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ORAL MUCOSA AS GRAFT MATERIAL FOR THE PURPOSES OF RECONSTRUCTIVE UROLOGY

Abstract

Introduction: Despite the significant technological advances in recent years, numerous challenges still face the field of reconstructive urology. One of the main issues is the lack of universal graft material.

Aim: The present study aims to conduct a retrospective analysis of the functional results following the use of free mucosal graft harvested from the oral cavity.

Material and methods: For a period of twenty years (2000-2021) a total of 521 cases of reconstructive surgery with the use of oral mucosa were performed. They are divided into 5 main groups, based on the organ involved:

I. Urethroplasty in urethral strictures - 427 (82%)

II. Urethroplasty in complicated (crippled) hypospadias - 70 (13.4%)

III. Ureteroplasty in ureteral stricture - 1(0.2%)

IV. Substitute corporoplasty for Peyronie's disease - 15 (2.8%)

V. Organ - preserving operations in carcinoma of the penis -8 (1.5%)

Results: Depending on the source of the substitute material harvested:

- 1. Buccal mucosa (BMG) 368 (70.6%)
- 2. Lingual mucosa (LMG) 135 (25.9%)
- 3. Lower lip mucosa- 18 (3.5%)

No major complications resulting from graft harvesting were observed. The main type of operations were:

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- one-act operative techniques 460 (88.3%)
- two-act operations 38 (7.3%)
- operations on the penis 23 (4.3%)

Functional results were reported according to the type of operation. In the largest group – urethroplasty, a success rate of 84.29% was achieved.

Conclusion: Currently, reconstructive surgery of the urinary tract and penis using free oral mucosa graft is the most widely used surgical technique in modern urology. This operative technique requires strict patient selection and substantial professional experience.

Keywords: oral mucosa graft (BMG, LMG), urethroplasty, ureteroplasty, corporoplasty, organ-sparing operations for penile cancer

Despite the significant technological advances in recent years, numerous challenges still remain in the field of reconstructive urology. One of the main issues is the lack of universal graft material. Reconstructive surgeries involving the male urethra (the majority of cases), ureter, and penis require the development of easily accessible and adaptive graft material. In the last 20-25 years, free tissue grafts from oral mucosa have been established as such ^{1, 2, 3, 4, 5, 6}. Buccal mucosa has become the gold standard for reconstructive urethroplasty ^{7, 8}. An increasing number of urological centers around the world are adopting this approach, which is facilitated by regular specialized sessions at European and World Forums, as well as annual independent congresses on this topic. Many retrospective, extended, long-term analyses and articles on the topic appearing in specialized literature support the effectiveness of this method ^{9, 10, 11, 12}. Our experience in this field spans over 25 years, allowing us to draw reliable scientific and practical conclusions ^{13, 14, 15, 16, 17, 18}.

In this article, we present a retrospective study of the use of oral mucosa as graft material in reconstructive urology.

Material and methods.

For a period of twenty years (2000-2021) a total of 521 cases of reconstructive surgery with the use of oral mucosa were performed.

They are divided into 5 main groups, based on the organ involved:

I. Urethroplasty in urethral strictures -427(82%).

II. Urethroplasty in complicated (crippled) hypospadias - 70 (13.4%).

III. Ureteroplasty in ureteral stricture - 1 (0.2%).

IV. Substitute corporoplasty for Peyronie's disease -15 (2.8%).

V. Organ - preserving operations in penile cancer -8 (1.5%).

Depending on the source of the graft material:

I. Buccal mucosa (BMG) - 368 (70.6%).

II. Lingual mucosa (LMG) - 135 (25.9%)

III. Mucosa of the lower lip - 18 (3.5%).

The specific technique of sourcing each graft is described in the respective chapters. (Fig 9, Fig 10)

According to the type of operative technique, the cases can be divided into:

I. One-stage techniques - 460 (88.3%).

1. Urethroplasty in urethral strictures.

1.1. Onlay augmentation techniques.

- 1.1.1. Dorsal onlay technique 262 (59.9%). (Fig 1)
- 1.1.2. Ventral onlay technique 58 (12.6%).(Fig 2)
- 1.1.3. Combined onlay-inlay technique 8 (1.7%).
- 1.2. Augmentation-anastomotic urethroplasty 97 (21.1%). (Fig 4)
- 1.3. One-stage operations in crippled hypospadias 38 (8.3%). (Fig 3)

II. Two-stage operative techniques - 38 (7.3%).

- 1. Local fixation of the graft 12 (31.5%)
- 2. Perineal fixation of the graft 7 (18.4%).(Fig 5)
- 3. Two-stage operations in crippled hypospadias 16 (42.1%).

III. Operations involving other localizations - 4.6%

- 1. Ureteroplasty 1 (0.3%). (Fig 8)
- 2. Replacement corporoplasty 15 (2.8%). (Fig 6)
- 3. Organ-sparing operations for penile cancer 8 (1.5.5). (Fig 8)

The following methods were used in the retrospective analysis:

1. Diagnostic methods.

Along with the generally accepted methods, anamnesis, physical examination, interventional ultrasound, specialized imaging, and examination methods were used: retrograde and voiding cystourethrography; cavernoso-graphy; CT- urography; MRI; uroflowmetry.

2. Surgical methods - the basic operating techniqu s used are described and illustrated briefly:

2.1. Surgical techniques for urethral strictures.

2.1.1. Ventral onlay urethroplasty. (Fig 2)

2.1.2. Dorsal onlay urethroplasty. (Fig 1)

- graft preparation (Fig 9, Fig 10)

- urethroplasty

2.1.3. Augmentation-anastomotic urethroplasty. (Fig 4)

2.2. Combined urethroplasty in crippled hypospadias (Fig 3)

2.3. Reconstructive operations in cases of absent part of the urethra. (Fig 5)

2.4. Reconstructive surgery for Peyronie's disease (Fig 6)

(replacement corporoplasty)

2.5. Organ - preserving operations in localized penile cancer (Fig 7)

2.6. Reconstructive operations for ureteral stricture. (Fig 8)

3. Methods for evaluation of therapeutic results:

3.1. Methods for assessing the patency of the urethra (ureter) and the degree of urine flow:

3.1.1. Uroflowmetry.

3.1.2. Retrograde and voiding cystourethrography.

3.1.3. CT urography.

3.1.4. MRI

3.2. Methods for assessing erectile function after reconstructive surgery of the male urethra and penis.

We used a modified questionnaire ¹⁹ for erectile function after reconstructive surgery, as well as some physical tests - papaverine test; Morales test; Doppler of blood vessels.

Dorsal onlay urethroplasty

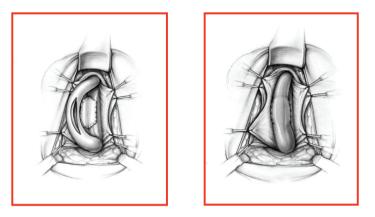


Fig 1.1 – Schematic drawing of dorsal onlay urethroplasty A. Liberation of the bulbar urethra, its' rotation and dorsal longitudinal incision of the stricture until reaching healthy tissue, fixation of the graft on the ventral surface of corpora cavernosa B. Fixation of the graft along the incised strictured segment and reconstitution of the normal anatomical position of corpus spongiosum

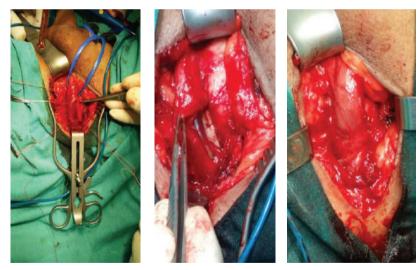


Fig 1.2 – Intraoperative images of ventral onlay urethroplasty A.Liberation of the bulbar urethra, its' rotation and dorsal longitudinal incision of the stricture until reaching healthy tissue. B fixation of the graft on the ventral surface of corpora cavernosa C. Fixation of the graft along the incised strictured segment and reconstitution of the normal anatomical position of corpus spongiosum

Ventral onlay urethroplasty

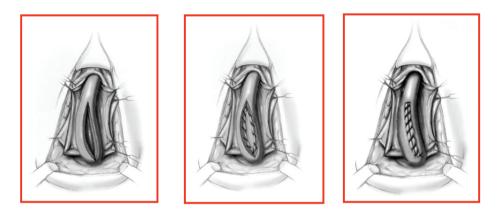


Fig 2.1 – Schematic drawing of ventral onlay urethroplasty A.Ventral longitudinal incision of the stricture until reaching healthy tissue. B. Ventral fixation of oral mucosa graft
C. Second layer of the urethroplasty from corpus spongiosum

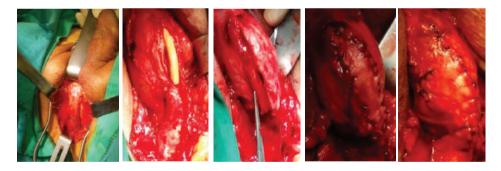


Fig 2.2 – Intraoperative images of ventral onlay urethroplasty A.Transperineal approach to the stricture. B. Ventral longitudinal incision of the stricture until reaching healthy tissue and assessment of the length of the needed graft. C. Ventral fixation of oral mucosa graft – initial sutures in the proximal and dorsal ends of the graft. D. Ventral fixation of oral mucosa graft – fixation with interrupted sutures along the circumference of the graft E. Second layer of the urethroplasty from corpus spongiosum

Combined urethroplasty

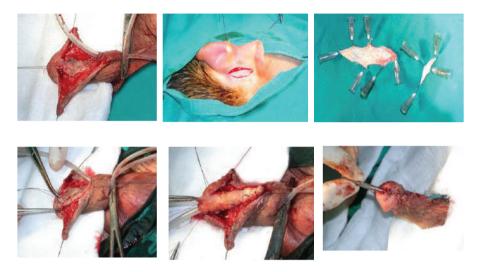


Fig 3 – Intraoperative images of combined urethroplasty A. Initial incision and preparation of the urethral plate in case of crippled hypospadia B.Harvesting of graft of retroauricular skin C. grafts on completion D. incision of the urethral plate –type Snodgrass (TIP, "Snodgraft" with inlay retroauricular skin graft) E.Onlay fixation of BMG F. Complete reconstruction

Anastomotic-augmentation urethroplasty

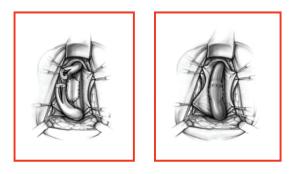


Fig 4.1 – Schematic drawing of augmentation urethroplasty A. Complete transection of the urethra in the strictured segment with eventual excision of obliterated part of the urethra and spatulating of theproximal and distal ends, followed by fixation of the graft on the ventral surface of corpora cavernosa B. Completion of the urethroplasty with both anastomotic and augmentation suture lines

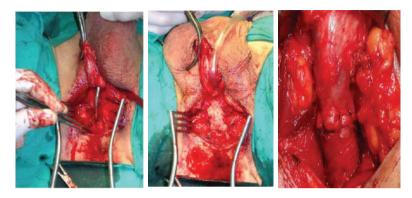


Fig 4.2 – Intraoperative images of ventral onlay urethroplasty A. Complete transection of the urethra in the strictured segment with eventual excision of obliterated part of the urethra and spatulating of theproximal and distal ends B. fixation of the graft on the ventral surface of corpora cavernosa C. Completion of the urethroplasty with both anastomotic and augmentation suture lines

Reconstructive surgery in long missing part of the urethra

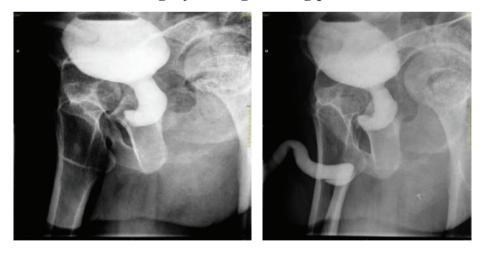


Fig 5.1 – preoperative urethrography in case of missing part of the urethra A. Antegrade cystography through previously fixed cystostomy tube, delineating the proximal end of the defect B.Simultaneous retrograde urethrography, delineating distal end of the defect and its overall lenght



Fig 5.2 – First stage of the urethroplasty in case of missing part of the urethra A.Previously fixed cystotomy tube B.transperineal approach to the defect yperpara C. fixation of the graft along the axis of the missing segment of the urethra D. Graft appearance after 6 months with good vascularization



Fig 5.3 – Second stage of the urethroplasty in case of missing part of the urethra A. mobilization of the BMG B.Formation of a perineal based flap C.reconstruction of the missing part of the urethra through tubularization of the flap



Fig 5.4 – Urethrography in case of missing part of the urethra 6 months after second stage – full patency of the reconstructed segment

Reconstructive surgery in Peyronie's disease



Fig 6.1 – Schematic drawing of plaque excision and corporoplasty with oral mucosa in Peyronie's disease A.Degloving of the penis in incision of Buck's fascia B. Dissection of dorsal neuro-vascular bundle of the penis C.excision of the plaque and covering of the defect with BMG

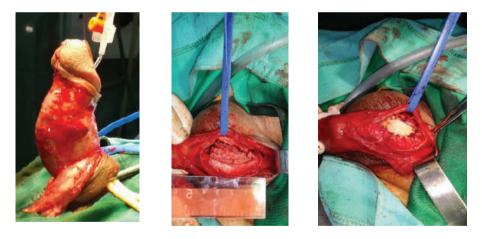


Fig 6.2 – intraoperative images of reconstructive surgery in Induration penis plastica
A.degloving of the penis and artificial erection for assessment of the plaque and curvature
degree B. Dissection of dorsal neuro-vascular bundle of the penis and excision
of the plaque C. covering of the defect in tunica albuginea with BMG

Organ preserving surgery in penile cancer/melanoma



Fig 7 – Organ preserving surgery in penile cancer A. penile cancer near sulcus glandis penis B. Glansectomy along Buck's fascia C.formation of neo-glans from the tips of corpora cavernosa D. Covering of the defect with BMG

Ureteroplasty



Fig 8 – Ureteroplasty in case of recurrent ureteral stricture – A. preoperative US and B. CT-KUB of hydronephrosis in a case of recurrent iatrogenic ureteral stricture C. Onlay fixation of BMG along DJ-stent protection in the strictured area D. postoperative CT-KUB one month after DJ extraction with absence of hydronephrosis

Oral mucosa graft harvesting

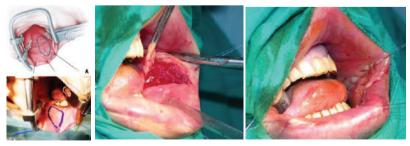


Fig 9 – Buccal mucosa graft harvesting – A. Schematic drawing B. Intraoperative marking of the graft. C Excision of the graft. D. Restoration of the graft site

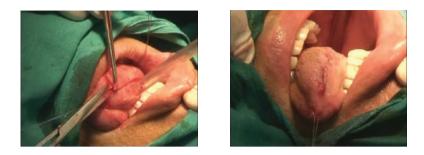


Fig 10. Lingual mucosa graft harvesting – A. Intraoperative marking and excision of the graft onto dorso-lateral surface of the tongue B. Restoration of the graft site

Operative technique

The Kilner-Doughty or other type of mouth retractor is used or stay sutures; three of which are placed along the edge of the mouth to stretch the oral mucosaThe Stensen duct is mandatory to be identified in proximity of the second molar Solution, containing local anesthetic (Lidocain, Bipuvacain) and Adrenaline 1/20.000, is injected at the donor site to achieve hemostasis and hydro-dissection. The dissection plane of the graft is between the mucosa and the muscle. The donor site is closed with running 5-0 resorbable sutures.

Results and discussion.

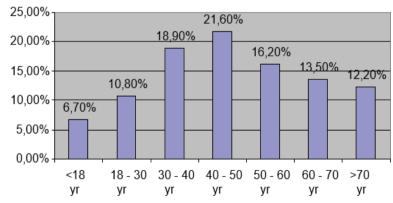


Figure 11 shows the age distribution of patients with urethral strictures:

Fig 11 - Incidence rate of strictures based on age

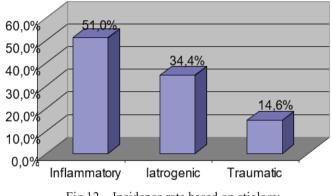


Fig 12 – demonstrates the etiologic distribution:

Fig 12 – Incidence rate based on etiology

In reconstructive operations on the male urethra, the recovery of patency was noted in 84.29%. Recurrence was found in 10%, with only 4.6% requiring re-urethroplasty. According to the erectile function questionnaire, there was an improvement of 9.4% compared to the questionnaire prior to surgery.

The age distribution in our patients varies widely (from 14 to 88 years). The majority was in the range between 30 and 60 years of age. This is largely due to the fact that some of the most common etiological factors (inflammatory and traumatic) mainly involve this age group 20 .

The obtained results show that age is not a significant factor in influencing the harvesting of the graft material and its revascularization after urethroplasty. About 40% of cases are of idiopathic etiology ²¹. The widespread use of endoscopic operations and procedures in urology is one of the most common causes of iatrogenic trauma to the urethra. It is now known that urethral strictures are found in 300 per 100,000 men and are a significant challenge in urological pathology ²². Their treatment is one of the main issues faced. Excision of the stricture with subsequent urethroanastomosis gives the best long-term results - over 90% ²³. However, the application of this approach is limited to short strictures located mainly in the bulbar urethra. That is why the introduction of urethroplasty with the oral mucosa flap is considered revolutionary. In 1996, Barbagli, G. outlined

the technique of dorsal "onlay" urethroplasty with a free graft of buccal mucosa, and since then this approach has been adopted in many countries around the world ²⁴. The use of different modifications of this technique (dorsal inlay, dorso-lateral onlay, ventral onlay) is a matter of preference for the surgical team ^{9, 13, 25}. The success of augmentation anterior urethroplasty in the long-term ranges from 73 to 90% ^{1, 6, 26}. A comparative analysis between onlay and inlay techniques shows almost identical results in long-term outcomes - 88% vs. 86.4% ²⁷.

Augmentation anastomotic urethroplasty is mostly used in the bulbar and posterior urethra ^{4, 28}.

The morphometric evaluation of the free buccal mucosa graft shows a high degree of vascularization - 4.9%. Maximal excision of stricture tissues, well into the healthy tissue, is an important factor for the success of urethroplasty ²⁹.

Currently, oral mucosa is typically harvested from the cheek, the tongue, and the lower lip ³⁰. Buccal mucosa has been the main donor site for years, due to the ease of access and possibility of harvesting a wider graft⁷. Despite these advantages, BMG is associated with a series of inconveniences and discomfort for the patients: perioral numbness, difficulty with opening of the mouth, oral cavity dryness, etc.⁸.

Using the tongue as a donor site – lingual mucosa graft (LMG) was first been proposed in 2006^{31} . Subsequently, this technique has gained popularity and has further been developed and perfected.

In the recent years (2006-2017) there have been over 20 publications in the English literature regarding LMG^{5, 10, 11, 17, 32}. The usual technique of graft harvesting is from the lateral and ventrolateral side of the tongue, between the papillae on the dorsal and sublingual mucosa. This approach allows harvesting longer grafts – over 7 centimeters¹¹. Using LMG for anterior urethroplasty shows highly positive functional results, with very few complications and patient inconvenience. This is supported by our observations^{17, 32}. Additionally, using LMG allows tabularization for a wider urethral lumen. In this technique the graft is sutured horizontally, forming a wide luminal diameter and outstanding functional results – 91.6% effectiveness¹⁰. Results of reconstructive urethroplasty with LMG are comparable to those with buccal grafting in addition to the smaller risk of complications associated with the procedure³³.

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Other substantial challenges in reconstructive urology are the long and complicated urethral strictures, as well as the treatment of recurrence 34 , 35 . Even in these cases, oral mucosa grafting is associated with a high success rate – over $81\%^2$. In most cases, such complicated strictures are reconstructed in two stages³⁶, with the second stage being after six to nine months.

In high-degree strictures and especially when part of the urethra is missing, following combined trauma, we developed and introduced a two-stage surgical technique utilizing buccal mucosa¹⁸. Our results in the treatment of seven patients give us reason to regard this approach as an alternative in this serious pathology.

Few studies demonstrate the results of the so-called Redo-urethroplasty in recurring strictures. Even here, the use of oral mucosa is a preferred technique, mainly with a buccal graft¹².

An important aspect in male urethral reconstructive surgery is vascular, nerve, and muscle sparing, which is associated with better functional results and fewer complications 3 .

Ureteroplasty.

Using oral mucosa as graft material in reconstructive surgery of the ureter has been gaining popularity^{37, 38} because of the high risk of complications associated with using an intestinal segment or auto transplantation.

Acquired ureteral strictures are relatively rare and usually due to:

1 complications of ureterorenoscopy (1%);

2 impacted ureteric stone (5-24%);

3 radiotherapy for an adjacent neoplasm $(2.3\%)^{39.}$

Other, more rare causes are trauma, retroperitoneal fibrosis, endometriosis.

Treatment of ureteral strictures is a serious challenge in reconstructive urology. Long and proximal strictures, as well as those involving the mid-third of the ureter, are especially challenging. The use of endoscopic methods is on the decline because of the unsatisfactory results and the necessity of follow-up surgeries and procedures⁴⁰. Using buccal or lingual mucosa is emerging as an alternative for ureteroplasty. In this study we put forward a personal observation in a patient with a mid-third ureteric stricture, resulting from several endoscopic procedures for an impacted stone. We used a 7 centimeter segment of lingual mucosa, grafted with the "onlay" technique. One year later results show no evidence of hydronephrosis.

Literature review regarding this approach demonstrates high success rates for ureteroplasty with oral mucosal graft and low rates of complications with both types of surgery – open or laparoscopic. Unfortunately, there are only 72 cases reported in the accessible literature, and more reports and later results have yet to be published.

Corporoplasty with buccal mucosal graft.

Another serious challenge in urologic practice is the presence of abnormal curvature of the penis (Peyronie's disease).

Peyronie's disease (PD) is an acquired condition, characterized by fibrosis of the tunica albuginea and leads to abnormal penile curvature with erectile dysfunction (ED) as a result.

PD affects 3.2 to 13% of men, and it is seen in men ranging from 50 to 60 years $old^{41, 42}$.

Predisposing etiological factors are diabetes mellitus, previous prostatectomy, hyperlipidemia, arterial hypertension, and tobacco smoking. Nevertheless, this disease's pathophysiology still is not completely clear. Recently it is thought that penile microtrauma plays a central role, causing fibroblastic proliferation and abnormal collagen deposition in the tunica albuginea⁴³. PD's course is biphasic: acute and chronic, and is characterized by pain and inflammatory elements, after which permanent curvature of the penis develops. Surgical therapy is indicated in cases with difficult or impossible penetration during intercourse and is subdivided into three categories based on the angle of deviation⁴⁴:

1. shortening of the opposite side of the penis (plication technique);

2. straightening by plaque excision and grafting of the defect with suitable material

3. penile implant placement

The second category includes multiple options for grafting material after plaque excision:

1. derma⁴⁵

2. venous graft⁴⁶

- 3. cadaveric or animal pericardium⁴⁷
- 4. dura mater⁴⁸
- 5. synthetic materials⁴⁹
- 6. intestinal submucosa⁵⁰
- 7. tissue-engineered graft⁵¹.

Over time, all these techniques could not establish themselves as methods of choice, and the results are variable. Buccal mucosa as a graft material was first proposed in 2005⁵². This approach has been developed and there are currently publications on using lingual mucosa for the same purposes^{53, 54}.

In our analysis, substitution corporoplasty in PD has been carried out in 15 (2.8%) patients. For all of them, the following have been assessed:

1. IIEF

2. curvature angle measurement with follow-up for 9 to 18 months.

Regarding the first index, 86% of cases have achieved satisfactory coitus, and, in 72%, penis straightening has been observed¹⁴.

Oral mucosal tissue with its elasticity and autology is an optimal alternative to the many proposed options for graft material in PD treatment – with highly positive cosmetic and functional effects.

Organ-sparing surgery for carcinoma of the penis.

Carcinoma of the penis is a rare neoplasm affecting around 1% of the male population in the USA⁵⁵ and up to 10% in developing countries⁵⁶.

Despite this, traditional treatment methods – partial or total penectomy – impose a serious and dramatic effect on the quality of life and psychological condition of patients. In some cases, there is a feasible alternative to total or partial penectomy, which still effectively eliminates the tumor and preserves the sexual function with a maximal cosmetic effect⁵⁷.

Most tumors involve the glans penis and preputium, which allows for such type of surgery. Despite this, patients should be carefully selected, taking into account the anatomical specifics – during cavernous body resection the borders have to be clear of tumor invasion⁵⁸.

Tumor excision and glansectomy are part of the organ-sparing techniques for carcinoma of the penis. The problem of what grafting material is to be used arises. Most often this is a skin graft – the "split-thickness" approach^{59, 60}.

Buccal mucosa as a substitute material is seldom used in urologic practice and dermatological surgery⁶¹. We have carried out 8 (1.5%) such procedures with very good functional and oncologic results⁶². In one patient with malignant melanoma, 18 months after surgery, generalization of the disease was found. In this particular case, organ-sparing surgery was performed despite inguinal nodal invasion, due to the patient's exclusive demand⁶¹.

Conclusion:

Oral mucosa has recently been proven to be superior as a graft material in reconstructive urology. Its advantages are

1. high accessibility and ease of harvest

- 2. low rate of infection
- 3. compatibility with the permanent contact with urine
- 4. thick epithelium and thin lamina propria
- 5. early revascularization and tissue adhesion.

Reconstructive surgery using free oral mucosal graft demands strict patient selection, possession of more operative techniques, and specialized professional experience. Oral mucosa as grafting material is the most widely used approach in modern urology because of the positive results of its application.

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ЛИГАВИЦА ОТ УСТНАТА КУХИНА КАТО ПЛАСТИЧЕН МАТЕРИАЛ В РЕКОНСТРУКТИВНАТА УРОЛОГИЯ

Абстракт

Увод.

Въпреки големият технологичен напредък в медицината, остават сериозни предизвикателства пред реконструктивната хирургия в урологичната практика. Липсата на универсален пластичен материал при заместващите операции на уро-гениталната система при мъжа е един от основните проблеми.

Цел.

Целта на настоящата студия е да се направи ретроспективен анализ на функционалните резултати от използването на свободни лигавични ламба от устната кухина.

Материал и методи.

За период от 20 години (2000-2021) са проследени 521 пациенти, при които е извършена реконструктивна заместваща операция с използване на свободни лигавични ламба от устната кухина. Те са разпределени в 5 основни групи, според органа върху който е извършена реконструктивната операция: 1/ Уретропластика при стриктури на уретрата – 427 (82%); 2/ Уретропластики при осакатена хипоспадия – 70 (13.4%); 3/ Уретеропластика при стриктури на уретера – 1 (0.2%); 4/ Заместителна корпоропластика при болестта на Пейрони – 15 (2.8%); 5/ Органсъхраняващи операции при карцином на пениса – 8 (1.5%).

Резултати.

Като заместителен (пластичен) материал от зоната на устната кухина са използвани три места:

1.	Букална лигавица (BMG)	- 368 (70.6%)
2.	Лингвална лигавица (LMG)	- 135 (25.9%)

Лигавица от долната устна - 18 (3.5%)

Не са отбелязани по-сериозни усложнения от добиването на графта.

Основен вид операции са били: едноактни оперативни техники 460 (88.3%), следвани от двуактните операции – 38 (7.3%) и операции върху половия член – 23 (4.3%).

Функционалните резултати са отчетени според вида на операцията, като в най-голямата група – уретропластиките е постигнат успех в 84.29%

Заключение.

Понастоящем реконструктивната хирургия върху пикочните пътища и половия член при мъжа с използване на свободни ламба от лигавицата на устната кухина е най-застъпената оперативна техника в модерната урология. Този вид дейност изисква стриктен подбор на пациентите и сериозен професионален опит.

Ключови думи. лигавица от устната кухина (BMG, LMG), уретропластика, уретеропластика, корпоропластика, органсъхраняващи операции при Са на пениса.