reported to be a risk factor for the development of testicular cancer [21].

According to the EAU guidelines, in the presence of testicular microlithiasis associated with other risk factors (previous germ cell tumour, history of cryptorchidism, testicular volume <12 ml, etc.) and in the absence of an obvious focal mass in either gonad, annual ultrasound follow-up and self-palpation is recommended [21].

During our long-term ultrasound follow-up (average 12 years), testicular microcalcifications were found in 52% of the cases, with no correlation with the volume of the twisted gonad but a correlation with a pathological volume of less than 15 ml (andrological lower limit associated with hypospermatogenesis).

So, following data that have emerged, it would be useful to propose an annual check-up to all patients, especially those with testicular volume <15 ml, combined with self-examination. At present there are no data in medical literature about this condition and long time follow-up (testicular torsion and microcalcifications).

Spermiogram and hormone tests

With reference to spermiogram outcomes, some authors report that unilateral testicular torsion significantly interferes with spermiogenesis in about half of the cases, and that in a further 20%, it causes borderline changes in the seminal fluid. Subfertility, understood as a sperm count <20 million/mL, affects, according to some studies, almost 40% of patients operated for testicular torsion, with normal seminal fluid examination in only 5-50% of cases [9].

Although the sample of patients who underwent a spermiogram at the time of the study was rather limited, it is interesting to note that in none of these cases were significant alterations in the spermiogram. This is true if we consider the W.H.O. criteria, but as reported in the results section, it was possible to show a difference in semen quality between patients. These data are important because semen analysis is not only a range.

Finally, in accordance with the findings of Arap et al. [22], the blood sample taken from 14 of the 22 patients showed an average FSH level higher than the general healthy population, albeit within the normal range. This supports the concept that testicular torsion, even unilateral, can alter the hormonal axis. This is further supported by evidence of a statistical difference between FSH levels in subjects with testicular volume <15 ml and >15 ml. This correlation is essential if associated with semen quality [23].

Our study showed some limitations: 1- basic clinical data concerning torsion were missing, as medical records were not consulted. Therefore, it was not possible to associate the time of onset of symptoms and the time of torsion before surgery with the long-term instru-

mental and clinical findings; 2- the patients were operated on by different surgeons and therefore the choice of removing the testicle or derotating and retaining it could be based on different evidences and clinical aspects; 3- even the interpretation of the extent of torsion could be relative to the individual surgeon, therefore it is not possible to be sure of what described at surgery.

Among the strengths of our study, on the other hand, there is first of all that of highlighting the absence of correlation between the morphological quality of the pathological testicle in the long term (12 years after surgery) and the degree of torsion, thus demonstrating that the severity of the torsion is not fundamental in the decision to preserve the gonad at surgery. We correlate the clinical-instrumental data with the results obtained from the recent Pediatric fertility lab studies, we can state that: 1- as demonstrated in vitro, the state of suffering of the peritesticular tissues corresponds to the state of suffering of the testicular parenchyma and therefore a reduced volume, an inhomogeneous parenchyma and the presence of microcalcifications correspond to an altered gonadal function (FSH with higher levels); 2- in vitro, it has been demonstrated that the use of HCG can increase both vascularisation and cell proliferation at scrotal and testicular level, and this data translates into a clinic with a greater volume and better parenchyma. Our results showed exactly that the pathological testis in the pre-pubertal patient grows less than the pathological testis in the pubescent or developing patient, a growth that is evidently secondary to the development-related hormonal input. In vivo, therefore, a treatment with HCG in the postoperative period, as demonstrated in vitro, could mimic the hormonal stimulus of the peripubertal period, with subsequent increase in vascularization and cell proliferation, allowing greater gonadal recovery [24, 25].

Conclusions

There are few studies in the literature reporting long-term data on testicular torsion, the quality of the preserved gonad and the andrological appearance of these patients [26-30].

Our results demonstrate that long time follow-up is essential for these patients because monorchid patient operated on in the pre-puberal period had their testes that grows more than the healthy testis of the patient operated on in the pre-pubertal period but with a preserved pathological testis; patients with testicular torsion may have different hormonal and semen fluid alterations and this means that it is important to follow them till adulthood to avoid problems with fertility. Many doubt still remain among pathological testes and the influence of abnormal testicular function on the healthy one. This could be due to the fact that the preservation of a functionally impaired gonad can alter the hormonal axis affecting the growth of the healthy contralateral testis.

Disclosure of conflict of interest

None.

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