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Article type : Original Article

# Sperm retrieval rates in non-mosaic Klinefelter patients undergoing testicular sperm extraction: what expectations do we have in the real-life setting?

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Short title: Sperm retrieval in Klinefelter men

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**ABSTRACT**

Background: A recent meta-analysis (Corona et al, 2017) reported positive sperm retrieval rates (SRR) in 50% of patients with Klinefelter syndrome (KS) undergoing testicular sperm extraction (TESE). However, these results do not reflect the rates of SR that we observe in clinical practice. We assessed the rate and potential predictors of SR in Klinefelter patients in the real-life setting.

Materials and Methods: We reviewed clinical data of 103 KS men who underwent TESE between 08/2008 and 03/2019 at 5 tertiary referral Andrology centers. Patients underwent testis ultrasound, hormonal evaluation and genetic testing. All patients were azoospermic based on the 2010 WHO reference criteria. Conventional (cTESE) or microsurgical TESE (mTESE) were performed based on the surgeon's preference. We used descriptive statistics and logistic regression models to describe the whole cohort.

Results: Median (IQR) patient's age was 32 (24-37) years. Baseline serum FSH and total testosterone levels were 29.5 (19.9-40.9) mUI/mL and 3.8 (2.5-11.0) ng/mL, respectively. Conventional and mTESE were performed in 38 (36.5%) and 65 (63.5%) men, respectively. The sperm retrieval rate was 21.4% (22/103 men). Fifteen patients used sperm for ICSI and 5 ended in live birth children. Patients with positive SR were similar to those with a negative TESE in terms of clinical, hormonal and procedural parameters (all $p>0.05$). Logistic regression analyses confirmed the lack of association between clinical, hormonal and procedural parameters with SR outcome.

Discussion: Given the conflicting results in the literature regarding SRR in KS, patients should be carefully counselled regarding TESE outcomes based on data from published literature and local results.

Conclusions: In the real-life setting we observed a lower SRR (21.4%) than that reported in meta-analyses in our cohort of KS patients. No associations between clinical, hormonal and procedural variables with TESE success were found.

KEYWORDS. Male infertility; Klinefelter syndrome; sperm retrieval; azoospermia; predictors

## INTRODUCTION

Klinefelter syndrome (KS) is the one of the most frequent chromosomal disorder affecting 1/500–600 male newborns in the general population (Lanfranco et al., 2004). The vast majority of the cases shows the 47,XXY karyotype, although mosaicism (46,XY/47,XXY) or higher-grade X aneuploidies can be rarely detected (Lanfranco et al., 2004). Despite its high incidence, KS frequently remains undiagnosed and it is suspected later in adulthood after a diagnostic workup for hypogonadism, couple's infertility, and/or sexual dysfunction (Bojesen et al., 2003; Corona et al., 2010; Vignozzi et al., 2010).

Approximately 90% of adult men with homogeneous KS suffer from nonobstructive azoospermia (NOA) (Forti et al., 2010), while fertility in mosaic KS seems to be less severely affected (Aksglaede and Juul, 2013). Fathering is an important aspect for Klinefelter patients. Maiburg et al. performed a survey on 260 adults with KS and showed that most couples would like to have children and show a positive attitude toward assisted-reproductive techniques (ART) (Maiburg et al., 2011). Infertility has been considered an untreatable disease in Klinefelter patients for many years. However, testicular sperm extraction (TESE), associated with ART, were found to be a valuable option for azoospermic men with KS to father a child, due to the presence of residual foci with preserved spermatogenesis (Aksglaede and Juul, 2013; Foresta et al., 1999). A recent systematic review and meta-analysis evaluated the outcomes of sperm retrieval by conventional TESE (cTESE) and by microsurgical TESE (mTESE) in 1248 individuals with KS (Corona et al., 2017). Authors reported an average sperm retrieval rate (SRR) of 44% (43% and 45% after cTESE and mTESE, respectively) (Corona et al., 2017), which is similar to that reported for men without KS (Deruyver et al., 2014). However, these meta-analytic data do not necessarily reflect the rates of SR that physician observe in clinical practice, which is typically lower than 50%. Moreover, results of meta-analysis should be interpreted according to the limitation of the study itself (inclusion of small, single center studies, effect of unadjusted confounders) (Corona et al., 2017).

These observations prompted us to conduct a multicenter collaborative study to investigate the rate of and potential predictors of sperm retrieval by TESE in a cohort of azoospermic patients with KS presenting for primary couple's infertility in the real-life setting.

## MATERIALS AND METHODS

### Patient population

After institutional review board approval, we retrospectively reviewed data from 103 consecutive patients with non-mosaic KS assessed at five academic Andrology centers for couple's primary infertility between September 2008 and March 2019.

### Infertility evaluation

According to the World Health Organization (WHO) criteria, infertility was defined as not conceiving a pregnancy after at least 12 months of unprotected intercourses regardless of whether or not a pregnancy ultimately occurs ("World Health Organization web chapter on couple's infertility. 2017. http://www.who.int/reproductivehealth/topics/infertility/definitions. Accessed May 2, 2019.," n.d.). Primary infertility was defined when a couple was never able to conceive ("World Health Organization web chapter on couple's infertility. 2017. http://www.who.int/reproductivehealth/topics/infertility/definitions. Accessed May 2, 2019.," n.d.).

Patients were assessed with a thorough self-reported medical history including age and comorbidities. The Charlson Comorbidity Index (CCI) was used to score health-significant comorbidities, coded using the International Classification of Diseases, 9$^{th}$ revision (Charlson et al., 1987; Salonia et al., 2009). Body mass index, defined as weight in kilograms by height in square meters, was calculated. Testicular volume and morphology were evaluated with ultrasound scanning and varicocele was clinically assessed in every patient (Jungwirth A. et al., 2017).

Venous blood samples were drawn from each patient between 7 AM and 11 AM after an overnight fast. Circulating serum hormone levels including follicle-stimulating hormone (FSH), luteinizing hormone (LH) and total testosterone (tT) were measured in every patient after cessation of any testosterone replacement for at least 6 months. Chromosomal analysis and genetic testing were performed in every patient (karyotype analysis and tests for Y-chromosome microdeletions and cystic fibrosis mutations) (Ventimiglia et al., 2016). Conventional R-banded karyotypes were performed with a resolution of more than 450-band level of at least 30 peripheral blood leucocytes.

Non-obstructing azoospermia (NOA) was defined as the absence of sperm due to non-obstructive causes in two consecutive semen analyses after centrifugation of the sample (Cooper et al., 2010) and

after a complete history, physical examination, endocrine profile, and chromosomal analysis. Semen samples were collected by masturbation and analysed within 2 h according to the WHO criteria.

None of the patients had hormone treatment before surgery to improve SRR (e.g. human chorionic gonadotropin, oestrogen receptor modulators or aromatase inhibitors).

**Surgical techniques**

Patients were scheduled for cTESE or mTESE based on the surgeon's preference. Informed consent was obtained after a thorough explanation of results in the literature and the invasiveness of the surgical technique. Conventional TESE was performed, under general or local anesthesia, through a small horizontal incision in the median part of the scrotal, the skin, dartos muscle, and tunica vaginalis were opened to expose the tunica albuginea. The tunica albuginea was incised for about 5 mm at the middle of the testis. Multiple testicular specimens were excised and dispersed between two glass slides, and the embryologist observed the samples under the optic microscope. If no sperm were seen in the initial sample, subsequent samples were taken from other locations, in the upper and lower pole of the testis, and eventually from the contralateral testis. Micro-TESE was performed according to the procedure reported by Schlegel et al. (Schlegel, 1999). Fourteen procedures were performed with the stepwise micro-TESE approach that included three-steps: single conventional TESE biopsy, micro-TESE on the same testis and contralateral multiple TESE (Franco et al., 2016). At the same time of testicular intervention in both procedures, a small tissue specimen was placed in Bouin's solution and sent for histopathological examination.

**Sperm identification procedure**

Immediate intraoperative evaluation of the specimens is performed by a member of the IVF laboratory in the operating room, but a subsequent and deeper research is always carried out in the laboratory. Intraoperatively, specimens are placed in human tubal fluid culture medium; isolation of individual tubules from the mass of coiled testicular tissue is achieved by initial dispersal of the testis biopsy specimen with two sterile glass slides or syringe needles, stretching the testicular parenchyma to isolate individual seminiferous tubules. Subsequently, mechanical dispersal of the tubules is accomplished by mincing the extended tubules. Intraoperatively, a "wet preparation" of the suspension is examined under phase contrast microscopy at 100X and 400X power. This intraoperative sperm assessment may require about 15-20 minutes. If no spermatozoa are seen,

contralateral procedure is performed. The samples are then further analyzed in the lab where all testicular samples are subjected to centrifugation at 1400-1800G with 5 mL human tubal fluid and carefully examined to determine the presence of spermatozoa in the pellet. In most cases, a positive research is completed in 60-90 minutes. Extra time is used in case of unsuccessful retrieval.

**ICSI procedure**

Infertility treatments, including hormonal stimulation, oocyte retrieval, oocyte vitrification, embryo culture, vitrification and transfer methods were performed as described in details elsewhere (Busnelli et al., 2014, Corti et al., 2013, Intra et al., 2016, López-Regalado et al., 2014, Restelli et al., 2014, Sarais et al., 2016). Briefly, either GnRH agonist or GnRH antagonist daily protocol was used for pituitary downregulation. The gonadotropins used for ovarian stimulation included human menopausal gonadotropins or purified urinary FSH, recombinant LH or recombinant FSH. The FSH starting dose and the type of protocol were determined according to ovarian reserve assessment, patient's age, basal hormonal status and antral follicular count. The dosage of gonadotropins varied according to the patient's ovarian response and ranged from 150 to 450 IU administered daily. Cycle monitoring was conducted with ultrasonography ovarian transvaginal and serum estradiol measurements and the frequency of patient's monitoring was dependent of the ovarian response to ovarian hyperstimulation (Corti et al., 2013). Human chorionic gonadotropin (hCG) for ovulation trigger was administered to those patients who had at least one mature follicle ≥17 mm. Vaginal oocyte retrieval was performed 36 h after the administration of hCG or recombinant hCG by transvaginal ultrasonography-guided needle aspiration under anesthesia. ICSI cycle was performed by standard techniques (Restelli et al., 2014). Embryos were transferred to the uterus either 3 days (cleavage stage) or 5 days (blastocyst stage) after oocyte retrieval. The number of embryos transferred was established according to the American Society for Reproductive Medicine guidelines (Practice Committee of the American Society for Reproductive Medicine; 2009).

In terms of sperm activation procedures, pentoxifylline is frequently used for stimulating sperm motility and improving ICSI outcomes among the five centers (Navas et al., 2017).

**Statistical methods**

Data collection followed the principles outlined in the Declaration of Helsinki. All patients signed an informed consent agreeing to share their own anonymous information for future studies. Distribution

of data was tested with the Shapiro–Wilk test. Data are presented as medians (interquartile range; IQR) or frequencies (proportions). A 95% CI was estimated for the association of categorical parameters. Exploratory analyses were initially applied to all variables; variables were retained for analysis when deemed clinically significant to the results. Descriptive statistics tested the association between clinical and hormonal variables and the sperm retrieval rate. The categorical variables between the groups were analysed using the Chi-squared and Fisher's exact tests. The continuous variables between groups were analysed using the Mann–Whitney U test.

Statistical analyses were performed using SPSS v.23 (IBM Corp., Armonk, NY, USA). All tests were two sided, and statistical significance level was determined at $P < 0.05$.

**RESULTS**

Table 1 lists clinical characteristics of 103 azoospermic patients with nonmosaic KS. Figure 1 shows the distribution of patients among the five centers. Median (IQR) patient's age was 32 (24-37) years. Baseline serum FSH and total testosterone levels were 29.5 (19.9-40.9) mUI/mL and 3.8 (2.5-11.0) ng/mL, respectively. Above all, 15 (14.5%) patients have been on chronic testosterone replacement therapy (TRT) prior to surgery (either by injection or transdermal rout). Conventional TESE, mTESE and stepwise TESE were performed in 38 (36.5%), 51 (49.5%) and 14 (13.6%) men, respectively. A bilateral procedure was performed in 88 (85.4%) patients. The sperm retrieval rate was 21.4% (22 out of 103 men). Eighteen patients cryopreserved spermatozoa for subsequent ART procedures while 4 used fresh spermatozoa for injection for a concurrent cycle of ICSI. A median of 2.54 (2-4.5) blocks was stored for sperm banking. Out of 22 men who had a positive SR, fifteen patients used sperm for ICSI and 5 ended in live birth children (four of which with frozen sperm).

Histologic reports showed Sertoli cell-only syndrome and maturation arrest in 86 (83.5%) and 17 (16.5%) patients, respectively. Median Johnsen score was 2 (2-30). Only 2 (1.9%) patients had complications related to surgery (1 scrotal haematoma and 1 wound infection).

Table 2 details patients' characteristics according to sperm retrieval outcome. Patients with positive sperm retrieval were similar to those with a negative TESE in terms of clinical, hormonal and procedural parameters (all $p>0.05$). In particular we noted a trend toward a younger age, lower FSH values and larger testicular volume in patients with positive SR than those with a negative TESE, but differences between groups were not statistically significant. The Johnsen score was higher in Klinefelter men with positive SR than those with negative sperm retrieval ($p=0.01$).

Logistic regression analyses conformed the lack of association between clinical, hormonal and procedural parameters with SR outcome (Table 3). Patient's age, FSH and testosterone values, testis volume, the use of TRT prior to surgery, the TESE approach and SCOS histology were not found to be associated with SR outcome (all $p>0.05$) (Table 3).

## DISCUSSION

With the recent improvements of TESE and ICSI procedures infertility has been no longer considered an untreatable disease in Klinefelter patients. In this context, most studies investigating TESE outcomes in patients with KS depicted conflicting results, in spite of having been generally rated of limited quality (Aksglaede and Juul, 2013; Corona et al., 2017). A recent review showed that SRR in Klinefelter patients was approximately 50% world wide, thus similar to that of men without genetic abnormalities (Deruyver et al., 2014). However, these results appear to be unrealistic and even far from what physicians typically observe in the clinical practice.

The aim of this cross-sectional, real-life study was to investigate the prevalence of and possible factors associated with a positive SR in a cohort of white-European azoospermic patients with KS undergoing TESE at five academic Andrology centers. Of clinical relevance, we found that only one out of five KS men had positive SR in the real-life setting. Moreover, we failed to find any clinical, hormonal or procedural factors associated with SRR. At least, these findings confirmed previous studies, where in contrast meta analytic data reported a significant higher SRR (Corona et al., 2017).

So far, there is a lack of reliable clinical and biological predictors for sperm retrieval success in NOA patients with KS (Franik et al., 2016; Garolla et al., 2018; Vicdan et al., 2016). Advanced paternal age has been considered a negative predictive factor for SR in Klinefelter men undergoing TESE (Emre Bakircioglu et al., 2006; Sabbaghian et al., 2014). Ozer at al. (Ozer et al., 2018) showed that TESE had better outcome before the critical age of 30.5 years, while other Authors suggested that TESE should be performed before 35 years (Okada et al., 2005). Recent evidence, however, support the lack of association between age and SR outcome (Corona et al., 2017; Franik et al., 2016; Garolla et al., 2018; Vicdan et al., 2016). It has been shown that performing TESE between 15 and 23 years did not increase the SR rate compared to adult KS patients (25–29 years) (Plotton et al., 2015). We also confirm that SRR was not influenced by patient's age in a real-life study with a large cohort of Klinefelter men. According to this view it has been postulated that the progressive hyalinization and fibrosis of seminiferous tubules that is accelerated with the onset of puberty in KS is not ubiquitous and it is possible to observe tubules with normal residual activity (Franik et al., 2016; Gies et al., 2016). The impaired spermatogenesis could also be caused by an intrinsic problem of the germ cells,

possibly linked to (epi)- genetics of the X surplus chromosome (Aksglaede and Juul, 2013; Franik et al., 2016; Gies et al., 2016).

Testicular volume has been considered a possible factor associated with TESE success in Klinefelter patients. Madgar et al. (Madgar et al., 2002), for example, showed that testicular volume was significantly higher in men with positive SRR. However, there are several studies reporting that testicular atrophy does not affect the success of SR (Corona et al., 2017; Franik et al., 2016; Garolla et al., 2018; Majzoub et al., 2016; Ozer et al., 2018; Vicdan et al., 2016). Garolla et al. (Garolla et al., 2018), indeed, observed a 23% SRR even in KS patients with testicles <1 mL. Our results support these findings since we failed to find any relationship between testicular volume and SRR in NOA patients with KS.

There are conflicting results showing the association between serum hormones levels and TESE outcome in Klinefelter patients. Higher serum testosterone levels were found in Klinefelter men with positive SR as compared to those with negative SR (Ozer et al., 2018; Sabbaghian et al., 2014). Similarly, the combination of high testosterone levels and low levels of LH was considered as positive predictive marker for SR in in both adolescents and adults with KS (Cissen et al., 2016; Rohayem et al., 2015). Conversely, recent meta analytic data showed that serum hormones levels did not influence SRR in Klinefelter patients (Corona et al., 2017; Franik et al., 2016). We also showed that testosterone, FSH and LH levels were not different according to TESE outcome in our cohort of Klinefelter patients; however, additional studies are needed to explore the predictive value of serum hormones levels in KS.

Testosterone treatment in KS has been previously considered as a negative factor for sperm recovery (Schiff et al., 2005). In our population TRT was not associated with worse SRR as compared to that of men who did not received any supplementation. Our findings are in line with previous studies that did not show any impact of testosterone treatment on spermatogenesis in adolescents and adults Klinefelter men (Corona et al., 2017; Franik et al., 2016; Garolla et al., 2018; Plotton et al., 2015). Therefore, some authors did not recommend postponing androgen treatment in adolescent boys with KS for fear of impairing their TESE results (Franik et al., 2016).

Lastly, the superiority of mTESE as compared to cTESE in NOA men has been extensively investigated in the previous literature but with conflicting results (Corona et al., 2019). This is

particularly true also in the Klinefelter population. Only few reports have shown that mTESE could be associated with better SRR than cTESE (Majzoub et al., 2016; Mehta and Paduch, 2012). Conversely, our results, in agreement with recent studies (Corona et al., 2017; Vicdan et al., 2016), showed that TESE technique is not associated with SRR.

The clinical strength of our study is several-fold. First, we showed a low rate of positive sperm retrieval (up to 21%) in azoospermic men with KS in the real-life setting, thus suggesting that the crude data coming from meta-analytic studies cannot be routinely used in the everyday clinical practice. Second, we cross-sectionally showed that clinical, hormonal and procedural factors are unable to predict the SRR in patients with KS. In this context, we believe that Klinefelter patients should be carefully counselled regarding their chance of retrieving spermatozoa after TESE.

Further strength of present study is that we have comprehensively investigated a large homogenous group of patients with a detailed hormonal evaluation, and an accurate assessment of possible confounders for impaired semen parameters, such as recreational habits and health comorbidities (Iwatsuki et al., 2017; Ragab et al., 2018). However, none of these parameters were found to be associated with SRR.

Our study is not devoid of limitations. First, this study was a multicenter-based cross-sectional investigation, thus raising the possibility of selection biases. Second, despite the fact that we analyzed a relatively large, homogeneous, same-race cohort of infertile KS men, our study could be underpowered to infer association between predictors and SR outcome; thereof, larger studies are needed to validate our findings. Third, our data did not allow us to investigate patient's compliance to TRT. Lastly, because of the low number of events (n=22) we were unable to perform a multivariable logistic regression analysis to better explore potential predictors of positive SR in KS. However, since the univariable analysis showed no association between any predictors and SR, it is unlikely that these results would change after adjustment.

## CONCLUSIONS

The results of this cross-sectional, multicenter study revealed that the SRR (21.4%) in a large cohort of azoospermic KS patients submitted to TESE is lower than that reported in recent meta-analysis but it is probably reflective of a real-life setting. Of clinical importance, no associations between clinical, hormonal, and procedural parameters with TESE success were found.

Overall, these observations pointed out the importance of an accurate counselling for Klinefelter patients in terms of sperm recovery based on data from published literature and local results. Given the conflicting evidence in the literature on this topic, further large cohort studies are needed to corroborate our results.

ACKNOLEDGEMENTS: None.

**Author contributions**

L.B. designed the study, collected data, performed statistical analyses and wrote the manuscript.

F.P. designed the study, collected data and performed statistical analyses.

M.P; M.S; P.C; designed the study and collected data.

A.F.; E.RC.; J.SG.; L.BA; collected data

F.S.; A.S.; G.G.; M.F.; M.T.; C.C.; F.G. collected data, interpreted results, revised the manuscript critically.

L.T.; F.C.; L.R.; P.G.; F.M.; P.G.; F.M.; J.SC.; A.S.; E.M. interpreted results, revised the manuscript critically

All authors and co-authors approved the final version of the manuscript to be published

DISCLOSURE STATEMENT: No conflict of financial interest to declare.

FUNDING: No funding source.

**Figure caption**

Figure 1. Distribution of patients among the five Andrology centers.

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**Table 1: Characteristics and descriptive statistics of the whole cohort (No.=103)**

| | |
|---|---|
| Age (years) | |
| Median (IQR) | 32.0 (24-37) |
| Range | 18 – 55 |
| BMI [Kg/m2] | |
| Median (IQR) | 25.0 (22.7-26.2) |
| Range | 18.0 – 37.0 |
| CCI [No. (%)] | |
| CCI 0 | 96 (93.2) |
| CCI≥ 1 | 7 (6.8) |
| Testicular volume (ml) | |
| Median (IQR) | 3.0 (2-6) |
| Range | 1 – 10 |
| Current Smokers [No. (%)] | 31 (30.1) |
| Varicocele [No. (%)] | 6 (5.8) |
| Cryptorchidism [No. (%)] | 7 (6.8) |
| FSH (mUI/mL) | |
| Median (IQR) | 29.5 (19.9-40.9) |
| Range | 3.0 – 100.0 |
| LH (mUI/mL) | |
| Median (IQR) | 17.6 (12.8-22.8) |
| Range | 6.0 – 50.0 |
| tT (ng/mL) | |
| Median (IQR) | 3.8 (2.5-11.0) |

| | |
|---|---|
| Range | 0.3 – 24.9 |
| TRT prior to surgery [No. (%)] | 15 (14.5%) |
| Surgery Type [No. (%)] | |
| cTESE | 38 (36.5) |
| mTESE | 51 (49.5) |
| Stepwise mTESE | 14 (13.6) |
| Bilateral surgery [No. (%)] | 88 (85.4%) |
| Positive SRR [No. (%)] | 22 (21.4) |
| Fresh/Frozen sperm | 4/18 |
| Histologic reports [No. (%)] | |
| Maturation arrest | 17 (16.5) |
| Sertoli cell-only syndrome | 86 (83.5) |
| Johnsen score | |
| Median (IQR) | 2.0 (2.0-3.0) |
| Range | 1.0 – 9.0 |
| Postop. complications [No. (%)] | 2 (1.9) |

Keys: BMI = body mass index; CCI = Charlson Comorbidity Index;
TRT = Testosterone replacement therapy; SRR = Sperm retrieval rate.

**Table 2: Characteristics and descriptive statistics of patients according to SRR (No.=103)**

| | **Positive SR (N = 22; 21.4%)** | **Negative SR (N = 81; 78.6%)** | **p value*** |
|---|---|---|---|
| Age (years) | | | 0.14 |
| Median (IQR) | 30.0 (22.5-35.0) | 33.0 (24.5-38.0) | |
| Range | 18 – 49 | 18 – 55 | |
| BMI [Kg/m2] | | | 0.81 |
| Median (IQR) | 25.0 (20.5-26.4) | 25.0 (22.8-26.3) | |
| Range | 20.5 – 37.0 | 18.0 – 33.8 | |
| CCI ≥ 1 [No. (%)] | 2 (9.1) | 5 (6.2) | 0.91 |
| Testicular volume (ml) | | | 0.42 |
| Median (IQR) | 3.5 (2.7-7.0) | 3.0 (2.0-5.0) | |
| Range | 2.0 – 10.0 | 1.0 – 10.0 | |
| Current Smokers [No. (%)] | 6 (27.3) | 25 (30.8) | 0.54 |
| Varicocele [No. (%)] | 1 (4.5) | 5 (6.2) | 0.87 |
| Cryptorchidism [No. (%)] | 2 (9.1) | 5 (6.2) | 0.73 |
| FSH (mUI/mL) | | | 0.27 |
| Median (IQR) | 24.1 (15.6-38.7) | 30.3 (21.1-41.3) | |
| Range | 10.3 – 68.9 | 3.0 – 100.0 | |
| LH (mUI/mL) | | | 0.74 |
| Median (IQR) | 18.8 (11.1-25.3) | 17.3 (13.4-22.0) | |
| Range | 6.7 – 32.4 | 6.0 - 50.0 | |
| tT (ng/mL) | | | 0.06 |
| Median (IQR) | 4.9 (3.2-12.9) | 3.7 (2.4-10.1) | |

| | | | |
|---|---|---|---|
| Range | 2.5 – 19.3 | 0.3 – 24.9 | |
| TRT prior to surgery [No. (%)] | 2 (9.1) | 13 (16.0) | 0.12 |
| Surgery Type [No. (%)] | | | 0.15 |
| cTESE | 9 (40.9) | 29 (35.8) | |
| mTESE | 9 (40.9) | 42 (51.8) | |
| Stepwise mTESE | 4 (18.1) | 10 (12.3) | |
| Bilateral surgery [No. (%)] | 16 (72.7) | 72 (88.9) | 0.09 |
| Histologic reports [No. (%)] | | | 0.59 |
| Maturation arrest | 4 (22.7) | 13 (14.9) | |
| Sertoli cell-only syndrome | 17 (77.3) | 69 (85.1) | |
| Johnsen score | | | 0.01 |
| Median (IQR) | 3.5 (2.0-8.0) | 2.0 (2.0-2.0) | |
| Range | 1.0 – 9.0 | 1.0 – 8.0 | |

Keys: BMI = body mass index; CCI = Charlson Comorbidity Index; TRT = Testosterone replacement therapy; SRR = Sperm retrieval rate.

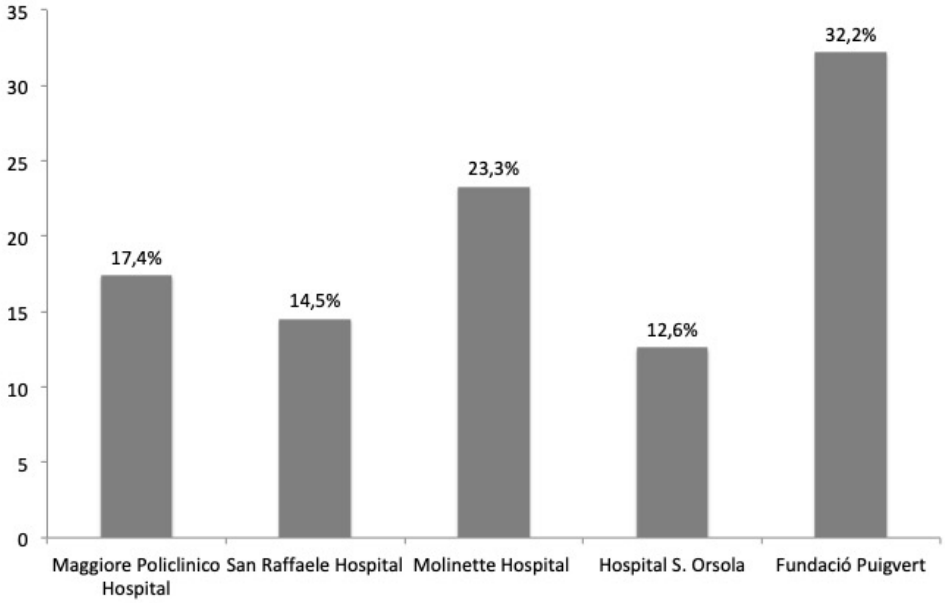
* p value according to the Mann-Whitney test and Chi Square test, as indicated.

**Table 3: Univariable logistic regression models predicting positive SR (OR; *p* value [95%CI])**

**in the whole cohort of patients (No.=103)**

| | OR | p-value | 95%CI |
|---|---|---|---|
| Age | 0.96 | 0.18 | 0.92; 1.02 |
| FSH | 0.98 | 0.36 | 0.95; 1.02 |
| Testis volume | 1.11 | 0.25 | 0.93; 1.29 |
| Total testosterone | 1.06 | 0.16 | 0.97; 1.15 |
| TRT prior to surgery | 0.96 | 0.25 | 0.91; 1.03 |
| mTESE vs. cTESE | 1.8 | 0.13 | 0.89; 2.34 |
| SCOS histology | 0.44 | 0.32 | 0.09; 2.09 |

Keys: TRT = Testosterone replacement therapy; SR = Sperm retrieval; SCOS = Sertoli cell-only syndrome

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