Kitap Bölümü Nasıl Hazırlanır?

Prof. Dr. Muammer Kendirci

İstinye Üniversitesi Tıp Fakültesi Üroloji AD

Liv Hospital Ulus

Akademik Gelişim Programı Geleceğin Akademisyenleri Toplantısı, 05 Nisan 2019, İstanbul

Kimlere ve neden davet yapılır?

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- PRKÇ
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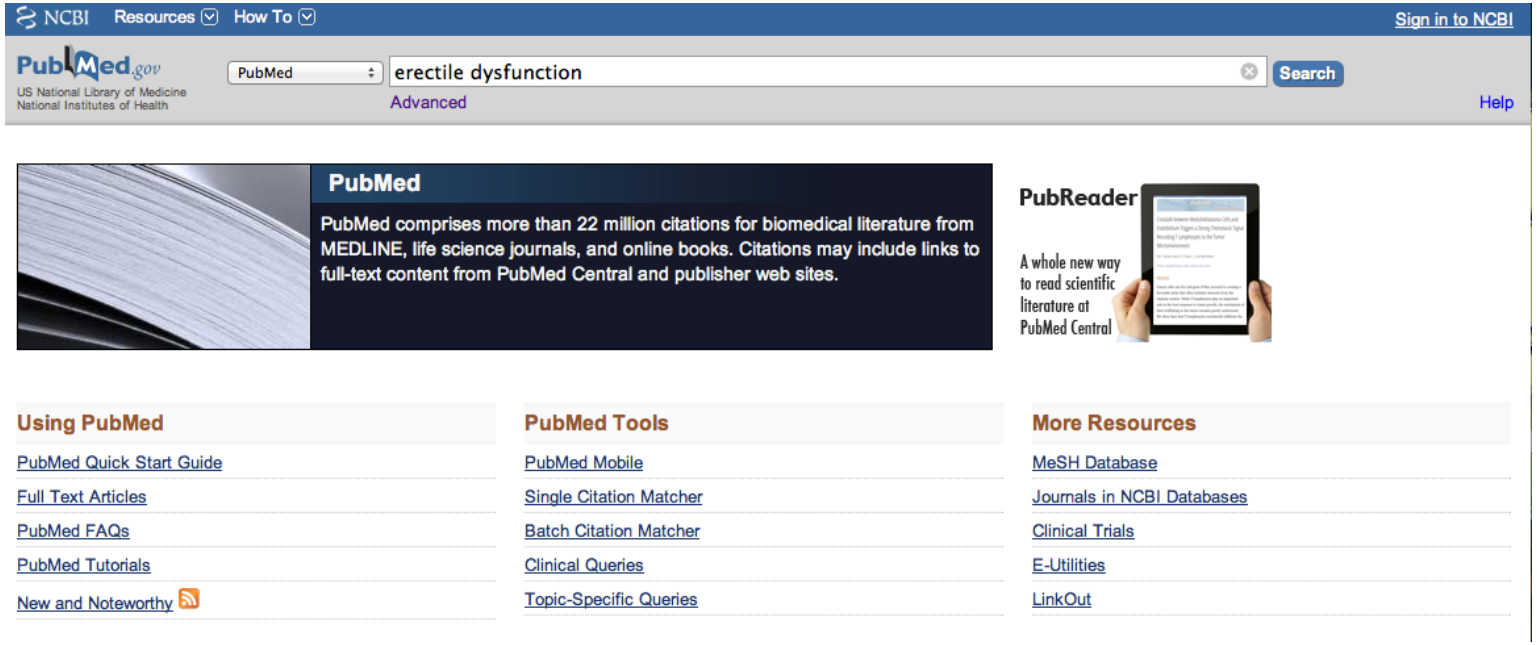
- Sistematik derlemeler
- Kılavuzlar
- Uzman görüşleri
- **KENDİ DENEYİMLERİNİZ**



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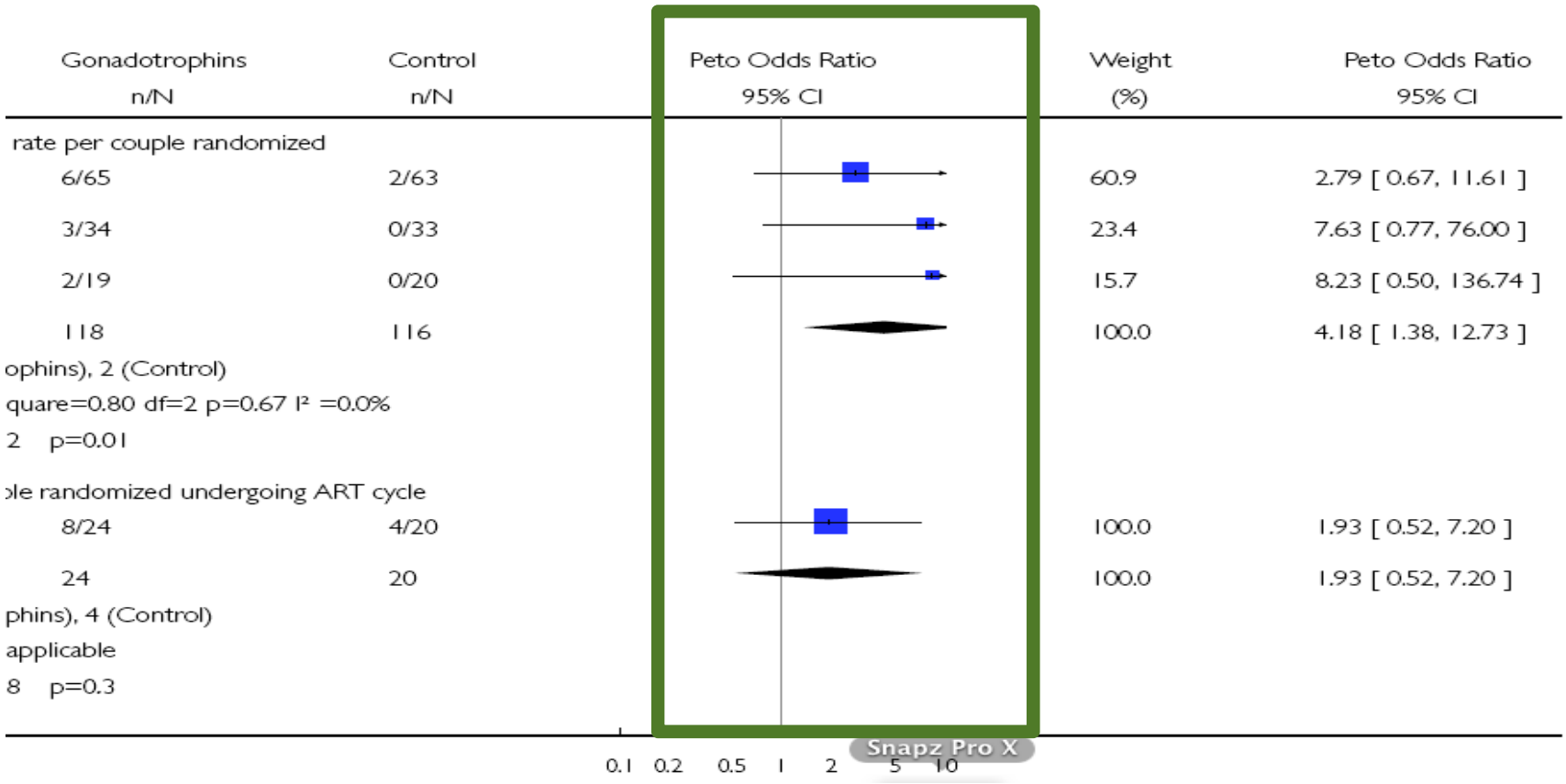

Sistematik derleme

- “Sağlık literatürünün bir özeti”
- Kritik çalışmalar ve geçerli veriler toplanır
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- Geçmişte elde edilen verileri değerlendirme
- "Archival analysis"
- **Mevcut durum ile (SCC) geçmişte olan bir olayı (Sigara kull) ilişkilendirmeye yönelik çalışmalar**

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- "Sıfır" zamandan başlayarak, ileriye dönük
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- "Taraf tutmayı engellemenin en iyi yolu"
- Bir olayın uygulanmasının (BPH'da ARB kull) zaman içinde yaratacağı durumu (Perioral dermatit) araştıran çalışmalar

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- Prospektif
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- Körleme
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1. A) RKÇ`ların metaanalizinden elde edilen veriler

   B) En az bir tane RKÇ`dan elde edilen veriler

2. A) Randomizasyon olmaksızın iyi düzenlenmiş kontrollü bir çalışmadan elde edilen veriler

   B) İyi düzenlenmiş en az bir girişimsel çalışmadan elde edilen veriler

3. A) İyi düzenlenmiş, girişimsel olmayan çalışmalardan elde edilen veriler (karşılaştırmalı çalışmalar)

   B) Tek vaka-kontrol

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C. Şüpheyle önerilir (Doğrudan uygulanabilecek iyi kalitede çalışmaya dayanmayan, ancak bulguları bazı sonuçlar çıkarmaya elverişli)

D. Önerilmez (Konuyla ilgili yeterince kanıt yok)

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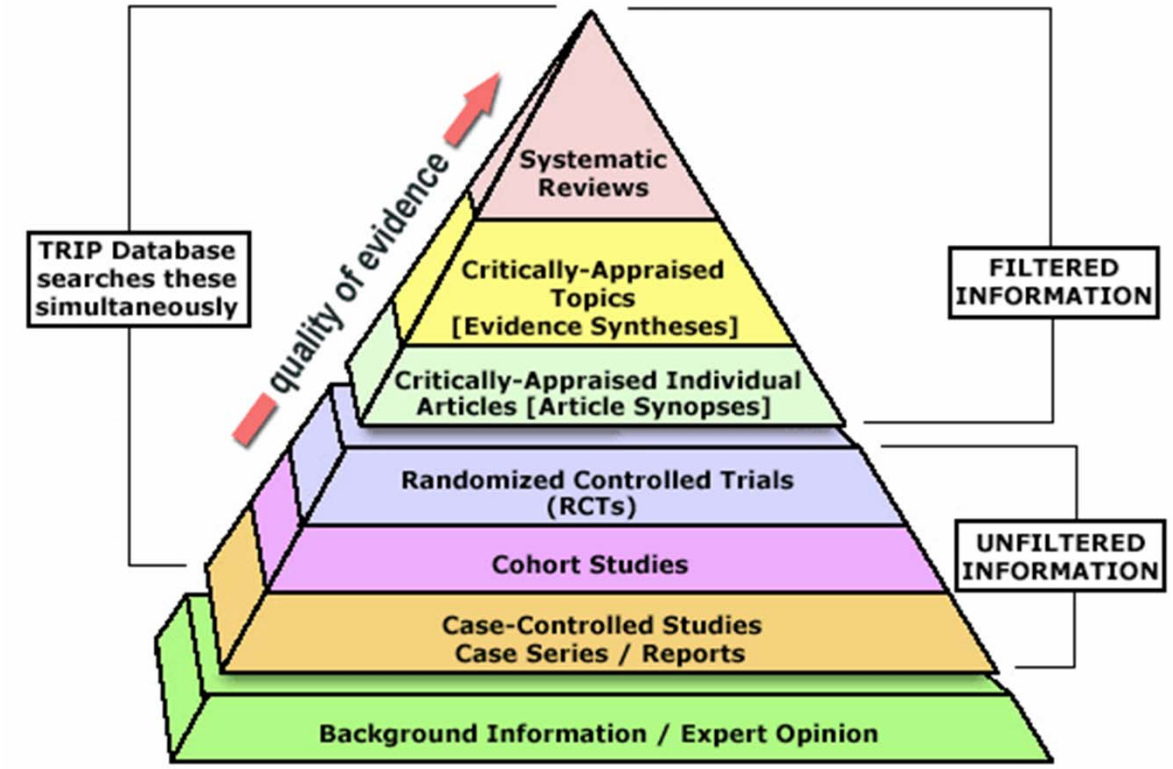


Hacim

RKÇk
RKÇ
Vaka-kontrol
Vaka serileri
Editoryal
Hayvan araştırmaları
İn vitro araştırmalar

Geçerlilik
Güvenilirlik

Chapter

TRANSPLANTATION OF STEM/PROGENITOR CELLS: POTENTIAL TREATMENT FOR ERECTILE DYSFUNCTION AFTER RADICAL PROSTATECTOMY

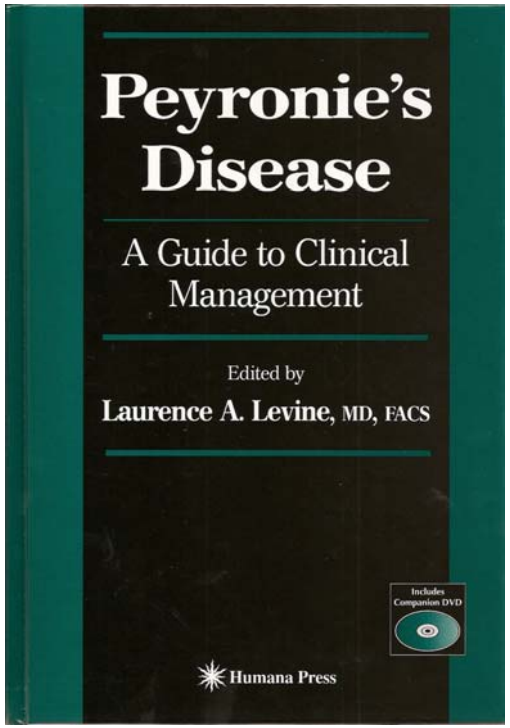
Muammer Kendirci

Cover Page
"Title=Başlık"

Running Head: Stem cells in erectile dysfunction

Keywords: Erectile dysfunction; Prostate cancer; Radical prostatectomy; Stem cells, Progenitor cells, Cell-based treatment

Correspondence:
Muammer Kendirci, MD
Associate Professor of Urology
İstanbul Cerrahi Hastanesi,
Üroloji Kliniği, Istanbul, Turkey
Pbox: +90 (212) 444 44 24
Fax: + 90 (212) 219 27 53
E-mail: mkendirci@superonline.com



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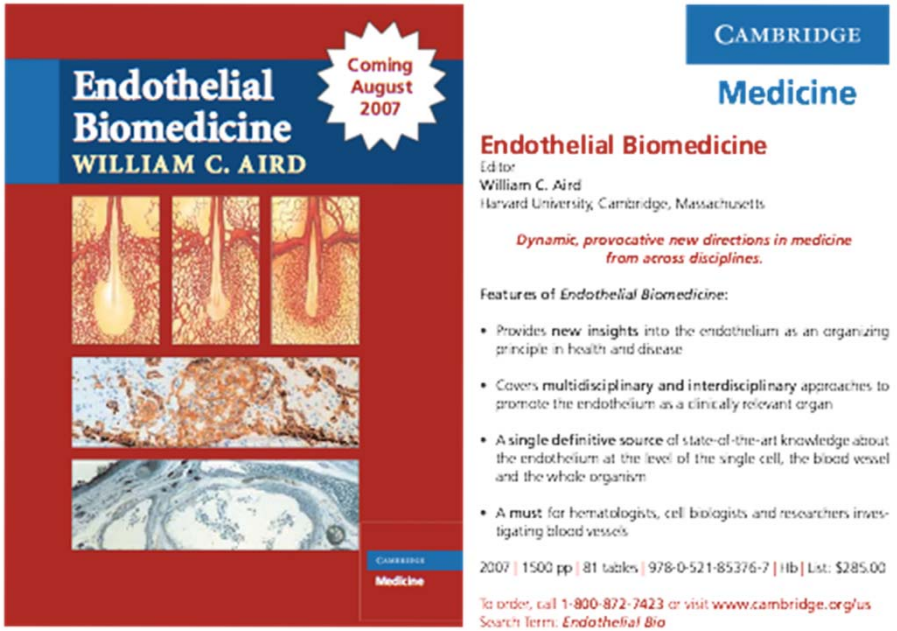
Intralesional Treatment of Peyronie's Disease

Muammer Kendirci, MD, Landon Trost, MD and Wayne J. G. Hellstrom, MD, FACS



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Muammer Kendirci and Wayne J.G. Hellstrom

Tulane University Health Sciences Center, New Orleans, Louisiana

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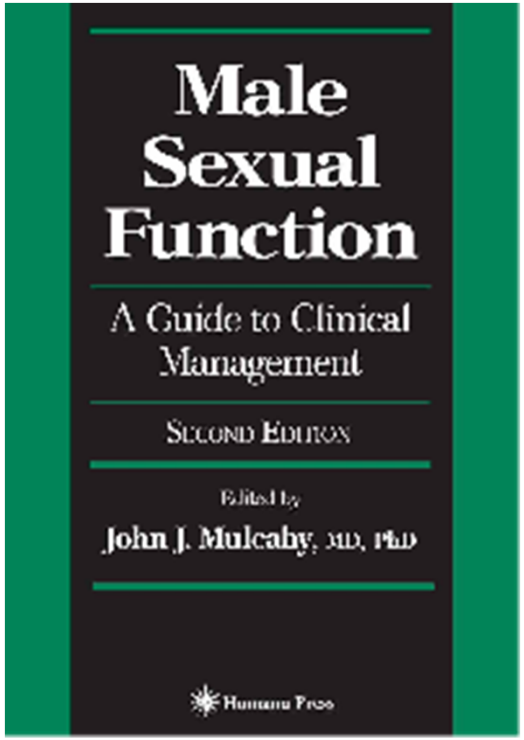
Radical Prostatectomy and Other Pelvic Surgeries

Effects on Erectile Function

Muammer Kendirci, MD, Jeffrey Bejma, MD, and Wayne J. G. Hellstrom, MD, FACS



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Correspondence:
Muammer Kendirci, MD
Associate Professor of Urology
İstanbul Cerrahi Hastanesi,
Üroloji Kliniği, Istanbul, Turkey
Pbox: +90 (212) 444 44 24
Fax: +90 (212) 219 27 53
E-mail: mkendirci@superonline.com

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"Authors=Yazarlar"

Chapter

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Muammer Kendirci

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Correspondence:

Muammer Kendirci, MD

Associate Professor of Urology

İstanbul Cerrahi Hastanesi,

Üroloji Kliniği, Istanbul, Turkey

Pbox: +90 (212) 444 44 24

Fax: + 90 (212) 219 27 53

E-mail: mkendirci@superonline.com

Cover Page
"Running Head
Kısa Başlık"

Chapter

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Muammer Kendirci

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Correspondence:

Muammer Kendirci, MD

Associate Professor of Urology

İstanbul Cerrahi Hastanesi,

Üroloji Kliniği, Istanbul, Turkey

Pbox: +90 (212) 444 44 24

Fax: + 90 (212) 219 27 53

E-mail: mkendirci@superonline.com

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"Keywords"

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Muammer Kendirci, MD

Associate Professor of Urology

İstanbul Cerrahi Hastanesi,

Üroloji Kliniği, Istanbul, Turkey

Pbox: +90 (212) 444 44 24

Fax: + 90 (212) 219 27 53

E-mail: mkendirci@superonline.com

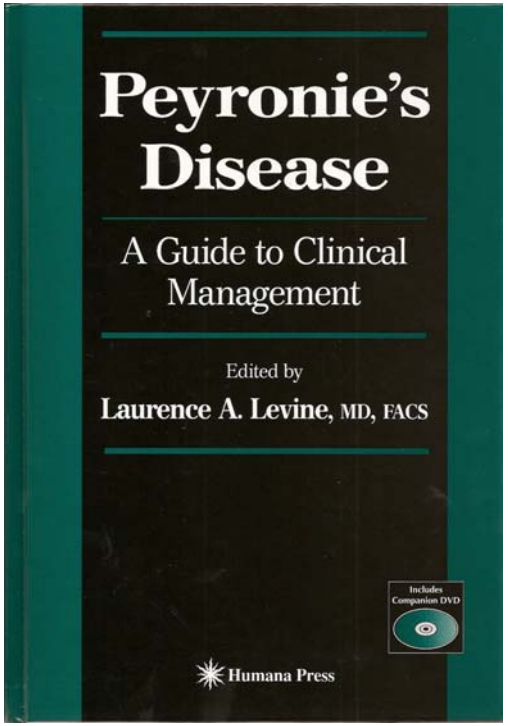
Cover Page
“Correspondence”

INTRALESIONAL TREATMENT OF PEYRONIE'S DISEASE

Muammer Kendirci, M.D.
Research Fellow
Tulane University School of Medicine,
Department of Urology
New Orleans, Louisiana

Sepehr Nowfar, M.D.
Tulane University School of Medicine,
Department of Urology
New Orleans, Louisiana

Wayne J.G. Hellstrom, M.D., F.A.C.S
Professor of Urology
Chief, Section of Andrology
Tulane University School of Medicine,
Department of Urology
New Orleans, Louisiana



Running Head: Intralesional treatment of Peyronie's disease

Keywords: Peyronie's disease; intralesional treatment, interferon, verapamil, steroid, collagenase, therapy, nonsurgical, minimally invasive.

Correspondent Author:

Muammer Kendirci, M.D.
Associate Professor of Urology
Department of Urology
Tulane University Health Sciences Center
1430 Tulane Avenue, SL-42
New Orleans, LA 70112
Phone: (504) 988-7308
Fax: (504) 988-5059
E-mail: mkendirci@superonline.com

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POSTOPERATIVE REHABILITATION OF ERECTILE FUNCTION

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BASIC SCIENCE STUDIES ON CAVERNOUS NERVE INJURY-INDUCED ERECTILE DYSFUNCTION

STEM/PROGENITOR CELLS IN ERECTILE DYSFUNCTION

STEM/PROGENITOR CELLS IN CAVERNOUS NERVE INJURY-INDUCED ERECTILE DYSFUNCTION

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Summary
"Özet"

SUMMARY

Peyronie's disease (PD) is a pathological condition of the penis that is most likely linked to the repetitive minor trauma that occurs during intercourse. The initial inflammatory process in some genetically susceptible individuals gives way to a subsequent persistent low-level autoimmune response. At the cellular level, this disorder involves increased deposition of collagen and glycosaminoglycans in the tunica albuginea of the penis, which leads to fibrosis and eventual plaque formation. The fibrous plaque can cause structural alterations in penile anatomy and sexual dysfunction. Experimental research in PD has invoked a role for cytokines and fibroblast activity, which has motivated clinicians to explore a number of nonsurgical and minimally invasive treatment options. With the experimental in vitro success of calcium channel blockers and interferons in counteracting the fibrotic process in PD, researchers have initiated a number of clinical studies with these agents. Both intralesional verapamil and interferon α-2b have demonstrated significant clinical benefits to men with PD regarding a decrease in penile curvature and plaque size, reduction of penile pain on erection, and improved sexual function. Intralesional injection therapy can be initiated in most cases of PD but must be individualized to each man's presentation based on the onset and severity of the disease, the patient's motivations, and realistic expectations from this therapy.

"İçeriğe bakmaya karar verdirtecek kısım"

Introduction
"Giriş"

INTRODUCTION

Peyronie's disease (PD) is a localized connective tissue disorder characterized by an inelastic, fibrous scar in the tunica albuginea of the penis *(1)*. Most authorities believe that PD is a result of repetitive trauma that occurs during intercourse, which in turn incites an inflammatory process and subsequent low-level autoimmune response *(2)*. This process results in increased deposition of collagen and glycosaminoglycans, which eventually leads to fibrosis of the tunica albuginea and plaque formation. The fibrous plaque often

- → Bir kaç paragraf
- → Sonunda bu bölümün amacı/ları
- → EN SON YAZ!
- → Sayfa numaraları eklemeyi unutma!

Body of Text
“Ana Yazı/Bölümler”

- → Çift satır aralığı
- → Paragraflar arası boşluk
- → Alt başlıkları numaralandır
- → Tablo/şekilleri metin içinde belirt

corporal smooth muscle, modification of channel function is a logical target for molecular and pharmacologic intervention in the treatment of ED.

3.5. RhoA/Rho-kinase

The contracted state of the penile vasculature is thought to be mediated by the release of norepinephrine, endothelin 1, and a host of other vasoconstrictors [39]. Vasoconstrictor agents elevate intracellular calcium and activate myosin light-chain kinase (MLCK), causing myosin phosphorylation and cross-bridge activation. In addition, calcium sensitisation is activated through agonist stimulation of heterotrimeric G protein-coupled receptors and activation of RhoA through the exchange of guanosine triphosphate (GTP) for guanosine diphosphate (GDP). Activated RhoA, in turn, activates Rho-kinase, which inhibits myosin light-chain phosphatase (MLCP), resulting in a net increase in myosin phosphorylation and force at a constant calcium level [40,41]. Chitaley et al. examined the role of Rho-kinase on cavernosal tone based on the hypothesis that antagonism of Rho-kinase caused corporal smooth muscle relaxation, initiating the erectile response independent of NO [42]. The fact that Rho-kinase antagonism stimulates penile erection in rats independently from the NO pathway introduces a potential alternative avenue for the treatment of ED.

3.6. Superoxide dismutase

Endothelial cells produce reactive oxygen species (ROS) in response to shear stress, endothelium-derived agonists including acetylcholine and bradykinin, and also in various vascular disease states [43]. Potential sources of ROS in endothelial cells include nicotine amide adenine dinucleotide phosphate (NADP) oxidase (generates superoxide anion), lipoxygenase, cyclooxygenase, peroxidases, cytochrome P-450s, xanthine oxidase, and eNOS [44]. The reaction of superoxide anions and NO in the vascular endothelium or smooth muscle cells triggers the formation of the highly toxic molecule, peroxynitrite [45]. Due to its toxic effects, peroxynitrite can cause direct tissue injury, alterations in vascular tone, oxidation of vascular proteins and lipids, and overall organ dysfunction [46]. The antioxidants superoxide dismutase (SOD), catalase, the endothelial and cavernosal smooth muscle cells [47]. Increased levels of superoxide anions in the endothelium and cavernosal smooth muscle cells contribute to ED by causing endothelial dysfunction and reducing cavernosal NO biosynthesis. Overall, increased oxidative stress and superoxide anion production alter penile vasculature homeostasis and impair endothelial-derived NO in the erectile tissues [14,48]. Therefore, overexpression of SOD in the penile vasculature can reduce superoxide anion and restore NO bioavailability, thus representing another potential molecular target.

3.7. Peptides

3.7.1. CGRP

CGRP is a potent vasodilator in a number of peripheral vascular beds, whereas in the penis, its proerectile effects occur by relaxation of corporal smooth muscle cells by hyperpolarisation via K channel opening and activation of adenylate cyclase, with subsequent increases in intracellular cAMP [49,50].

3.7.2. Vasoactive intestinal peptide

Vasoactive intestinal peptide (VIP), which is a 28-residue polypeptide originally isolated from porcine duodenum, is a potent vasodilator and smooth muscle relaxant [51]. Some studies suggest that NO and VIP act as neural comediators for penile erection [52]. After release into the corpus cavernosa, VIP stimulates the activity of adenylate cyclase, resulting in increased cAMP. The increased cAMP activates protein kinase A, with subsequent closure of Ca^{2+} channels and opening of K^+ channels, thereby inducing corporal smooth cell relaxation with subsequent penile vasodilation [53,54]. VIP has been localised to the terminals of the major pelvic ganglia, penile arteries, and cavernosal smooth muscle cells [55]. Additionally, VIP-containing secretory vesicles found within cholinergic nerve endings in the penis undergo exocytosis during penile erection [56].

4. Ideal vector system

The ideal vector for gene transfer is one that allows for efficient transduction and long-term stable transgene expression while resulting in few

Conclusion

CONCLUSION

NSRP is the "gold standard" surgical approach for men with organ-confined prostate cancer. Other pelvic surgical procedures have adopted the nerve-sparing technique to improve postoperative erectile function. ED following pelvic surgery and radical prostatectomy challenges most urologists because of the lower-than-anticipated success rates, despite currently available oral and minimally invasive treatments. Postoperative pharmacological penile rehabilitation programs employing oral, transurethral, and intracavernosal vasoactive drugs are suggested to be beneficial for most patients, allowing a faster and more complete recovery of erectile function. PDE-5 inhibitors provide improved postoperative prostatectomy erectile function in approximately half of men who undergo NSRP. Alternatives include VEDs and the implantation of an IPP. New data on cavernous nerve interposition grafts, peri-operative nerve protection procedures, and prophylactic agents that promote neuro-regeneration will likely evolve into a new therapeutic avenue for patients who undergo radical pelvic surgery. The ultimate aim is to increase the quality of life in patients diagnosed with prostate cancer.

KEY POINTS

- Approximately 52% of men aged 40 to 70 years have some degree of ED. Normal penile erection requires a coordinated arterial endothelium-dependent vasorelaxation and cavernosal endothelium-dependent smooth muscle relaxation. Endothelial and erectile dysfunctions have a multifactorial origin and share similar risk factors and pathophysiologies. Vascular risk factors, such as diabetes, hypertension, atherosclerosis, advanced age, hypercholesterolemia, and coronary artery disease, are associated with impaired vascular endothelial and erectile function. As a corollary, the onset of ED should direct clinicians to search for underlying vascular risk factors. Erectile function mirrors endothelial and vascular health.
- Penile erection is a neurovascular event that relies on neural integrity, a functional vascular endothelial system, and healthy cavernosal smooth muscle.
- A healthy vascular endothelium plays an important role in erectile function. Any alteration in the vascular endothelium of the penis may result in a decreased responsiveness to vasodilator mediators or an increased sensitivity to vasoconstrictors, with the net effect being ED.
- Common consequences of vascular risk factors on the endothelium are impairment in NO bioavailability and decreased eNOS enzyme activity.

Future Goals

- To advance our understanding of the pathophysiology of endothelial dysfunction, thus leading to novel prevention strategies and EC-based pharmacological and gene-related therapies to correct ED

Key Points
“Ana Noktalar”

Acknowledgements

- Teşekkür
- İkrar
- Doğruluğunu kabul etmek

Kaynakları ekleme

THOMSON REUTERS

- Belirtilen kadar kaynak
- Önerilen formatta
- Olabildiğince güncel
- Olabildiğince güvenilir
- **Turkish Journal of Urology**

Legends
“Açıklama Yazısı”

- Yalnızca şekiller için
- Kaynaklardan hemen sonra, şekillerden önce
- Şekli tam olarak ifade eden
- Şekildeki kısaltmaların, okların, işaretlerin açılımlıyla

Table 167-1: Common Risk Factors for Erectile Dysfunction

Vascular diseases
Coronary artery disease
Peripheral vascular disease
Atherosclerosis
Hypercholesterolemia
Hypertension
Smoking
Diabetes mellitus
Aging
Neurological disorders
Hormonal disorders
Psychological conditions
Radical prostatectomy
Oxidative stress
Drug-induced
Lifestyle issues

Tablolar

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European Association of Urology

Review – Sexual Medicine

Gene Therapy for Erectile Dysfunction: Fact or Fiction?

Muammer Kendirci [a], *Patrick E. Teloken* [b], *Hunter C. Champion* [c], *Wayne J.G. Hellstrom* [d], *Trinity J. Bivalacqua* [e,*]

Table 1 – Molecular targets used in gene therapy preclinical studies in animal models of various diseases

Molecular targets	Expected effects
Nitric oxide: NOS isoforms	Restore endothelial-derived and neuronally derived NO—ageing, diabetes
Ion channels: Maxi-K channel	Increased hyperpolarization of corporal myocyte—ageing, diabetes
Neurotransmitters: CGRP, VIP	Improve corporal cAMP synthesis—ageing, diabetes
Growth factors: VEGF, BDNF, NT3	Increase eNOS, nNOS expression, improve neovascularization—ageing, diabetes, cavernous nerve injury, vasculogenic
RhoA/Rho-kinase	Inhibition reduces corporal vascular tone, improve eNOS expression/activity—ageing, diabetes
Superoxide dismutase	Antioxidant, improve endothelial-derived NO—ageing, diabetes

NOS = nitric oxide synthase; NO = nitric oxide; CGRP = calcitonin gene-related peptide; VIP = vasoactive intestinal peptide; cAMP = cyclic adenosine monophosphate; VEGF = vascular endothelial growth factor; BDNF = brain-derived nerve growth factor; NT3 = neurotrophin 3; eNOS = endothelial nitrous oxide synthase; nNOS = neuronal nitrous oxide synthase.

Table 1
Proposed Mechanisms and Side Effects
of Various Agents Used in Intralesional Injection Therapy of PD

Drug	*Mechanism of action*	*Side effects*
Steroids	Anti-inflammatory, decreasing collagen synthesis	Local tissue atrophy, skin thinning, fibrosis
Collagenase	Collagen breakdown	No reported side effects
Orgotein	Anti-inflammatory, superoxide dismutase activity	Pain, swelling, stiffness, prickling or burning sensations, skin rashes, feeling of heaviness at the injection site
Interferon	Inhibition of fibroblast proliferation, stimulation of collagenase activity, inhibition of collagen production	Flulike symptoms, sinusitis, arthralgia, ecchymosis
Verapamil	Alters the balance of collagen synthesis and degradation	Penile bruising, ecchymosis, nausea, lightheadedness, pain

Table 3
Results of Intralesional Treatment With IFN-α-2b Regarding Dose, Number of Patients, Duration of Treatment, and Improvement Rates With Various Parameters

Reference	*Patients (n =)*	*Dose (units)*	*Duration*	*Pain relief*	*Decrease in curvature*	*Decrease in plaque size*	*Improvement in sexual function*	*Plaque softening*
33	25	1×10^6	Weekly, 5 wk	96%	4%	28%	?	?
34	30	3×10^6	Weekly, 3 wk	97%	3%	3%	?	?
35	10	1.5×10	3 times/wk, 3 wk	60%	60% (mean 20°)	33%	?	60%
36	21	1×10^6	Biweekly, 6 mo	90%	65%	85%	57%	100%
43	34	10×10^6	Biweekly, 14 wk	94%	47%	From 56.7 to 12.7 (mean, mm^2)	79%	?
38	23	2×10^6	3 times/wk, 3 wk	100%	5%	0%	—	?
39	25	2×10^6	Biweekly, 6 wk	80%	67%	71%	5/7 patients	?
40	117 (IFN = 55; Plc = 62)	5×10^6	Biweekly, 12 wk	28.1% Plc, 67.7% IFN	8.8% Plc, 27.0% IFN (% mean decrease)	19.8% Plc, 54.6% IFN (% mean decrease, cm^2)	5.96% Plc, 13.53% IFN (% mean increase in EF score)	11.1% Plc 33.3% IFN (% mean decrease)

The dose of IFN-α-2b is expressed as units. Plc, placebo.

[a]An additional three patients served as control with saline injection. No changes were observed in these placebo patients.

[b]Of 21 patients with PD, 7 were in the saline placebo arm. None of the men in the placebo group showed improvement after completion of intralesional injections.

[c]The injections were applied subcutaneously next to the plaque area. Patients who had erectile dysfunction at baseline were excluded from the study.

Treatment Outcomes With PDE-5 Inhibitors After Radical Prostatectomy

Authors	*Assessment*	*PDE-5 inhibitor*	*Nerve preservation*	*Response %*
Zippe et al. *(60)*	Successful penetration rate	Sildenafil (50–100 mg)	Bilateral	71.7
			Unilateral	50.0
			None	15.4
Zagaja et al. *(61)*	Mail survey	Sildenafil (50–100 mg)	Bilateral, <55 yr	80
			Unilateral, <55 yr	40
			Bilateral, >56–65 yr	45
			Unilateral, >56–65 yr	0
			None, any age	0
Raina et al. *(66)*	SHIM	Sildenafil	Bilateral	76.0
			Unilateral	53.5
			None	14.2
Brock et al. *(67)*	GAQ	Vardenafil (20 mg)	Bilateral	71.1
		Vardenafil (10 mg)	Bilateral	59.7
		Placebo	Bilateral	11.5
Montorsi et al. *(68)*	GAQ	Tadalafil (20 mg)	Bilateral	71
		Placebo	Bilateral	24

Adapted from ref. *127*.

SHIM, Sexual Health Inventory of Men; GAQ, Global Assessment Question.

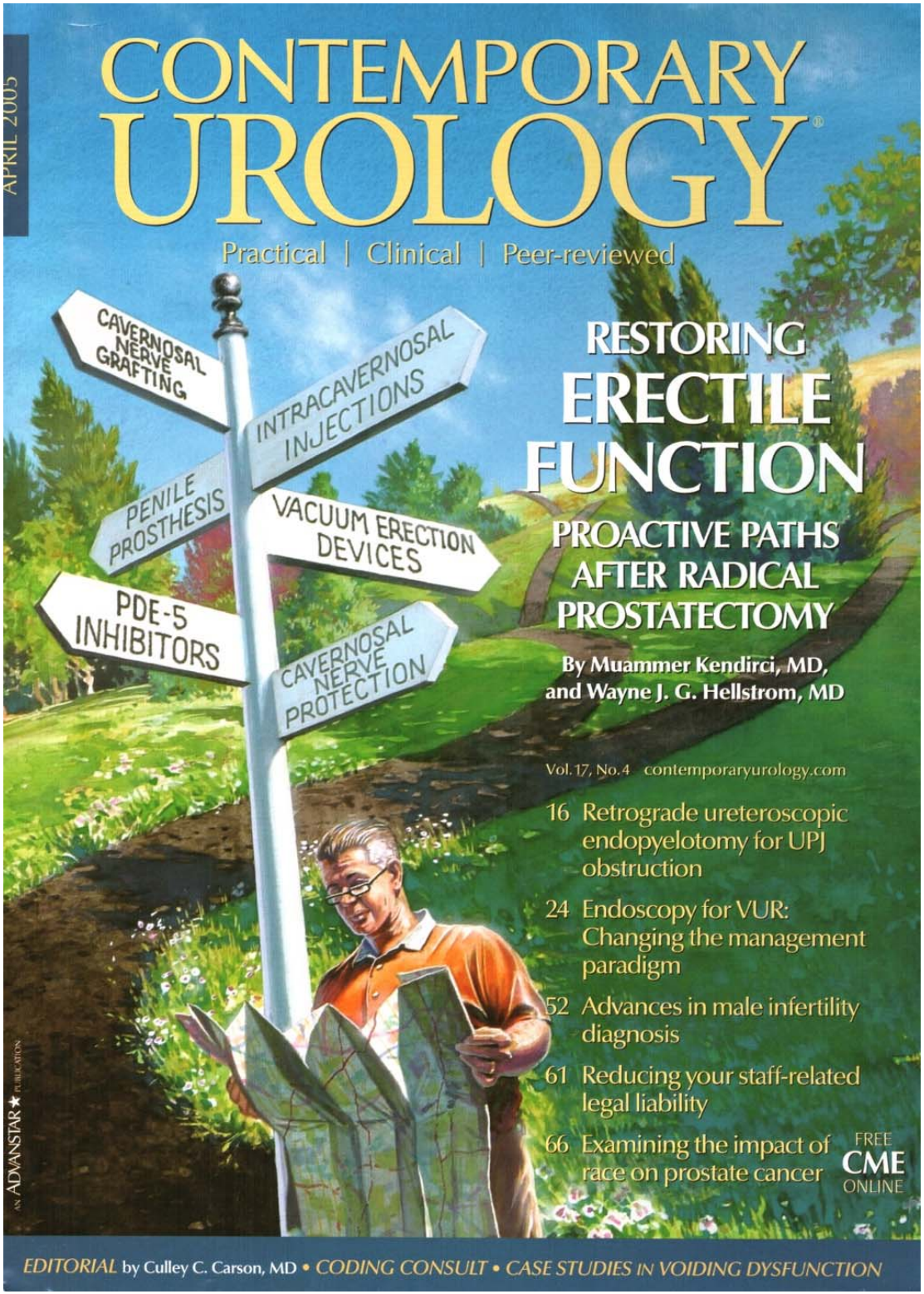
Table 2
Predictive Factors for Postprostatectomy Recovery of Erectile Function

Factors		*Advantages*	*Disadvantages*
Related to prostate cancer	Grade	Low	High
	Stage	≤T2	>T3
	Localization	Organ-confined	Advanced
Related to the patient	Age	≤65 yr	>65 yr
	Associated comorbidities	Absence	Presence
Related to the surgery	Degree of nerve preservation	Bilateral	Unilateral/no
Related to the pre-operative erectile function		SHIM ≥15	SHIM <15

Adapted from ref. *127*.
SHIM, Sexual Health Inventory of Men.

Table 1: Sexual function and bother in 1,213 prostate cancer survivors who underwent radical prostatectomy in the *Prostate Cancer Outcomes Study*. Adapted from Ref.[18]

Measure (level)	Baseline	6 mo	12 mo	24 mo	60 mo
% Sexual activity interest level					
None	7	29	15	17	18
Little/some	53	53	61	63	59
Lot	40	18	24	21	23
% Sexual activity frequency					
None	15	62	44	44	46
1/mo or greater	37	22	30	30	28
1/wk or greater	49	16	26	26	26
% Erections firm enough for intercourse					
No	17	89	81	75	71
Yes	81	9	17	22	28
% Difficulty maintaining erections					
None	51	2	5	8	9
Little/some	30	8	13	18	21
Lot	11	12	17	17	14
No erections	9	78	65	57	55
% How big a problem is sexual function					
No problem	57	12	15	18	23
Small	23	18	24	28	31
Moderate-to-large	20	70	61	54	46



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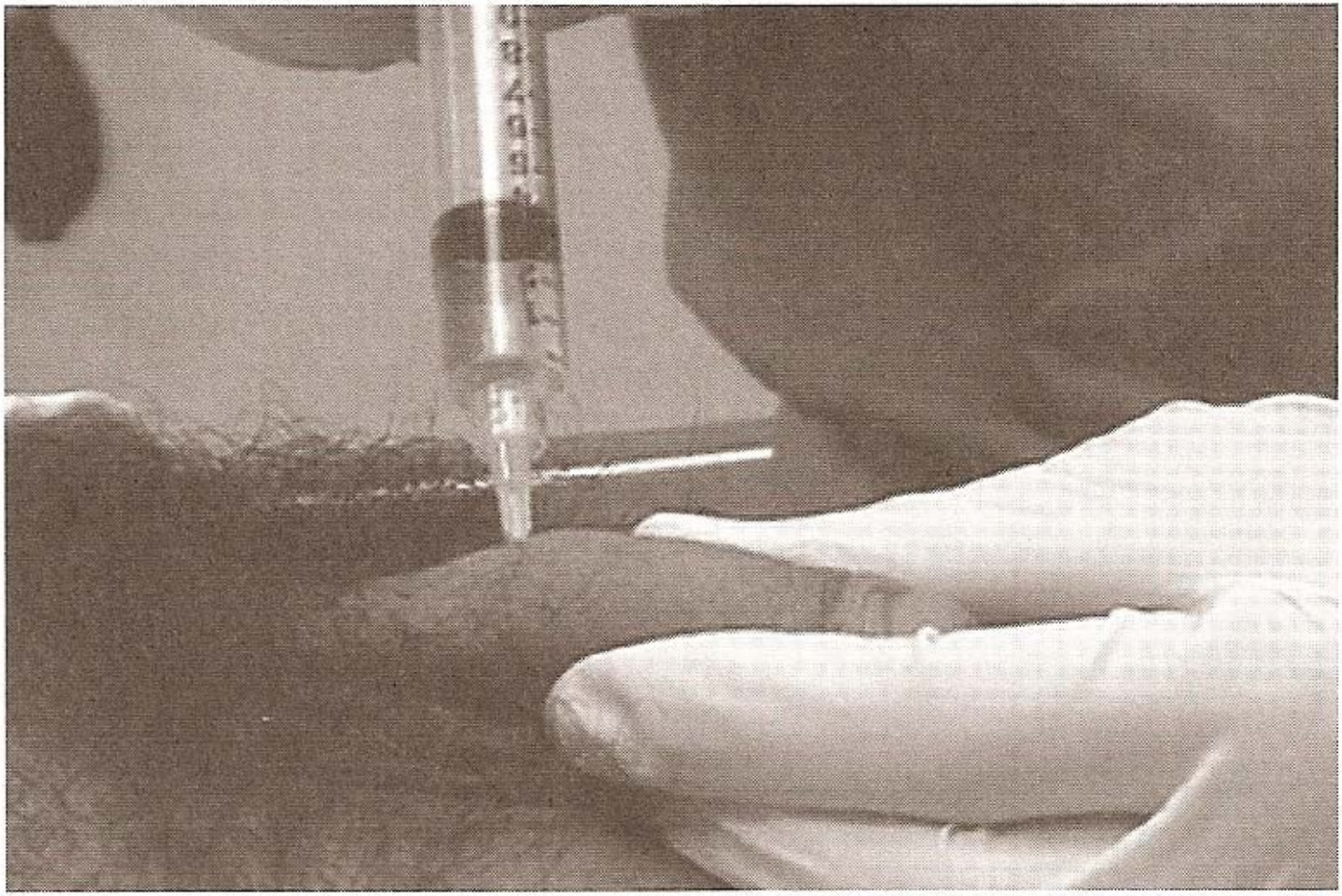

Fig. 1. Intralesional injection of IFN-α-2b into the Peyronie's disease plaque.

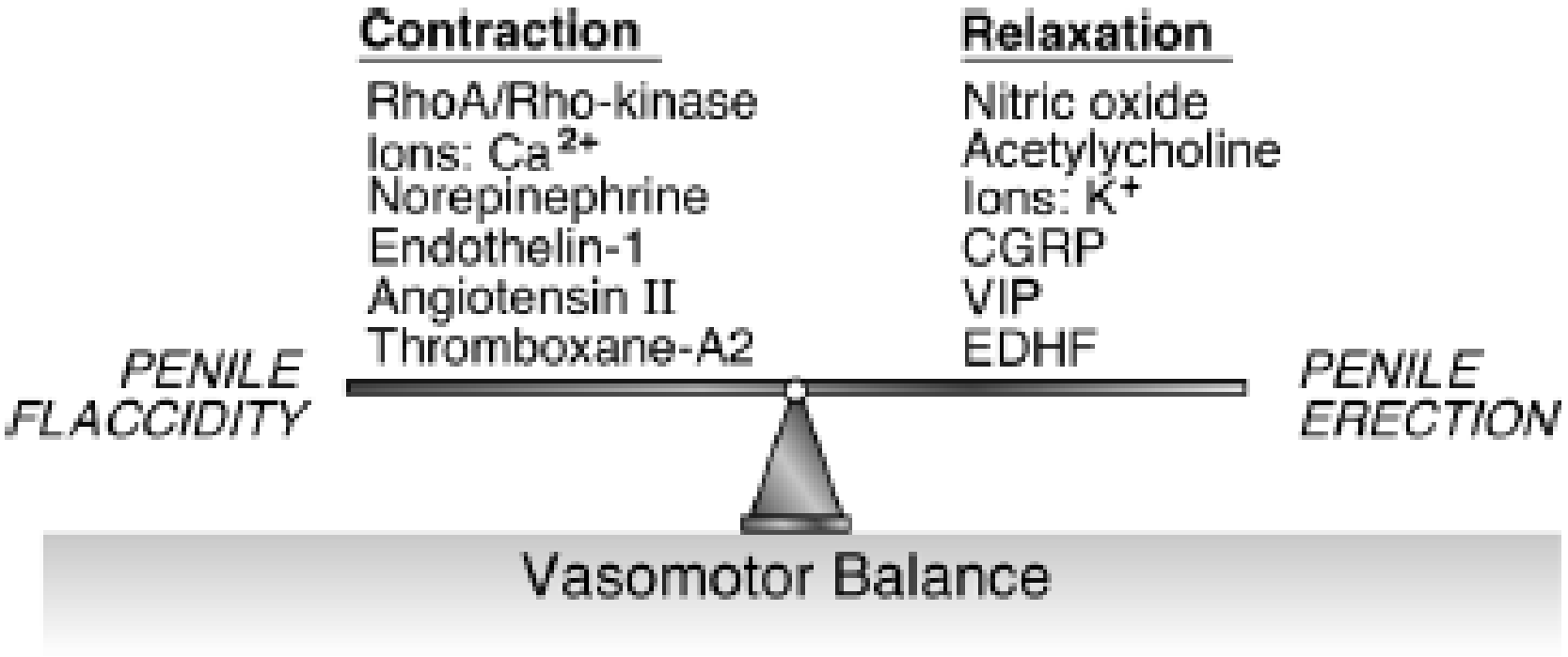

Figure 167.1. Endothelial, neural, and humoral factors mediating vasoconstriction and vasodilation in penile erection and flaccidity.

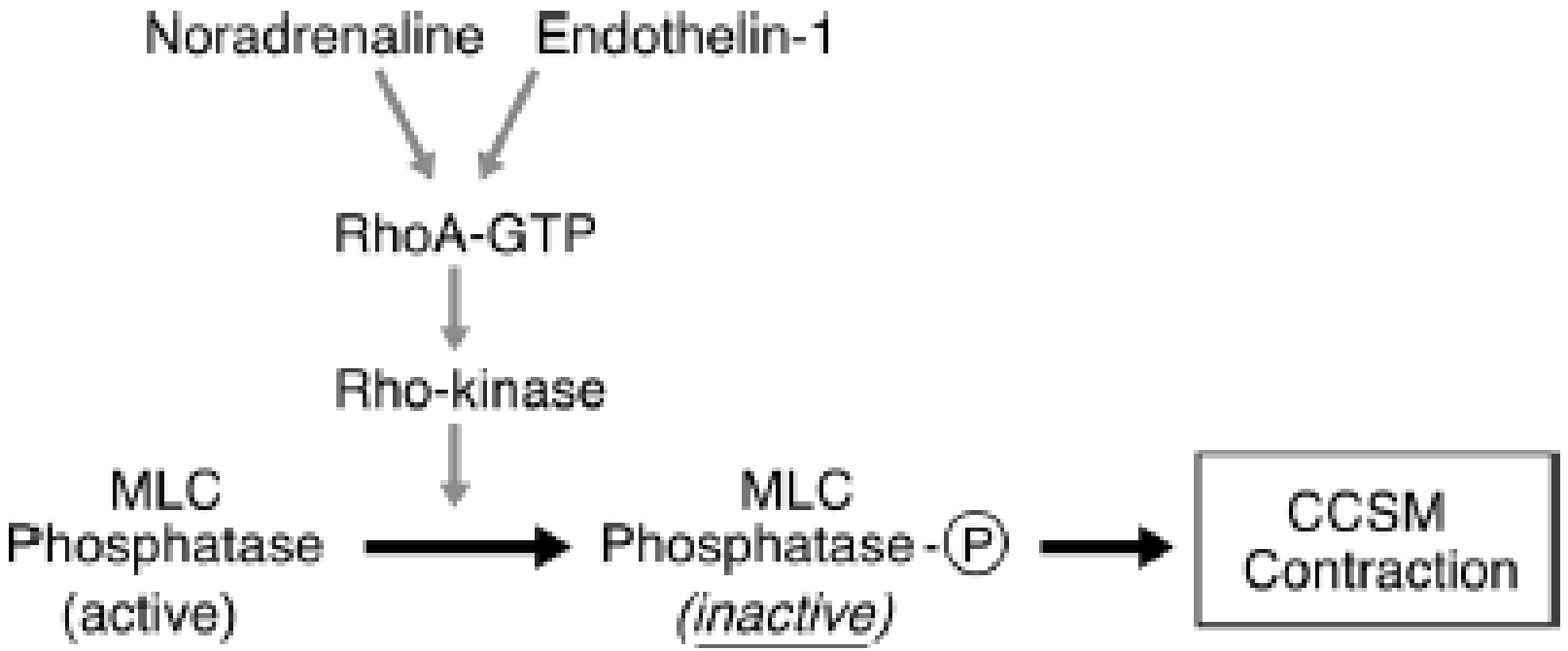

Figure 167.2. Rho-kinase pathway. The detumescent state of the corpus cavernosum smooth muscle (CCSM) is considered to be mediated by release of contractile neurotransmitters or modulators including noradrenaline and ET-1. GTP-RhoA activates Rho-kinase and inhibits MLC phosphatase, increasing MLC20 phosphorylation by basal level activity of MLC kinase. The resulting myosin phosphorylation and subsequent CCSM contraction occur without a change in sarcoplasmic Ca^{2+} concentration. (Adapted with permission from Andersson KE. Erectile physiological and pathophysiological pathways involved in erectile dysfunction. *J Urol.* 2003;170(2 Pt 2):S6–13; discussion S-4.)

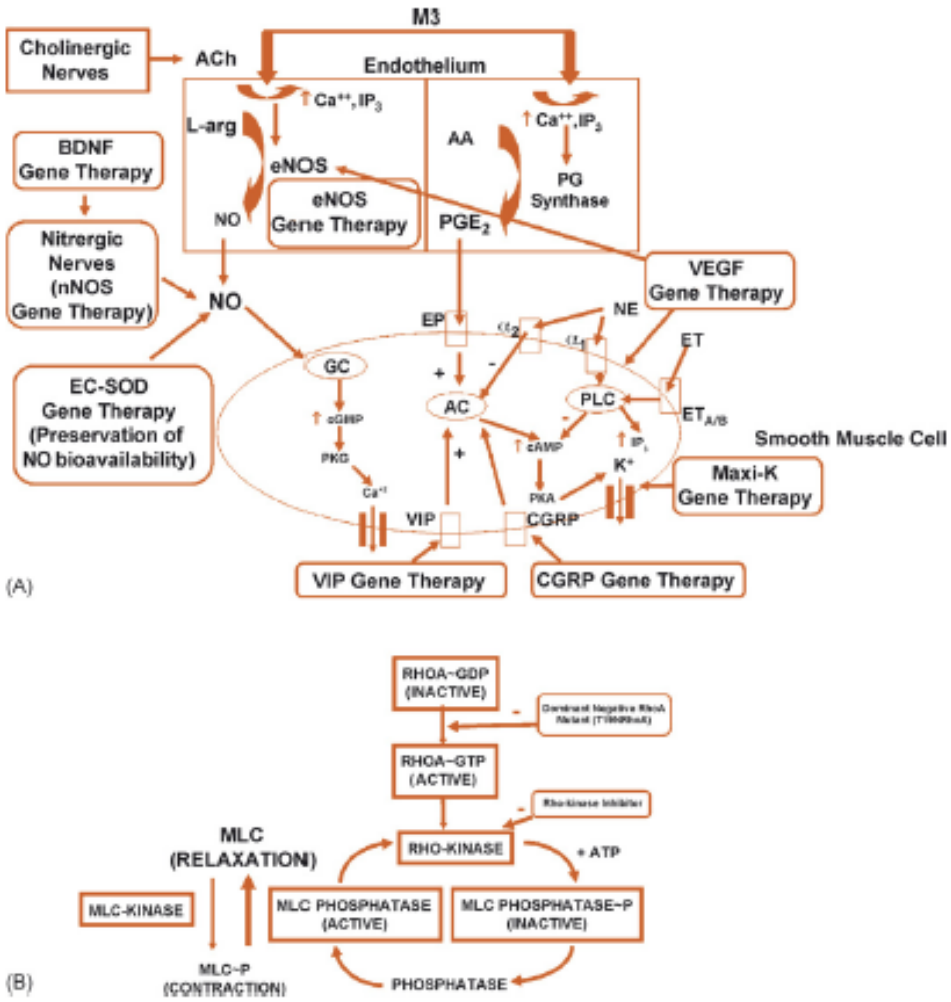

Fig. 2 – (A) Potential molecular targets that cause corporal smooth muscle relaxation. Endothelial nitric oxide synthase (eNOS) and vascular endothelial growth factor (VEGF) gene therapies increase endothelial-derived NO and promote corporal vasodilation. Additionally, VEGF preserves corporal smooth muscle integrity. Extracellular superoxide dismutase (EC-SOD) gene therapy reduces penile superoxide anion levels thus improving NO bioavailability and corporal smooth muscle relaxation. Neuronal NOS (nNOS) and brain-derived neurotrophic factor (BDNF) gene therapies increase nNOS expression and neuronal-derived NO. Vasoactive intestinal polypeptide (VIP) and calcitonin gene-related peptide (CGRP) gene therapies increase corporal cyclic adenosine monophosphate (cAMP) levels via activation of adenylate cyclase to increase corporal smooth muscle relaxation. Maxi-K channel (Ca^{2+}-sensitive potassium channel) hyperpolarises corporal smooth muscle to promote vasodilation. (B) Inhibition of RhoA or Rho-kinase using dominant-negative mutants promotes myosin light-chain (MLC) phosphatase to an activated form (nonphosphorylated), thus catalysing the dephosphorylation of MLC and thereby increasing corporal smooth muscle relaxation. Ach = acetylcholine; M3 = muscarinic receptor; L-arg = L-arginine; NO = nitric oxide; IP_3 = inositol 1,4,5-trisphosphate; AA = arachidonic acid; PGE_2 = prostaglandin E_2; PG = prostaglandin; GC = guanylate cyclase; AC = adenylate cyclase; PLC = phospholipase C; PKG = protein kinase G; PKA = protein kinase A; ET = endothelin; NE = norepinephrine; EP = prostaglandin receptor.

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Review – Sexual Medicine

Gene Therapy for Erectile Dysfunction: Fact or Fiction?

Muammer Kendirci[a], *Patrick E. Teloken*[b], *Hunter C. Champion*[c], *Wayne J.G. Hellstrom*[d], *Trinity J. Bivalacqua*[d,*]

The Role of Endothelium in Erectile Function and Dysfunction

Muammer Kendirci and Wayne J.G. Hellstrom

Tulane University Health Sciences Center, New Orleans, Louisiana

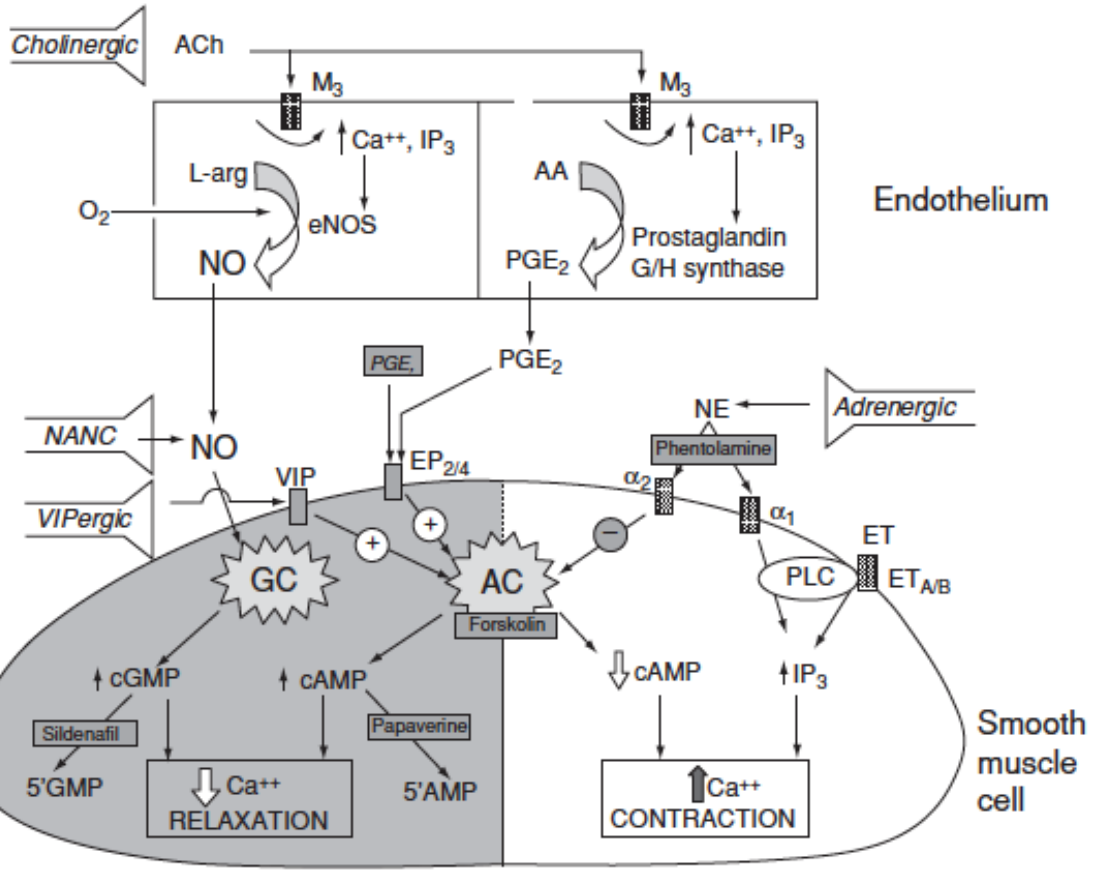
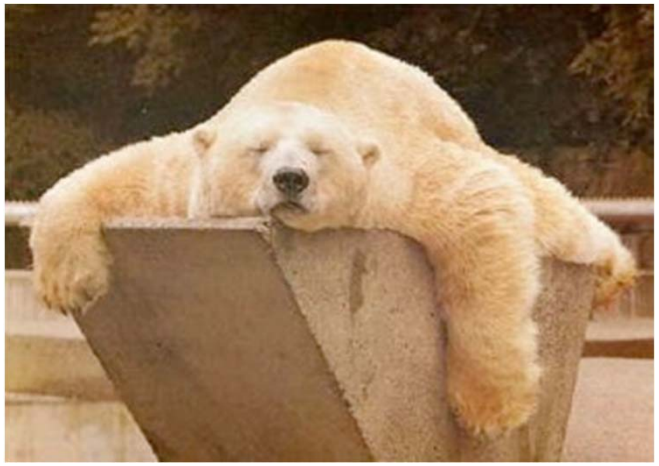


Figure 167.3. The interaction between vascular endothelium and cavernosal smooth muscle cells. (Adapted with permission from Moreland RB, Hsieh G, Nakane M, Brioni JD. The biochemical and neurologic basis for the treatment of male erectile dysfunction. *J Pharmacol Exp Ther.* 2001;296:225–234.)

Sonuçlandırma

- → Bir kaç kez oku
- → Dil konusunda tereddüt varsa “native writer” desteği (TÜD)
- → 2 hafta süreyle unut!
- → Son bir kez daha kontrol et!



[AU1]

30 Transplantation of Stem/Progenitor Cells: Potential Treatment for Erectile Dysfunction After Radical Prostatectomy

Muammer Kendirci

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Stem/Progenitor Cells in Cavernous Nerve Injury-Induced Erectile Dysfunction 000

Future Directions and Translational Issues 000

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Abstract

As the maintenance of a satisfactory quality-of-life is recognized as the principle concern for men and sexual dysfunction is an independent determinant of a worse general health-related quality-of-life, practicing urologists have focused on the understanding of the pathophysiology of erectile dysfunction (ED) following radical prostatectomy (RP) with the concepts of instituting prophylactic measures for prevention and early recovery from ED. ED following RP is often the result of inadvertent injury to the cavernous nerves that course along the prostate capsule and innervates the corpora cavernosa of the penis. The introduction of the nerve-sparing procedures to preserve erectile function has been embraced globally and has made for greater acceptance. However, as unassisted nerve regeneration is a slow process, denervation-induced damage, including cavernosal fibrosis and cavernosal smooth muscle apoptosis frequently develops following RP. Pharmacological penile rehabilitation postoperatively with oral or intracavernosal vasoactive drugs is theorized to be of benefit in most patients, allowing for faster and more complete recovery of erectile function. The current belief is that penile rehabilitation programs with available measures maintains erectile tissue integrity and prevents corporal smooth muscle atrophy and collagen production. Studies on neuroprotection and neuroregeneration will help to preserve erectile function following RP.

M. Kendirci (✉)
Department of Urology, Istanbul Surgery Hospital, Istanbul, Turkey
e-mail: mkendirci@superonline.com

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7 Radical Prostatectomy and Other Pelvic Surgeries

Effects on Erectile Function

Muammer Kendirci, MD, Jeffrey Bejma, MD, and Wayne J. G. Hellstrom, MD, FACS

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SUMMARY

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Key Words: Erectile dysfunction; radical prostatectomy; pelvic surgery; treatment; cavernous nerve; neuroprotection.

INTRODUCTION

Erectile dysfunction (ED) is defined as the consistent or recurring inability of a man to achieve and/or maintain an erection sufficient for satisfactory sexual performance or intercourse *(1)*. The Massachusetts Male Aging Study provided a detailed epidemiological report on ED, demonstrating the detrimental role of aging and other comorbidities regarding the erectile mechanism *(2)*. In this evaluation, men between the ages of 40 and 70 yr were asked to categorize their erectile function as complete, moderate, or minimal. Overall, 52% of these participants reported a certain degree of ED. Between age 40 and 70 yr, the probability of complete ED tripled from 5.1 to 15%; moderate ED doubled from 17 to 34%; and minimal ED remained at approx 17%. By age 70, only 32% of men studied portrayed themselves as free of any ED.

From: *Current Clinical Urology:*
Male Sexual Function: A Guide to Clinical Management, Second Edition
Edited by: J. J. Mulcahy © Humana Press Inc., Totowa, NJ

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Author's Proof

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AU3	Kendirci et al. (2004) which has been changed to Kendirci and Hellstrom (2004). Please check.	
AU4	Kendirci et al. (2005c) is cited in text but not given in the reference list. Please check and provide.	
AU5	Please provide in−text citation for Kendirci (2005).	
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The goal of cavernous nerve preservation has led several investigators to consider reconstruction of the nerve at the time of radical prostatectomy. Quinlan *(39)* and Ball *(40)* originally used the genitofemoral nerve as a replacement for the resected cavernous nerve in rats, with promising results. In humans, Kim et al. *(41)* applied the sural nerve as a conduit. These authors demonstrated promising outcomes, with a reported 26% rate of spontaneous, medically unassisted erections sufficient for sexual intercourse in 28 men who underwent radical prostatectomy and subsequent bilateral sural nerve grafting (mean follow-up: 23 mo) *(42)*. With the addition of four men who had partial erections sufficiently enhanced with sildenafil use, the overall potency rate for sural nerve grafting was reported as 43%. The authors similarly reported the benefit of unilateral grafting, with a potency rate of 78% *(42,43)*. In other clinical studies involving the sural nerve, Chang et al. *(44)* reported a 43% potency rate for bilateral grafting, and Anastasiadis et al. *(45)* demonstrated a 33% success rate for unilateral grafting with mean 23- and 16-mo follow-ups, respectively. Despite modifications, such as electrical stimulation to confirm the function and localization of the recipient nerve, the use of microsurgical instruments and loupe magnification, and grafting without tension, the procedure appears to be technically impractical and is infrequently used *(42–44,46,47)*. Furthermore, the candidates selected for nerve grafting often have high-stage cancer, which, as previously noted, is associated with a low probability of recovery of erectile function after surgery and would likely require adjuvant therapy; all of these factors further decrease the overall success rate *(44,48)*.

AU: high-stage cancer or late-stage cancer?

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Postoperative Rehabilitation

The introduction of the NSRP procedure by Walsh and Donker in 1982 as a means to preserve erectile function has been embraced globally and has inspired greater acceptance of surgical treatment approval for prostate cancer *(11)*. However, time has shown that this technique offers no guarantee that erectile function will be preserved *(14)*. The recovery time for return of erectile function following NSRP is not clear, and most patients do not recover erectile function as quickly as urinary continence. A study by Walsh et al. *(49)* suggested that maximal erectile recovery is not witnessed until a mean period of 18 mo after bilateral NSRP. Because several factors may affect the cavernous nerves during radical prostatectomy (including thermal damage, ischemic injury, mechanically induced nerve stretching, and the local inflammatory effects of surgical trauma), the cavernous

that innervate the corpus cavernosum. A detailed dissection in nine male cadavers revealed the midpoint of the pelvic plexus, which closely approximated the lateral margin of the seminal vesicle. Using the seminal vesicle as an intra-operative landmark, nerve-sparing radical cystectomy has improved potency rates measured by subjective questioning to 42 to 71% *(85,86)*. Furthermore, the percentage of patients subjectively reporting reduced or normal erections (compared with no erections) was evaluated in 331 patients who underwent attempted bilateral, unilateral, or non-nerve sparing cystoprostatectomies. Approximately 60% of the bilateral nerve-sparing group, 30% of the unilateral group, and 10% of the non-nerve sparing groups reported normal or reduced erectile function *(87)*. Although the results may not be as dramatic as the nerve-sparing approach to radical prostatectomy, preservation of the neurovascular bundle is paramount for potency in management of bladder cancer.

AU: Is reduced correct? Or should you say improved?

Very few studies have objectively studied erectile function and pharmacotherapy following radical cystoprostatectomy. Zippe et al. *(88)* used pre-operative, postoperative, and

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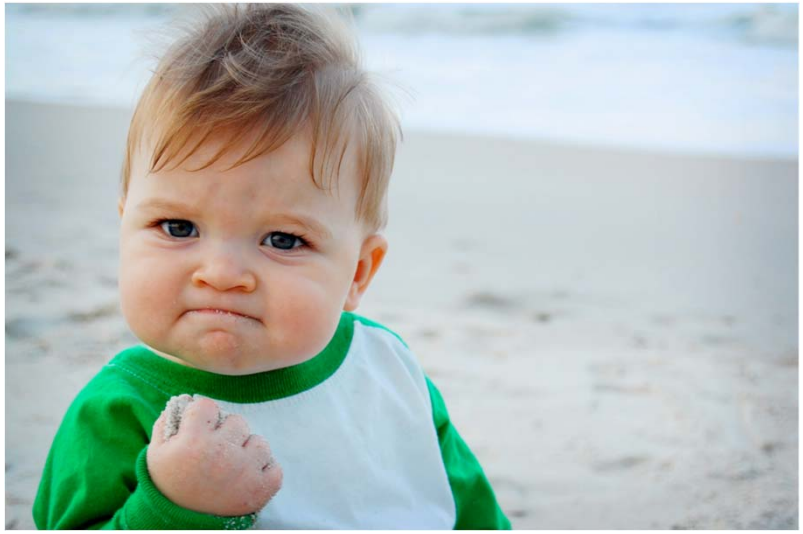
126. Kendirci M, Zsengellér Z, Bivalacqua TJ, et al. PARP inhibition preserves erectile function in rats after cavernous nerve injury. J Urol 2005: in press.
127. Kendirci M, Hellstrom WJG. Restoring erectile function: Proactive options after radical prostatectomy. Contemp Urol 2005; 17(4): 36–50.

AU: Ref 126: Update?

Sonuçlar



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