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PSA-based screening for prostate cancer: a more conscientious behaviour against the tenacity of a early diagnosis

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Prostate-specific antigen (PSA)-based screening for prostate cancer is among the most important and controversial issues of medicine with enormous health-care and health-economic relevance. Weighting the real effect of mass screening on prostate-cancer mortality and estimating the risk of overdiagnosis and overtreatment related to the use of PSA test in asymptomatic men were the most relevant unsolved questions in the last decades. The medical community has waited for many years definitive answers from two randomized controlled trials started in the early 1990s in United States (Prostate, Lung, Colorectal and Ovary [PLCO] trial) and Europe (European Randomized Screening for Prostate Cancer [ERSPC] trial), respectively. During such time, the availability of a “simple” and “safe” test to yield an early diagnosis of prostate cancer forced many urological and oncological societies to recommend periodical dosages of PSA in asymptomatic men over 50 years. For example, in the USA, both American Urological Association and American Cancer Society recommended that screening should be offered to men of 50 years or older. More recently, the National Comprehensive Cancer Network (NCCN) practice guidelines concerning the prostate cancer early detection suggested considering to offer baseline DRE and PSA dosage at the age of 40 years. In other words, waiting for the results of the two ongoing randomized controlled trials (RCTs) on prostate cancer mass screening, we assisted to the affirmation of the opportunistic PSA screening with the progressive lower of the cut-off points for “normality” and of age to start dosing PSA. Surely, this trend had larger fortune and impact in the clinical practice that the opposite recommendations of some other scientific societies. Specifically, the US Preventive Services Task Force (USPSTF) had concluded that the evidence was insufficient to recommend for or against PSA screening and the Advisory Committee on Cancer Prevention in Europe had stated that screening for prostate cancer was not recommended as health-care policy.

During these years, all the urologic community was hoping that the evident harms related to the screening could be balanced by the convincing evidence of significant reduction in cancer-specific mortality.
In a recent issue, the New England Journal of Medicine published the first reports of both ongoing RCTs evaluating the effects of prostate cancer screening on cancer-specific mortality. Unfortunately, although both studies are still ongoing and future updates were promised, their preliminary conclusions seem to be different.

The results of PCLO trial showed no mortality benefit from combined screening with PSA and digital rectal examination during a median follow-up of 11 years. Specifically, 10 years after the randomization, the Authors observed 92 prostate cancer-related deaths in the screened patients, compared to 82 in the control group (RR 1.11 - 95% CI 0.83-1.50). Although the follow-up of the PCLO trial is planned to continue until 13 years from randomization for all the patients, the persistence lack of a significant difference in the death rates between the two randomized groups supported the need to publish these preliminary results.

The match seems to be finished in favor of the opponents of the PSA screening. However, in the subsequent article of the same issue of the New England Journal of Medicine, Schroder et al, reported the results of the third pre-planned interim analysis of the ERSPC trial. Specifically, the authors found that PSA screening without digital rectal examination was associated with a 20% relative risk reduction in the cancer-related death rates at a median follow-up of 9 years (RR 0.80 - 95% CI 0.65-0.98), with an absolute risk reduction of about 7 prostate cancer deaths per 10,000 men screened. In a very balanced final message, the Authors highlighted that the introduction of population-based screening must take into account population coverage, overdiagnosis, overtreatment, quality of life, cost, and cost-effectiveness.

The match remains opened and the players could probably play very long over time. Some considerations can be done. The New England Journal of Medicine presented two different messages concerning the same topic coming from two studies with different potential drawbacks. Obviously, the controversy remains life but the confusion probably increases.

Table I summarizes the main characteristics of the two studies (Table I).

Looking at the PCLO trial, we can note that the conclusions of this study were based on US patients aged between 55-74 years who underwent annual screening and prostate biopsy for total PSA value higher than 4 ng/ml and/or suspicious digital rectal examination. The compliance to the screening protocol was 85%, slightly below the value of 90% planned during the design of the study. Vice versa, the contamination rate in the control group (i.e., the percentage of patients randomized to the control arm which, indeed, received PSA testing) ranged from 40 to 52%, which was significantly higher than the pre-planned 20%. On the whole, however, only 174 prostate-cancer deaths were observed and driving the power of the study. Interestingly, considering the high percentage of contamination in the control group of the PCLO, this trial could be considered as a comparison between a population-based and opportunistic screening. Moreover, the significant number of patients who underwent PSA and/or DRE test within past 3 years before the inclusion in the study might have selected a population of patients with lower risk of prostate cancer.

Considering the ERSPC trial, the conclusions of the study were based on a core of patients aged between 55-69 years, screened every 4 years with PSA who received indication for a sextant prostate biopsy for value of PSA > 3 ng/ml. In this study, the compliance to the screening protocol resulted 82% as planned, while the authors did not report any information on contamination in the control group, initially estimated to be as low as 20%. Similarly, no information were available concerning the number of PSA test performed before the enrollment in the trial. 540 prostate-cancer deaths were observed during the study.

On the whole, the PCLO trial was underpowered to detect the modest benefit in favor of the screening found by the ERSPC trial. Nevertheless, the wide confidence interval reported in the PCLO trial (95%CI 0.83-1.50) includes at its lower margin the point estimate effect from the ERSPC (95% CI 0.65-0.98).

At the same time, the results of ESRPC trial in favor of the screening are clearly outweighed by the high risk of overdiagnosis reported in the trial. In particular, our patients (and our governors) must be informed that 1410 men would need to be offered screening for each patients diagnosed with prostate cancer and that 48 men would need to be treated for cancer in order to prevent a single prostate-cancer death during a 10-year period. Although the number needed to screen is similar to the figures of breast and colon-rectal cancers screening, we do not have a curative “organ-sparing” treatment for prostate cancer and the risks of overtreatment and long-term complications related to such treatments are significantly more relevant.

In our opinion, based on these preliminary results and waiting for the final data of both the RCTs, the
indications in favor of early PSA testing, lowering both cut-off points to trigger biopsy and age to start the dosage should be clearly reduced. Nevertheless, I believe that our police will continue to be indicating the PSA test in well-informed patients required to entry in a program of early diagnosis for prostate cancer. However, we must reconsider with more caution the age to start the dosage of total PSA, PSA cut-off point, and potential role of static and dynamic PSA-derivates to indicate prostate biopsy. According to the results of ESRPC trial, the opportunistic screening could be reserved only for men aged between 55-70 years, the PSA test should be performed every 4 years and the cut-off value to indicate a prostate biopsy should be higher than 3 ng/ml. The appropriate and opportune number of cores to be sampled during prostate biopsies is another controversial issue which can multiply the risk of overdiagnosis reported in the two screening RCTs, where a minimal sextant protocol has been used.

In order to enrich the discussion and allow our reader to have a clearer opinion on such an interesting issue, in the present issue of the *Journal of Andrological Sciences* we report two editorials, one in favor and one against prostate cancer screening with PSA. We are sure that you will appreciate these contributions.

### References

2. Welch HG, Schwartz LM, Woloshin S. *Prostate-spe-


PSA and male sexual dysfunction

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Key words
Male sexual dysfunction • Erectile dysfunction • PSA • Infertility • Lower urinary tract symptoms • Fatherhood

The case for PSA screening in patients with andrological compliants

Why ask for prostate-specific antigen (PSA) check during an andrological assessment? This question provides numerous points with an interesting link to different aspects in the everyday clinical practice of both the sexual and the reproductive medicine fields. In this context, answers are certainly numerous and may be related to patients’ characteristics or to some pointed clinical condition.

1. Why does “age” matter? Patients coming to our andrological clinic can be 50 years old or more, complaining of erectile dysfunction (ED), ejaculatory disorders (EjDs), hypoactive sexual desire, and – surprisingly but more and more frequent – male infertility. According to the European Association of Urology (EAU) guidelines, men aged 50 or more would need PSA check-up every year if they do not have prostate cancer (PCa) familiarity, otherwise they should start prevention trial from 40 years of age. In this context, it has been highlighted that PCa risk can be estimated in individual men primarily using PSA, but also using prostate volume, previous biopsy status, family history and ethnicity (being these data certainly collected during a comprehensive andrological setup!). In our clinical practice it is very common to see “otherwise healthy” elderly patients with ED. This obvious consideration is the result of several prevalence studies, where, after adjusting for other co-risk factors, ageing is the strongest predictor of ED; data suggests a constant increase in the odds of ED with each decade after the age of 40 years. Moreover, the majority of old (namely, men older than 50 years) impotent patients refer some degrees of lower urinary tract symptoms (LUTS), which have been linked a number of times to male sexual health both clinically and from the patho-physiology standpoint, this certainly giving us the priority to check for PSA values.

2. Male infertility meets PCa risk. Basic science has already shown that men with disorders in fertility may lack certain checkpoint or regulatory genes predisposing them not only to abnormal spermatogenesis but also to abnormal control mechanisms for normal cell division and, hence, a potential increased incidence of cancer, PCa as well. This is the case for defects of DNA mismatch repair – a DNA repair mechanism that corrects mispaired

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bases during DNA replication errors – which play an important role in both fertility and cancers. Defective mismatch repair (MMR) proteins result in genome instability with detrimental consequences, that significantly contribute to male infertility and tumorigenesis. In this context, as previously described by Kolettis & Sabanegh, significant medical disorders can be detected during male infertility evaluation; significant PCa was found in a 38ys old man suffering from secondary infertility. He was just one case out of 536 patients screened (0.19%), but we think his young age (along with the aggressiveness of the tumor) is enough to justify in our daily practice a digital rectal examination to all patients and, in case any abnormalities are detected, a PSA check. This is certainly even more significant when considering our recent finding that male factor infertility (MFI) – by itself – accounts for a higher Charlson Comorbidity Index, which may be considered a reliable proxy of a lower general health status, regardless of the etiology of MFI. What does this really mean? We may speculate that our findings suggest that after adjusting for the patient’s age, body mass index –BMI, and educational status, a significantly lower general health was recorded for infertile patients as compared with fertile men. Therefore, why not screening for PSA values in men presenting for couple’s infertility? This strengthens the correlation between andrology and PSA!

3. Is fatherhood a risk factor? Interesting is the correlation between fatherhood and risk of developing PCa. A number of reports attempt and correlate the two, in scientific terms. Harlap et al. for instance, reported a significant association between childlessness and an increased risk of PCa in fathers from the Jerusalem Perinatal Study Cohort [RR of 1.40]. Prostate cancer cohort members had fathered significantly fewer sons (offspring male:female sex ratio, 0.94) than other men in the cohort (offspring male:female sex ratio, 1.06). They thus concluded that infertility and PCa could have a similar genetic background, probably in terms of Y chromosome abnormalities. In contrast, two different northern European groups reached opposite conclusions after their “local” case-control studies; a significant inverse association between the number of children and subsequent PCa risk was reported, indeed. Interestingly, men with sons seemed at lower risk than men with daughters only.

The above reported observations are only a few among those supporting the importance of screening for PSA during the andrological everyday clinical practice; PSA screening may be considered almost a screening for “male health”, rather than a simple PCa screening! In this context, we may conclude saying that age and male infertility are the two major clinical situations for checking PSA, although one must give attention to the cornerstone aspect that prostate is a fundamental part of the male sexual and reproductive system.

References

1. Fisch H. Older men are having children, but the reality of a male biological clock makes this trend worrisome. Geriatrics 2009;64:14-7.
Walsh TJ, Croughan MS, Schembri M, Smith JF, Chan JM, Turek PJ. Infertile men may have increased risk for non-germ cell cancers: data from 51,318 infertile couples. J Urol 2008;179(Suppl. 4):654.


The case for “PSA screening”: why being “pro” is mandatory!

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Two large trials on PSA (prostate-specific antigen) screening, which were published simultaneously in March 2009, came to opposite conclusions. The European Randomized Study of Screening for Prostate Cancer randomized 162243 men between the ages of 55 and 69 to undergo PSA screening at an average of once every 4 years or to a control group. Most of the participating centers used a PSA level of 3.0 ng/ml as an indication for biopsy. At an average follow-up time of 8.8 years, 214 men had died for prostate cancer (PCa) in the screening group, as compared with 326 in the control group, for an adjusted rate ratio of 0.80 (95% CI 0.65-0.98, p = 0.04). In other words, screening decreased the risk of death due to PCa by 20%.

The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, conducted in the United States, came to the opposite conclusion: there is no benefit from PSA screening in terms of PCa-specific mortality reduction. This study was smaller, with 76693 men between ages 55 and 74, randomly assigned to receive PSA testing every year for 6 years and digital rectal examination for 4 years, or usual care in the control group. A PSA level of more than 4.0 ng/ml was considered to be positive for PCa. At 7 years of follow-up, of those who reported undergoing no more than 1 PSA test at baseline, 48 men had died of PCa in the screening group, as compared with 41 in the control group (rate ratio 1.16, 95% CI 0.76-1.76).

The designs of the two trials are different and provide complementary insights. The PLCO investigators offered several explanations for their negative results. First, the PSA threshold of 4 ng/ml that was used in that study may not be effective. Second, more than half the men in the control group actually had a PSA test in the first 6 years of the study, potentially diluting any effect of testing. Third, about 44% of the men in the study had already had one or more PSA tests at baseline, which would have eliminated cancers detectable on screening from the study. Fourth, not all men who were advised to undergo biopsy actually did so. Fifth, the follow-up time may not yet be long enough for the benefit to be apparent. Sixth, treatment for PCa improved during the years of the study, so that fewer men than expected died of PCa in both the

Key words
Prostate cancer • PSA • Screening
screening and the control groups. Moreover, though the PLCO trial has shown no significant effect on PCa mortality to date, the relatively low number of end points begets a wide confidence interval, which includes at its lower margin the point estimate of effect from the ERSPC trial. Finally, the smaller difference in screening intensity between the two study groups in the PLCO trial, as compared with the ERSPC trial, is reflected in a smaller risk of overdiagnosis (23% vs. more than 70%) and a less impressive shift in cancer stage and grade distributions. Therefore, important differences between the two studies can be found. In the European study, all patients with a PSA ≥ 3.0 ng/ml were advised for a prostate biopsy, and the adherence to this advise was very high (86%). Conversely, in the PLCO trial the trigger PSA for a biopsy was higher (4.0 ng/ml), and the biopsy was performed only in 40% of patients, therefore limiting the possibility to diagnose significant prostate cancers in these patients, and limiting the possible benefit related to the screening. Moreover, in the European study only 10% of recruited men had already had a PSA testing before entering the study. Therefore, the risk of having eliminated the most aggressive cancers that would have been found through the screening was extremely low. Conversely, in the American study more than 40% of the men had already had a PSA testing before entering the randomized study, so that the possibility that many PCa would have been diagnosed before the beginning of the study and excluded from the study itself is quite high. This bias makes the American study weaker when compared to the European one.

In the European study, the effect of PSA testing on cancer-specific mortality began to be evident starting from 7 years after the beginning of the study, and became statistically significant after 10 years. Therefore, since PCa is a slow growing tumor, the European study will demonstrate an increasing benefit of PSA screening in the future years. Conversely, the American study will not show this increasing benefit due to methodological biases.

In conclusion, the European study showed that there is a PSA screening-related benefit in PCa-specific mortality, and the future results of this study might show that the benefit is higher than a 20% reduction of PCa-specific mortality. Conversely, the PLCO study, which is affected by serious methodological biases might not demonstrate such a benefit. However, the longer follow-up results are awaited to better understand the significance on PCa screening trial.

References
A complex biology, men’s *weltanschauung*, and communication challenges

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When asked about PSA testing and screening for prostate cancer (PCa), I try to do my best at giving transparent and objective information. In order to be complete, I must say about the limitations of the test, their influence on the subsequent decisions, and the uncertainty surrounding the whole subject. I feel committed to make it clear that patients should see beyond that comprehensible naïve curiosity that moves some people, most of us all actually, when checking the state of our own health. I can remember of countless times when at the end of a thoughtful interview facing my patients, and patients’ spouses, putting all my communicational skills to shine the reaction was: “OK. Thank you Doctor, we appreciate it. Mmm ... now then, and your suggestion is ...?”.

Screening for prostate cancer remains controversial with multiple reasons for being disoriented. How can we work it out, physicians and patients alike? Cancer has a complex biology and the peculiarities of PCa make it a wonderful example of such complexity. Among the total number of men diagnosed with prostate cancer, there is a proportion of men for whom treatment is not necessary and, notably, treatment can be still effective if delivered at a delayed time after diagnosis. The follow-up data of prospective, active surveillance studies represent a convincing demonstration. Interestingly, the same conclusion can be obtained from retrospective analyses, where no difference was observed for patients who remained without treatment for 7.7 ys until delayed treatment was instituted, in comparison to immediate treatment. When looking at retrospective analyses caution has to be used as *ad hoc* principles for selection, as well as, pre-scheduled actions for monitoring the potential progression of stage and grade of the disease were not explicitly in place, in other words, the probability of oversight can not be ruled out completely. But still, PCa mortality did not differ between the two groups.

The results of both retrospective analysis and prospective trials counter our “early detection and early treatment” axiom, at least for some forms of the disease (low stage and grade). Besides, PCa is not destined to remain a single example, as the policy of surveillance...
is currently being extended also to tumours of other organs (i.e. kidney, bladder, etc.).

Vice versa, for another proportion of men at the other end of the spectrum, cure is not attained even with immediate active treatment, including multiple treatments association, because of high-risk, poor responsive disease already present from the onset, uninfluenced by early detection 7.

In the adult male population we witness a "self-managed" PSA screening and, as a result, PCa diagnosis is the highest in countries where PSA testing is highest 4.

Two monumental trials were recently closed and the results yielded are a negative one, and a positive one, respectively 5 6. Both excellent trials have received attention deservedly, along with comments and criticisms 7 8. Among the latter, outdated PSA cut-off, crossover contamination, mis-classifications of the causes of death, insufficient discriminatory power, have weakened the results of the negative study. In essence, what the results prove is that screening for prostate cancer has shown no survival advantage, or only small, at best.

Among the screened men in the positive trial, the rate of over-diagnosis, that is, the diagnosis of prostate cancer in men who would not have clinical symptoms during their life-time, was prudently estimated at 50%, and the number of men that need to be treated to spare one death was calculated as 49. Both figures that we'd better bear in mind when looking back again at the results of the trial from the clinical and also from the economical standpoints. The results of those trials are likely to be included within the (already thick) list of documents that some patients download from the net before walking through our offices’ doors. For some of them, or basically their spouses, the decision of being screened was already made. Some others, or their spouses, will simply seek for orientation. How can we help them out?

Weltanschauung is a German word composed of two parts, welt or world, and anschauung or vision, therefore, it is generally translated in “vision of the world”. It applies to single persons, human groups, peoples, or societies. Not existing an equivalent word in other languages than German, it is relatively difficult to render an authentic translation. For a more thorough representation, the weltanschauung can be regarded also as the sense of existence providing a framework for generating, sustaining, and applying knowledge.

We give information, striving for objectivity and hinging solidly on evidence, and the way it will be received within anyone weltanschauung constitutes a communication challenge. Some men need to be reassured from a generic sense of threat posed by the idea of a disease per se. Men and women are alike with respect to this. In breast cancer, the incidence of mastectomy is rising again despite the evidence accumulated so far in favour of breast conserving surgery (BCS) 9. After the results of six randomised trials, breast conserving surgery, followed by breast irradiation, became the treatment of choice for women with early stage breast cancer, in the nineties 10. Nevertheless, the rate of mastectomy increased 1.8-fold from 2004 to 2007 in comparison to 1994 to 1998 9. Local recurrence after BCS has been a concern for patients and doctors both, although in the face of evidence.

The desire of being safe, beyond the medical literature, has a central role in the choice.

Men too, just like women, need to be reassured. If a test could tell something about your future health, even with some lack of precision, it would be appealing to most people.

The controversy surrounding PSA screening is likely not to be the point. With regards to screening for PCa, presently, we are but bystanders. The key challenge is to diffuse evidence based information. With early, low stage and grade PCa, the general culture in favour of “early detection and treatment” has probably found an exception.

As the PSA driven increase in PCa diagnoses will inevitably fuel treatment, over-diagnosis will engender over-treatment. This is where we have to be the most vigilant, as doctors are more prone “to recommend interventions that they provide, rather than accurately disseminate information” 11. It can be added also that the most rewarding therapeutic options for doctors tend to be offered more frequently. A honest admission. For the time being, surgery, either standard open, or robotic assisted, is the most rewarding followed by external-beam irradiation and brachytherapy. Not the same for active surveillance that could probably serve best most of the cancers found by screening, as initial option,

It’s my opinion that the estimates of over-diagnosis, and the number needed to treat in order to spare one single death from the disease represent an excessive toll to pay for screening of PCs, to men and society, both.

However, I admit, this is how it looks to me or, more precisely, to my weltanschauung.
References
   Active surveillance for prostate cancer: a review of the literature. Cancer
   Prospective study of determinants and outcomes of deferred treatment or
   watchful waiting among men with prostate cancer in a nationwide cohort. J Clin
3. D’Amico AV, Moul J, Carroll PR, Sun L, Lubeck D, Chen MH. Cancer specific
   mortality after surgery or radiation for patients with localised prostate cancer
4. Ross LE, Brerkowitz Z, Ekwueme DU. Use of the PSA among U.S.
   men: findings from the 2005 National Health Interview Survey. Cancer
   Epidemiol Biomarkers Prev 2008;17:636-44.
   PLCO Project Team. Mortality results from a randomised prostate cancer
   Screening and prostate cancer mortality in a randomised European study. J Clin
7. Barry MJ. Screening for prostate cancer. The controversy that refuses to die. N
9. Morrow M, Harris JR. More mastectomies: is this what patients really want? E
   pub ahead of print as 10.1200/JCO.2009.23.0078.
10. NIH Consensus Conference. Treatment of early stage breast cancer. JAMA
11. Wilt TJ. Uncertainty in prostate cancer care. The physician’s role in clearing
    the confusion. JAMA 2000;283:3258-60.
Health promotion in women with female genital mutilations

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Summary

Introduction. In 2008 WHO estimated that between 100 and 140 million of women have undergone female genital mutilations in the World and that every year about 3 millions of female children are mutilated in Africa. The Guidelines of the Italian Health Minister extrapolated that 93,809 immigrant women with residence permit have a genital mutilation in Italy and the 9th of January of 2006 the law 7/2006 for the specific crime of female genital mutilation was introduced in the Italian Penal Code.

Aim. The aim of this article is to present the Epidemiology, the Legal, Anthropological and Medical aspects of Female Genital Mutilation with particular reference to Italy.

Conclusion. Female Genital Mutilation is a socio-sanitary subject which requires skilled cultural mediators and trained medical professionals to take in charge these patients with competence, cure the related complications and finally prevent these practices. Defibulation is recommended for infibulated women especially in case of long-term complications.

Key words
FGM • Female genital mutilations • Infibulation • Defibulation • Sexuality and FGM

Laws and dialogue to avoid and cure practices nowadays present in the multiethnic society of Western countries, promoting health and creating a new awareness of women rights, including sexuality

In 2008 ISTAT (Italian National Institute of Statistics) published some data showing that there are 3,5 million legal immigrants in Italy and that, among them, 49.9% are women, the majority in fertile age. It is estimated that more than 93,000 of them have undergone a genital mutilation. The 18th of September of 2009 the Piepoli Institute in Rome revealed the results of a survey conducted in June and July 2009 for the Department of Pair Opportunities and for the Presidenza del Consiglio dei Ministri. It estimated a decrease of these practices: among 110,000 women from countries where genital mutilations are performed and with Italian residence permit, 35,000 underwent a genital mutilation. 4600 of these are less than 17 years old. In this survey, it was not taken into consideration the practice of stretching the clitoris and the labia minora (genital stretching), typical of some ethnic groups from Malawi, Burundi, Ruanda and Uganda.

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In a multiethnic society a good health promotion policy must include correct education, training and communication, result of experience, knowledge and cultural mediation.

Female genital mutilation is a socio-sanitary subject which requires skilled cultural mediators and trained medical professionals to interact with these women, their partners and their entire community. This is the way that makes possible to prevent these practices and cure the related complications.

**Epidemiology**

The practice of female genital mutilations is an ancient tradition strongly linked with the ethnic identity of the practitioners. Because of that, it crosses the frontiers of countries and where it is not global, its prevalence is concentrated in some areas which correspond to specific ethnic groups. Female Genital Mutilations exist in Central and Eastern Africa (Sudan, Nigeria, Ivory Coast, Uganda, Mali, Benin, Burkina Faso, Egypt, Ethiopia, Eritrea, Somalia, Djibouti), in Indonesia, Malaysia, part of the Persian Gulf, among some ethnic minorities in Yemen, Oman, Iran, Iraq and among the immigrant communities in Europe, Canada, United States, Australia and New Zealand.

In 2008 WHO (World Health Organization) estimated that between 100 and 140 million of women have undergone female genital mutilations in the World and that every year about 3 millions of female children are mutilated in Africa. Countries with the major incidence are Somalia (97.9% of women between 15 and 49 years old), Egypt (95.8%), Guinea (95.6%), Sierra Leone (94%), Djibouti (93.1%), Mali (91.6%) and Eritrea (88.7%). Some researchers reported that these practices exist in countries such as India, Indonesia, Iraq, Israel, Malaysia and United Arab Emirates, but national official estimations are not available. In addition, it is a changing phenomenon thanks to the feminist movements and to the local governments, the ngos’ and the international organizations’ actions.

It is difficult to estimate the number of women with female genital mutilations and of the children that are potentially at risk in Italy. The numbers presented in the Guidelines of the Italian Health Minister are extrapolations based on the total number of women from these countries with a regular residence permit (July 2006) and on the percentage of mutilation in the original country. Illegal immigrants are not considered. It is extrapolated that 93,809 women have a genital mutilation, 490 are less than 13 years old and 3,535 are between 14 and 18 years old. These ages are potentially at risk of genital mutilations. Women between 19 and 40 years old (age of the mothers) would be 62,710. Mature women (> 40 years old) would be 26,098.

**Italian law**

The Italian Code of Medical Deontology forbids any practice of female genital mutilations (art. 5).

The Italian Constitution safeguards inviolable human rights in the articles 2, 3 and 32. It recognizes social dignity and equality of all the citizens in front of the law and it guarantees health protection as a fundamental individual right. The article 5 of the Civil Code forbids the acts of body disposition when they cause a permanent damage to the physical integrity or when they are against the law, the public order or the public decency. It was not until the 9th of January of 2006 that the law 7/2006 for the specific crime of female genital mutilation (Disposizioni concernenti la prevenzione e il divieto delle pratiche di mutilazione genitale femminile) was introduced in the Italian Penal Code. Before that, the sanctions were
Health promotion in women with female genital mutilations

based on the articles 582 (personal lesions) and 583 (severe and very severe personal lesions). The law establishes the necessary measures to prevent and forbid female genital mutilations, considered as a violation of the fundamental human rights and personal integrity of women and children. This measure adds two articles to the Italian Penal Code (art. 583-bis and art. 583-ter) and establishes sentences of imprisonment ranging from 4 to 8 years in case of having performed a mutilation (clitoridectomy, excision, infibulation and any other practice that causes similar effects) in absence of a therapeutic reason. The law is applicable to crimes committed abroad by an Italian citizen or by a foreigner resident in Italy or when the mutilation is performed on an Italian citizen or on a foreigner resident in Italy. In case of medical professionals who perform a mutilation, the legally imposed ban on the profession will last between 3 and 10 years (art. 583-ter). The law contemplates the organization of informative and awareness campaigns for immigrants coming from countries where these practices are indigenous in order to develop socio-cultural integration. It also promotes labour and delivery training courses for infibulated women, information programs for the compulsory education teachers and the monitoring of the known cases of mutilated women by hospitals and the social and health services. Finally, it establishes education and training for medical professionals to guarantee correct diagnosis, cure and prevention of mutilations.

Anthropological aspects

Mutilations are very ancient practices, known since the time of the Pharaons (infibulation is still called pharaonic circumcision in many African countries). The word infibulation derives from the Latin word *fibula*, which was the brooch used by the Romans to fix the toga but used also on the genitals’ slaves to prevent them from having sexual activity.

Female genital mutilations are not prescribed by any religion. They are wrongly associated to Islam but exist among Christians (Copts, Orthodox, Protestants) as well as among Jews (Halascia in Ethiopia and their descendents in Israel) and Animists. Anthropologists talk about genital mutilations as an active institution to determine relations and exchanges on which the social organization of the major part of these communities is based. In these patriarchal societies, female sexual control happens through the tradition of genital mutilation to ensure chastity, which is essential for marriage and the honor of the entire community. In countries where the female genital mutilation is indigenous it represents a time honored and deep-seated social convention and it gives a social status to the child and her family. Not conforming to the practice leads to stigma, exclusion and shame. In these societies, the mutilation makes the child a woman. Biology by itself is not enough and the rite gives honor, value, identity, pride and sense of belonging to the cultural and social group. It also protects virginity and chastity defending a woman from her sexual drives and it guarantees a marriage. Furthermore infibulation is associated with beauty. Centuries of genital modifications have changed their aesthetic perception.

Talking about the meanings of these practices, some of them are typical of certain countries. For example in Somalia the mutilation is also an initiation rite with which the child becomes an adult and in Sudan the purpose is to decrease the vaginal opening to increase the sexual pleasure of the man.

The age at which children undergo the mutilation varies considering the type and the traditions of the community: it can be at the first week of life, during the childhood, the adolescence or before the pregnancy. In some regions after each delivery a woman can be reinfibulated.

For a medical doctor, even if respectful of other cultures, theses practices do not have the same social, gender, aesthetic, and personal implications as for the patients; but rather legal, biological and ethical implications considering the risk of unnecessary psychophysical damages for children and women and for the decreased value given to the woman’s dignity comparing to men. Besides, they are considered a violation of fundamental human rights.
Consequences and complications
Medical complications of female genital mutilations depend on different factors:
1. hygienic and economic conditions of the family (rural contexts versus richer ones);
2. the pre-existing health and nutritional conditions of the baby or child (disease or malnutrition);
3. the modalities and the instruments used (unhealthy or primitive sanitary and surgical tools such as acacia thorns vs sterile surgical thread, use of traditional curative mixtures instead of modern anesthetics and antibiotics, traditional practitioner or physician or nurse, etc.) and the post-mutilation period: hygiene, availability of water/antibiotics/medications. In case of infibulation the mutilation can be done a second time when the opening is considered too wide;
4. type of mutilation (Table I). In case of infibulation the vulvar vestibule, the urethral orifice and part of the vaginal opening are obstructed by the scar. In a virgin infibulated woman the small opening left is not wider than 2-3 mm from which menstrual blood and urine flow. The urethral orifice continues to be covered by the scar in sexual active women and after the delivery.
5. possible psychological, physical and psycho-physical complications, consequence of the experience of the mutilation.

It is important to distinguish between immediate complications after the operation and late complications which can characterize the entire life of a woman and which require sensitivity and attention considering that they are often not regarded as a problem by the patient, but rather as a normal condition of being a woman. Immediate complications can be extreme pain; urinary burning and acute urinary retention; hemorrhage and shock; different grades of anemia depending on the bleeding; death; infection and dehiscence of the injury, which can be sutured more times; urinary tract infections and septicemia; tetanus, infectious diseases like HIV or hepatitis in case of contaminated instruments in multiple operations.

Late complications depend on the type of the mutilation. The main ones are chronic pelvic infections, chronic or repeated vaginitis, especially after the first sexual intecourses, repeated urinary infections, dysuria, stones formation behind the scar because of the stagnation of the urine flowing in a difficult way. In infibulated women one of the more frequent complications is the severe dysmenorrhea, due to mechanical, inflammatory and psychosomatic factors. In addition, in case of a virgin infibulated woman, if the vaginal opening is too narrow, the blood can stagnates in the vagina or in the uterus producing hematocolpus and hematometra. We can find also drop by drop and prolonged miction (especially in virgin infibulated women) and cutaneous or sebaceous retention cysts in the scar, which can reach considerable dimensions or become an abscess in case of super infections. Finally there can be superficial and deep dyspareunia, especially at the beginning of sexual activity when the penetration is painful and difficult, sometimes impossible for the two partners.

During the labour it can be difficult to evaluate cervix dilation, to monitor the presentation progression and insert a urinary catheter. The expulsion period can be longer than usual with negative effects on the fetus and with possible perineal or anal sphincter lacerations sometimes responsible of incontinence and fistula (more common in developing countries than in western countries).

In some countries such as Sudan and Somalia, after the delivery a reinfibulation can be performed. It consists in re-stitching the scar of the infibulation previously cut to let the woman deliver.

Psychological complications can be often linked to the experience of the mutilation; however nowadays it is frequent that in young and adult women with genital mutilations living and growing in western countries psychological complications originate from the comparison and the differences of new different socialization and female identity construction models. The experience of the mutilation can be lived as negative: sense of humiliation, impotence, inhibition, betrayal of the family; or as positive: women feeling
proud of the mutilation, beautiful, not considering the mutilation as a possible cause of physical, psychological and sexual complications, thinking instead of some associated disorders as a normal condition of being a woman. In this case just with the dialogue with other women, especially if deinfibulated, these problems are recognized as they are. It is very important to be careful with the young patients who were mutilated in their country, where culture made them live the mutilation as a positive condition, and then migrated in a western country, where the new cultural environment makes them live the fact of being mutilated extremely negatively. The change of the image and of the perception of their genitals from beautiful to mutilated and very ugly, can cause a psychological mutilation inhibiting in particular any positive expectation of pleasure in sexuality. Sexual dysfunctions can be experienced even without a severe physical damage.

The real consequences on sexuality are variable. It is important to underline that in case of sexual dysfunction it should not be assumed that the cause is just the physical mutilation without investigating about the situation of the patient. She may probably be like any other woman with intact genitals and a sexual dysfunction, who needs a diagnosis and a treatment. Mutilated women with sexual dysfunctions can and must be cured with an appropriate sexual therapy involving the partner too. In case of infibulation the defibulation must be proposed.

**Surgery**

Defibulation let women have gynecological examinations and PAP tests.

Defibulation is a surgical operation which exposes the vaginal opening and the urethral meatus (partial defibulation) or the clitoral tissue and sometimes the whole intact clitoris (total defibulation) covered by the scar of the infibulation. Even if it is a simple operation from a technical point of view, it is part of a complex path for the patient. A path full of doubts, resistances, fear of exclusion by the own community, awareness and learning. It is a medical act which promotes women’s health by allowing gynecological screenings such as the PAP test, instrumental exams as hysteroscopy and transvaginal ultrasound. Furthermore it makes easier the vaginal delivery, solves urogenital infections and is part of the psychosexual therapy for dysfunctions such as impossible penetration and dyspareunia.

During the defibulation many are the possible forms of mutilations or the complications (reinfibulated genitals, adherences, retention cysts, bleedings). At the Regional Centre for Preventing and Curing Female Genital Mutilations of Careggi Hospital, Florence, there are 2 techniques of defibulation employed, both are ambulatory and performed with local anesthesia. The simpler and more frequent technique is the surgery with scissors or scalpel. It is used when the scar of the infibulation is thin and without complications and when it is possible to rebuild a sort of previous anatomy of external mutilated genitals. If there is a thick scar or a keloid, if there are retention cysts and in absence of tissue to rebuild some labia it is preferred to choose the laser surgery in collaboration with the service of colposcopy. In other centers the operation is done under total anesthesia.

After defibulation it is recommended accurate hygiene, daily manipulations with anesthetical and antibiotic creams to avoid the re-sealing of the borders of the scar during the healing process, which lasts about one week. The patient is advised to urinate in warm water, sometimes disinfected, to avoid urinary burnings.

| Type I: Partial or total removal of the clitoris and/or the prepuce (clitoridectomy) | Type Ia, removal of the clitoral hood or prepuce only; Type Ib, removal of the clitoris with the prepuce |
| Type II: Partial or total removal of the clitoris and the labia minora, with or without excision of the labia majora (excision) | Type IIa, removal of the labia minora only; Type IIb, partial or total removal of the clitoris and the labia minora; Type Iic, partial or total removal of the clitoris, the labia minora and the labia majora. |
| Type III: Narrowing of the vaginal orifice with creation of a covering seal by cutting and appositioning the labia minora and/or the labia majora, with or without excision of the clitoris (infibulation) | Type IIIa: removal and apposition of the labia minora; Type IIIb: removal and apposition of the labia majora |
| Type IV: Unclassified | All other harmful procedures to the female genitalia for non-medical purposes, for example, pricking, piercing, incising, scraping and cauterization |

**Table 1. Classification of FGM (WHO 2007).**
When the patient undergoing defibulation is a virgin woman coming with her future husband and their parents, they must be told that during the operation the hymen is not going to be damaged or touched after having previously explained that the physical virginity is not the artificial scar but the presence of the intact hymen, which is not always present and which can have different forms. The dialogue preceding the operation is also the appropriate moment for giving information and education to the couple and their families. It is the moment to explain that female genital mutilations are illegal in the World as also in the original country and that they are dangerous practices not recommended by the religion. In this way women and men will hopefully become responsible of the care of the integrity of their children and the mutilation will gradually stop being considered as indispensable in the choice of a wife. The dialogue does not have to be done with condemnation or sense of superiority. It is fundamental to give explanations and information about how the vulva is going to be after the operation and about the partial reconstruction of the labia to protect the vaginal opening. It is necessary to agree with the patient about where the opening of the scar is going to be stopped. Many women do not want to feel “completely opened” and prefer the incision to be stopped just after the urethral meatus to have a normal miction (and also to permit the insertion of a urinary catheter). It is vital to inform that the way of urinating is going to change, to avoid that a continuous urine flow, very different from a slow and drop by drop flow, frightens the patients. An informed and understood consentment must be signed.

At the Regional Centre for Preventing and Curing Female Genital Mutilations in Florence a significant and important cultural change has happened during the years. At the beginning defibulation used to be asked or accepted by a few number of married women and just if the husband agreed with it. The operation was secret because women who asked to be defibulated were scared to expose their husbands to ridicule from their own family and community. In their culture, the defloration of the scar of the infibulation is an important demonstration of virility. Hence, a man who allows his wife to be “opened” by a surgeon is criticized. However, recently young women have asked on their own to be “opened” before the planned wedding to improve their health. In one case of an infibulated minor the tutelary judge asked for a defibulation. Women talk among them and awareness and information about the dangers of infibulation and the beneficial effects of defibulation spread.

During pregnancy, defibulation can be performed during the first trimester, as soon as possible or during the labor. The recommendations are different depending on the country; in Italy it is preferred during the first trimester if possible. Intrapartum defibulation is performed with scissors or scalpel along the median line of the scar until the urinary meatus; then episiotomy is often done too.

After the delivery, the borders are sutured with simple and haemostatic stitches. Often the patient asks to be “closed” again. Because of that, it is important to talk before the labor, giving exhaustive explanations and saying that in Italy it is not legal. At the same time it is fundamental to restore the “normal” anatomy of the genitalia without leaving the vaginal opening too wide to avoid psychosexual distresses that may affect the life of the couple and that often push the woman to go back to her country to be reinfibulated. Finally, it is necessary to talk about the anatomical and physiological changes of the genitalia during the postpartum period and to propose eventually the pelvic floor re-education with Kegel exercises, which will help the patient to feel her genitalia pleasurable.
Straightening-reinforcing (S-R) technique with selected incisions in the treatment of congenital and acquired penile curvature: 10 years results of a simplification

F. Mantovani, R. Anceschi, S. Maruccia, G. Cozzi, V. Guarrella, F. Rocco

Summary

Objective. The correction of penile curvature is not anymore confined only to severe curvotorsions. Today Peyronie’s disease is precociously curable. Moreover, the demand of aesthetical correction for congenital curvatures, even minimal, is greatly increasing, especially from young patients requiring new suitable procedures.

Material and Methods. We perform the straightening-reinforcing technique in local anaesthesia, in day-hospital regimen. The first passage carries out the plicature while the second one seals it discharging the tension during erection. This technique is different from the simple Ebbehøj-Metz stitch, which plicates but doesn’t seal, exposing to relapse. In 10 years we performed 66 plicatures (50 congenital and 16 acquired) with a mean follow-up of two years.

Results. A penetrative activity was possible and satisfactory for every subject within 3 months. To report 6 relapses.

Conclusions. This technique is quicker and less invasive than the Nesbit’s corporoplastic technique and, with the appropriate indications, can provide the same goals, even on long term periods.

Introduction

Correction of penile curvature is not anymore confined to severe curvatures determining impossibility to penetrate or deformities aesthetically unacceptable (severe curvotorsions). At present, Peyronie’s disease is precociously curable with premature interruption of the progression and important reduction of morphofunctional damage. Moreover, the demand of aesthetical correction for congenital curvatures, even minimal, is greatly increasing, especially from young patients requiring new suitable procedures less invasive than traditional and nevertheless offering, for correct indications, same good results.
Material and Methods
We perform a straightening-reinforcing technique\(^1\) (Fig. 1) in local anaesthesia, in day-hospital. Until 45° of curvature we simply perform the plication of bulging albuginea with undetectables stitches under the dartos lining of the penile scalp. In our opinion this technique can be suitable also in stabilized Induratio Penis Plastica with mild curvature and mild coital interference. The first passage carries out the plication, while the second one seals it discharging the tension during erection, differently from the simple Ebbehøj-Metz\(^2\) stitch, which plicates but doesn’t seal. In case of ventral bending, we still prefer the subcoronal access: this approach favours a complete view of the dorsal anatomy, with special regard to the neurovascular bundle, that has to be preserved during placation (Fig. 2). However, in dor-

Figure 1. S-R technique step by step: a) in-out/in-out double stitch: tightening the suture results in straightening by albuginea plication; b) the reinforcing stitch is then performed with the same suture.

Figure 2. Coronal incision and full penile degloving focusing dorsal neurovascular bundle (correction of ventral curvature).

Figure 3. Peno-scrotal incision focusing urethra and ventral corpora (correction of dorsal curvature).

Figure 4. Half-coronal incision focusing controlateral corpora (correction of lateral curvature).

dosal curvatures, the peno-scrotal incision is for us the best choice, being in the degree to expose corpora cavernosa and urethra in the best way for the easiest and safest placation (Fig. 3).

Last but not least, in lateral bendings, an half coronal incision can be suitable (Fig. 4), exposing enough the corpora for the plication, preserving intact the prepuce with all connected advantages.

After the selected incision and penile degloving a hydraulic artificial erection is induced to assess the curvature. Two Allis forceps grasp the corpora cavernosa on the convex profile to achieve satisfactory straightening. The penis is deflected. Superficial Colles’ fascia is bilaterally opened exactly where the Allis have grasped. The S-R procedure is now
performed using 2/0 Prolene suture. In-between the marks left by the Allis, the needle enters the albuginea, exits, enters again and again exits, thus ensuring the “straightening”. Now comes the “reinforcing”: the needle enters the albuginea again at the beginning and exits at the end of the double stitch. The sutures on both corpora cavernosa are now tightened, and the result is checked by inducing an artificial erection. If readjustment is necessary, the knot can be loosened for suitable modification. Colles’ fascia and incisions are then closed. Please note that Buck’s fascia remains intact, preserving the strength of the albuginea and helping to prevent recurrence. Once the wound is dressed and the patient has left the operating theatre, he is usually able to leave hospital shortly after.

In 10 years we performed 66 plicatures (50 congenital and 16 acquired) with a mean follow-up of two years each.

Results
Penetrative activity was possible and satisfactory for every subject within 3 months. A total amount of 6 relapses is to be reported.

Restoration of a real fully satisfactory coital activity was however delayed of other 3 months because of some pain during erection. About one third of all patients had some problems with the coronal suture which disappeared 1 month after the operation; 15% reported a reduced sensibility of the glans. Four patients reported a light haematoma. Ten percent regarded the suture visible beneath the skin as unpleasant. Satisfactory straightening was achieved nearly in all the patients, both in their opinion and at photographic check up. Recurrence rate was low: only 3 patients, all of them with Peyronie, received no benefit from the operation: during follow-up, curvature recurred due to disease progression and the patients reported painful erection.

Discussion
S-R plication is not better than Nesbit procedure. However, for low degrees of penile curvature, both congenital and acquired, it is probably not absolutely necessary to perform an invasive operation requiring the opening of Buck’s fascia, detachment of the urethra or neurovascular dorsal bundle and albuginea excision (as in Nesbit operations or similar). Simple placation frequently cannot prevent recurrence. S-R plication improves the outcome of simple plication, preventing risk of relapse. Based on our experience, we feel S-R can be recommended as a minimally invasive procedure, particularly for aesthetic operations, which are increasing called for, especially by young males.

Conclusion
Because of the current sexual culture and the focus on physical perfection, even minimal curvatures are not acceptable to young patients, as they increase anxiety and stress in sexual relations. Modified S-R placation, in these cases, as in Peyronie’s curvatures, may be a minimally invasive and effective treatment suitable for most patients in day hospital and in local anaesthesia.

This technique is quicker and less invasive than the Nesbit’s corporoplasty procedure and, with the appropriate indications and selected incisions, it can provide the same outcomes, even on long term periods.

References
J. Abdulcadir, V. Orlando  
Health promotion in women with female genital mutilations  
Journal of Andrological Sciences 2009;16:159-164

Cycling and genitourinary symptoms: results from an observational analytical cohort study  

R. Boscolo-Berto, E. Bonandini, M. Gardiman, V. De Marco, M. Iafrate, G. Novara  
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Errata
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Preparation of semen samples
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If the entire volume exceeded 2 ml, it was divided into samples of 2 ml and layered onto a gradient comprising by the phases 40% and 80% in 15 ml conical centrifuge tubes. The samples were centrifuged at 300xg for 20 minutes, and the pellet obtained was then suspended in 2 ml of medium [Sperm Wash, Sage IVF (Cooper Surgical Group), USA], and centrifuged at 300xg for 7 minutes. The pellet obtained was again suspended in 4 ml of medium for insemination [Sperm Assist, Sage IVF (Cooper Surgical Group), USA] ready for insemination. Data on the volume, physico-chemical properties, concentration and type of sperm motility were recorded both before and after preparation of the semen.
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Corrige
p. 93

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• captions and legends for all tables and figures

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At the end of the text should appear the bibliography, the legends to the tables and figures.
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1. DENOMINAZIONE DEL MEDICALE Priligy 30 mg compresse rivestite con film. Priligy 60 mg compresse rivestite con film. 2. COMPOSIZIONE QUALITATIVA E QUANTITATIVA Ogni compresa rivestita con film contiene dapoxetina cloridrato, equivalente a 30 mg o a 60 mg di dapoxetina. Efficacità: Iattolitec. Per l'eccitamento completo degli eiaculanti, vedere paragrafo 6.1. 3. FORMA FARMACEUTICA Compresse rivestite con film. Le compresse rivestite con film da 30 mg sono di colore giallo chiaro, rotonde, confezionate con un latto "30" all'interno di un triangolo. Le compresse rivestite con film da 60 mg sono di colore giallo, rotonde, confezionate con un latto "60" all'interno di un triangolo. Le compresse presentano un aspetto uniforme e non sono distinte da altre sostanze in fase di preparazione. 4. DOSAGGI E PARAGRAFICO La compresse rivestite con film da 30 mg sono state utilizzate per definire la patologia nei studi clinici sull’EP - Tempo di latenza eiaculativa intravaginale (intravaginal ejaculation latency time - IELT) inferiore ai due minuti; e - Eiaculazione persistente o ricorrente alla minima stimolazione sessuale, prima, durante o appena dopo la penetrazione e prima che il paziente lo desideri; e - Spiccato disagio personale o difficoltà interpersonale conseguente all’EP; e - Scacco controllo dell'eiaculazione. 4.2 Precauzioni e di somministrazione Per urgenza. 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Il medico che opta per l'impiego di Priligy nel trattamento dell'eiaculazione precoce, deve valutare i rischi e i benefici riportati dal paziente in seguito all'assunzione del prodotto medicale dopo le prime quattro settimane di trattamento o dopo 6 dosi, per definire il rapporto rischio/beneficio e decidere se è opportuno continuare il trattamento con Priligy. Ancora (dit.e pari o superiori a 65 anni). I profili di efficacia e di sicurezza di Priligy non sono stati stabilì in pazienti di età pari o superiori a 65 anni a causa dell'insufficienza di dati a disposizione in popolazione di pazienti (vedere paragrafo 5.2). Bambini e adolescenti Priligy non deve essere impiegato in pazienti di età inferiore ai 18 anni. Patienti con condizioni multisoste e gravemente raccordate, come una rianimazione in pazienti con disfunzione renale grave (vedere paragrafi 4.4 e 5.2). 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conformitativo di Priligy e antidepressivi, fra cui gli SSRI e i SNRI, è controindicato (vedere paragrafo 4.3). Non è raccomandato sospendere il trattamento in atto per depressione o ansia, al fine di iniziare la somministrazione di Priligy per il trattamento dell’EP. Priligy non è indotto per disturbi psicosomatici e non deve essere impiegato negli uffici d’affari dal disturbo di altezza. Questo potrebbe essere un rischio di un disturbo psicofarmacologico di base o di una terapia farmacologica. I medici devono incoraggiare i pazienti a segnalare eventuali pensieri o sensazioni di ansia in qualsiasi momento e, se durante il trattamento si manifestano segni di depressione o ansia, è necessario sospendere l’assunzione di Priligy. Emorragia
Congiuntiva di SSRI sono state segnalate emorragie maioraniche. È pertanto necessario prestare attenzione nei pazienti che assumono Priligy, soprattutto in associazione a prodotti medicinali che aumentano il rischio di emorragia (es. aspirina, anticoagulanti orali, antiaggreganti piastrici o anticoagulanti (es. warfarin)), così come nei pazienti con un’anamnesi positiva per emorragie o disturbi della coagulazione (vedere paragrafo 4.5).

Disfunzione renale
Priligy non è raccomandato nei pazienti affetti da disfunzione renale grave e si raccomanda cautela nei pazienti con disfunzione renale di grado lieve o moderato (vedere paragrafi 4.2 e 5.2). Effetti di interazione tra farmaci E' stato segnalato che la sospensione repentina di SSRI somministrati cronologicamente, impiegati per il trattamento di disturbi depressivi cronici, garantisce i seguenti sintomi: disturbo, irritabilità, aggressione, capogiri, disturbi del sonno, depressione, ansia, agitazione, parestesia e tremori. In particolare, il disturbo del sonno e l’irritabilità possono persistere per diversi giorni dopo l’interruzione del trattamento. I sintomi possono spesso diminuire in pochi giorni, ma possono persistere per settimane o mesi. In alcuni casi, l’assunzione di SSRI in associazione con altri antidepressivi o benzodiazepine può aumentare la probabilità di sospensione improvvisa. Per questo motivo, è importante informare i pazienti che la sospensione di Priligy deve essere graduata e non interrotta bruscamente.

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La Tabella 1 illustra le reazioni avverse da farmaco che sono state segnalate. Le reazioni avverse segnalate nell'estensione a lunghi termini, in apporto, dello studio, sono state coerenti con quelle riportate negli studi in doppio cieco e non sono state segnalate ulteriori reazioni avverse da farmaco. 4.9 Sovradosaggio Non sono stati riportati casi di sovradosaggio. In uno studio di farmacologia clinica con Priligy non si sono manifestati eventi avversi inaspettati con dose giornaliere fino a 240 mg (due dosi da 120 mg somministrate a 3 ore di distanza). In linea di massima, i sintomi di sovradosaggio di SSRI comprendono reazioni avverse medicole della serotonina, come sonnolenza, disturbi gastrointestinali quali nausea e vomito, taquicardia, tremore, agitazione e capogiri. Nell'uso di sovradosaggio, se necessario, devono essere adottate misure di supporto a supporto. A causa dell'elevate legami proteici e del vasto volume di distribuzione della dapoxina circolato, è improbabile che diuresi forzata, dialisi, emoperfusione e scambio trasfusionale rechino benefico. Non è noto alcun antidoto specifico per Priligy. 5. PROPRIETÀ FARMACOLÓGICHE 5.1 Proprietà Farmacodinamiche Categoria farmacoterapeutica: altri urenologici, codice ATC: codice temporaneo G04BX, codice permanente non ancora assegnato Mecanismo di azione. Si suppone che il meccanismo d'azione della dapoxina nell'eiaculazione precoce sia correlato all'inibizione del riciclo neurobiologico del fenilecateramina e al conseguente potenziamento dell'eiaculazione nel caso osteoartrosico sugli scorticelli pre e post-sinapico. L'eiaculazione umana è principalmente mediata dal sistema nervoso simpatico. Il processo eiaculatorio trae origine da un centro del rifiuto spinale, mediato dal tronco cerebrale, che è inizialmente influenzato da numerosi nuclei spinali (nucleo preposto mediano e nucleo paraventricolare). Nel frattempo, la dapoxina inibisce il rilievo eiaculatorio dell'espulsione agendo a livello sopraspinale con il nucleo laterale paragigocellulare (LPGB) come struttura cerebrale necessaria per ottenere l'effetto. Le fibre nervose postgangliari simpatiche, che innervano le vescicelle semiinali, dolore deferente, prostata, muscoli bulbouretrali e collo vescicale, generano, in modo coordinato, la relativa contrazione degli organi innervati, per ottenere l'eiaculazione. La dapoxina modula questo rilievo eiaculatorio nei ratti, causando un aumentato della latenza di scacchi del riflesso dei motoneuroni del nervo pudendo (PMRD) e una riduzione della durata di scacchi (PMRD). Studi clinici suggeriscono che Priligy nel trattamento dell'eiaculazione precoce è stata stabilita in cinque studi clinic di doppio cieco, controllati con placebo, in cui sono stati randomizzati in totale 0.081 pazienti. I pazienti avevano un'età pari a superiore a 18 anni ed un'anamnesi positiva per EP nella maggior parte dei rapporto sessuali, nei 6 mesi precedenti l'arresto. Inoltre, in quattro dei cinque studi clinici, i pazienti avevano un tempo di latenza eiaculazione intravaginale (intragugial ejaculatory latency time - IELT, tempo intercorso dalla penetrazione vaginale all'eiaculazione intravaginale) ≥2 minuti in un limite del 76% di rapporto sessuali validi durante il periodo base. I pazienti con altre forme di disfunzione sessuale, compresa la disfunzione erettile, o quelli che utilizzavano altre forme di farmacoterapia per il trattamento dell'EP sono stati esclusi da tutti gli studi. In quattro studi clinici, l'endpoint primario dell'IELT medio è stato misurato mediante l'impiego di un cronometro, durante ogni episodio di rapporto sessuale. I risultati di tutti gli studi randomizzati sono stati coerenti. In uno studio clinico rappresentativo per la durata di trattamento più lunga (24 settimane), sono stati randomizzati 1.152 pazienti, 385 al trattamento con placebo, 388 al trattamento con una dose di Priligy da 30 mg al bispino e 389 al trattamento con una dose di Priligy da 60 mg al bispino. L'IELT medio al basale e all'endpoint dello studio per tutti i gruppi di trattamento è illustrata nella Figura 1. Gli aumenti della media aritmetica dell'IELT all'endpoint della settimana 24 sono stati statisticamente significativi (p=0.001) nel gruppi di trattamento con Priligy rispetto a quelli del gruppo placebo. L'entità del prolungamento dell'IELT è stata correlata all'IELT basale ed è risultata variabile fra i singoli pazienti. La rilevanza clinica degli effetti del trattamento con Priligy sono descritti di seguito in termini di tassi di risposta segnalati dai pazienti.

**Figura 1:** Media (+/- DS) dell'IELT medio (min) nel tempo - Studio R096769-PRE-5001

Oltre all'endpoint primario dell'IELT medio, il significativo beneficio farmacologico recato al paziente nello studio clinico sopra citato, è stato dimostrato utilizzando una definizione della risposta al trattamento composta ovvero costituita da un insieme di almeno un aumento di 2 categorie del controllo dell'eiaculazione più almeno una riduzione di 1 categoria del disagio correlato all'eiaculazione. In ogni gruppo di pazienti in trattamento con Priligy, una percentuale maggiore rispetto al gruppo placebo, in maniera statisticamente significativa, ha risposto al trattamento, iniziando dalla settimana 4 fino alla settimana 24 (p=0.003 per dapoxina 50 mg rispetto al placebo alla settimana 16, tutti gli altri confronti p>0.001). Sono stati osservati anche un significativo calo del disagio soggettivo e un significativo miglioramento della soddisfazione del paziente in merito al rapporto sessuale. I miglioramenti alle settimane 12 e 24 relativi agli endpoint chiave secondari, sono presentati nella Tabella 2.
Eredit?}