Korean clinical practice guideline for benign prostate hyperplasia

전립선비대증 진료권고안

대한비뇨기과학회
The Korean Urological Association

대한가정의학회
The Korean Academy of Family Medicine

대한배뇨장애요실금학회
Korean Continence Society

후원 : 근거창출임상연구국가사업단

인정

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대한비뇨기과학회 전립선비대증 진료권고안 발간에 부쳐

인체의 여러 장기들 중 전립선은 잘 드러나지 않는 곳에 있기에 그 기능과 해부가 의학적 견지에서 주목을 받게 된 것은 장기 자체보다 전립선비대증이라는 병명에 기인한 탓이 크다고 할 수 있습니다. 전립선의 해부학적 비대에 수반되어 발생하는 하부요로증상인 전립선비대증은 최근 수명연장과 더불어 급격하게 증가되어 궁극적으로는 장년 남성의 대부분에서 발병하는 증후군이라고 할 수 있습니다. 이러한 유병률의 증가는 의학적 연구와 치료 방법의 개발로 이어졌고, 여기서 파생된 다양한 접근방법 및 치료법들은 본 질환에 대한 사회적 관심의 환기와 아울러 표준화된 진료권고안이 필요한 배경이 되었습니다.

그간 국내의 의학은 주로 서양의 시스템과 치료를 소화하는 데 맞추어져 왔으나, 우리 비뇨기과학은 여러 선후배 교수님들의 열정과 노력을 통해 한국인에서의 전립선과 관련 질환에 대한 데이터를 꾸준히 축적해왔습니다. 본 진료지침은 비록 외국의 진료권고안들보다 그 출발이 다소 늦었고 일부 외국의 권고안들을 참고하였지만 우리나라 사람을 대상으로 한 최신의 치료경향을 포함하고 있습니다.

무엇보다 그 개발 과정에 있어 교육 워크숍과 여러 차례의 개발 회의를 통한 과학적이고 합리적인 방법론을 수용하고 두 차례의 공청회를 통한 다양한 의견들을 통합하여 임상진료의 일선에서 바로 적용할 수 있는 최적화된 내용을 담고 있는 점이 큰 장점이라 하겠습니다. 특히 진료권고안이 다학제를 통한 개발이어야 한다는 의학회의 지침을 충실히 반영하였고 근거창출 임상연구국가사업단의 과제로 수행되어 우수 평가를 받았습니다.

의학은 지속적으로 발전하는 것이기에 앞으로 나올 새로운 치료법에 의해 오늘의 내용이 달라질 수 있겠지만, 본 진료권고안의 가치는 현재의 지식은 물론 사회적으로는 비뇨기과를 넘어 우리나라 보건의료에서 추구할 공통적인 지향을 정리한 데 있다고 생각합니다. 이 어려운 개발 과정에서 수고해주신 김형지 개발위원장, 여정균 책임연구자 이하 모든 선생님들께 깊이 감사 드리며, 앞으로 전립선비대증과 씨름하는 모든 의료인들에게 이 책자가 값지게 쓰여지기를 희망합니다.

대한비뇨기과학회장 **주 명 수**

대한비뇨기과학회 전립선비대증 발간사

전립선비대증은 남성에서 하부요로증상을 일으키는 대표적인 질환으로 비뇨기과에서 중요한 자리를 차지해온 질환이지만 우리나라의 진료 상황을 반영하고 형식 또한 제대로 갖춘 가이드라인이 없었던 것이 사실입니다.

이번에 개발된 전립선비대증 진료권고안은 이러한 부분을 보완하여 1년간 공을 들여 만든 가이드라인이며 향후 개정판을 통하여 그 내용을 더욱 알차게 만들어 나갈 수 있는 토대가 될 수 있으리라 생각합니다.

특히 가이드라인 개발 방법을 잘 따르고 두 차례에 걸친 공청회를 통하여 개원의 선생님들의 의견을 충분히 듣고 반영할 수 있어서 더욱 의미가 깊다고 하겠습니다.

근거창출임상연구국가사업단의 연구비 지원을 받고 대한의학회 인증을 통하여 우수 평가를 받은 것 또한 다행스러운 일이라 하겠습니다.

본 책자가 비뇨기과 의사는 물론 전립선비대증에 관심이 있는 분들에게 큰 도움이 되기를 기대합니다.

끝으로 본 책자를 만들기 위해 노고를 아끼지 않으신 김형지 개발위원회 위원장님과 온갖 궂은일을 도맡아 진행하신 여정균 책임연구자를 비롯한 진료권고안 발간에 참여하여 주신 모든 분들께 깊은 감사의 말씀을 드립니다.

대한배뇨장애요실금학회장 **김 준 철**

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* PVR: post-voided residual urine, † IPSS: international prostate symptom score, ‡ QOL: quality of life,
‖ DRE: digital rectal examination, § PSA: prostate specific antigen, ¶ TWOC: trial without catheter

40세 이상 남성 하부요로증상 환자에서 진단 및 치료의 접근 방법과 관련 핵심질문

권고안 요약표

권고사항	권고등급	근거수준
1. 전립선비대증 환자를 처음 진료할 때 IPSS 설문지는 단순 병력 청취보다 진단에 도움을 주는가?		
1-1. 국제전립선증상점수(IPSS)는 치료에 대한 반응이나 추적관찰 중 증상악화를 판단하는 데 있어 중요한 요소이다. 따라서 치료를 시작하고자 하는 환자들에게 치료 전 IPSS를 작성하기를 권고한다.	Strong	B
2. 전립선비대증 환자를 진료할 때 배뇨일지는 단순 병력 청취보다 진단에 도움을 주는가?		
2-1. 배뇨일지가 병력 청취로부터 얻어진 정보를 명확히 하고 정확한 진단에 도움이 된다.	Strong	B
3. 전립선비대증 환자에서 요속검사 및 잔뇨량 측정은 치료법 결정에 도움을 주는가?		
3-1 하부요로증상이 있는 전립선비대증 환자에게 선택적으로 요속검사를 시행한다.	Strong	C
3-2. 하부요로증상이 있는 전립선비대증 환자에게 선택적으로 잔뇨량검사를 시행한다.	Strong	C
3-3. 하부요로증상이 있는 전립선비대증 환자에서 전문의의 평가가 필요한 경우 요속검사와 잔뇨량 측정을 시행한다.	Strong	B
4. 전립선비대증의 해부학적인 평가를 위해서 직장수지검사보다 초음파검사가 더 정확한 평가를 할 수 있는가?		
4-1. 정확한 전립선의 해부학적인 평가를 위해서는 직장수지검사 외에 전립선초음파가 필요하다.	Strong	B
5. 전립선비대증 환자에서 전립선특이항원 수치는 반드시 측정해야 하는가?		
5-1. 40세 이상의 하부요로증상을 호소하는 전립선비대증 환자에서 전립선특이항원 검사를 해야 한다.	Strong	A
6. 전립선비대증 환자에서 생활습관 개선은 증상 호전에 도움이 되는가?		
6-1. 경증의 전립선비대증 환자는 대기요법이 적절하다.	Strong	B
6-2. 하부요로증상을 가진 환자에게 약물 치료 전 또는 약물 치료와 동시에 생활습관 개선에 대한 교육을 시행하여야 한다.	Strong	B
7. 전립선비대증 환자에서 일차치료법으로 약물치료법이 수술적 치료보다 우선적으로 고려되어야 하는가?		
7-1. 전립선비대증으로 인해 중등도 이상의 증상을 보이는 경우는 약물치료가 일차적으로 권장된다. 그러나, 방광돌이 있는 경우, 방광기능장애를 동반한 방광게실이 있는 경우, 상부요로의 확장으로 인한 신기능부전이 동반된 경우, 약물치료에도 불구하고 요폐, 요로감염, 혈뇨가 반복되거나 배뇨증상, 배뇨 후 잔뇨량의 호전이 없는 경우에는 수술치료가 고려되어야 한다.	Strong	B
7-2. 5α환원효소억제제는 중등도 이상의 하부요로증상을 호소하는 환자에서 직장수지검사 또는 전립선초음파검사에서 전립선 크기가 크거나 혈청 전립선특이항원 검사에서 전립선비대증의 진행 가능성이 보이는 경우 장기간 처방을 고려해야 하는 치료약물이다.	Strong	A
7-3. 항콜린제는 중등도 이상의 하부요로증상을 보이는 환자 중 방광자극증상을 주로 호소하는 환자에서 고려될 수 있으며, 방광출구폐색이 심하거나 배뇨 후 잔뇨량이 많은 경우 신중한 사용이 필요하다.	Strong	A
7-4. 알파차단제는 중등도 이상의 하부요로증상을 보이는 전립선비대증 환자에게 우선적으로 고려되어야 하는 치료약물이다.	Strong	A
8. 전립선비대증 환자에서 병용요법이 알파차단제 단독사용보다 치료효과를 높일 수 있는가?		
8-1. 전립선비대증 환자에서 알파차단제와 5알파환원효소억제제 병용요법은 알파차단제 단독요법보다 하부요로증상 완화에 효과적인 치료방법이다.	Strong	A

8-2. 알파차단제와 항콜린제 병용요법은 중등도 이상의 하부요로증상을 갖는 환자에서 알파차단제 단독요법의 효과가 불충분할 경우에 시행한다.	Strong	A
8-3 알파차단제와 항콜린제 병용요법은 배뇨 후 잔뇨량이 많고 방광출구폐색이 의심되는 남성에서는 신중하게 시행한다.	Strong	A
8-4. PDE5 억제제와 알파차단제의 병용 투여는 중등도 이상의 하부요로증상을 감소시키는 데 있어 알파차단제 단독요법보다 효과적이다.	Weak	A
9. 전립선비대증 환자에서 급성요폐 발생 시 TWOC (Trial without catheter)는 수술적 치료 전에 우선적으로 고려되어야 하는가?		
9-1. 급성요폐 발생 시 TWOC는 수술적 치료 전에 고려할 수 있다.	Strong	A
9-2. 급성요폐를 치료하는 데 있어 요도 도관 유치 전후 알파차단제 사용이 도움이 된다.	Strong	B
9-3. 요도 도관은 급성요폐 후 2-7일간 유치하는 것이 도움이 된다.	Strong	B
10. 전립선비대증 환자에서 경요도전립선절제술은 개복전립선절제술에 비해서 우선적으로 고려되어야 하는가?		
10-1. 경요도전립선절제술은 전립선 비대증 수술에 우선적으로 고려된다.	Strong	C
10-2. 70 gm 이상의 큰 전립선 비대증 환자에서 경요도를 통한 내시경 수술은 개복전립선수술과 함께 1차 수술법으로 고려할 수 있다.	Strong	A
11. 전립선비대증 환자에서 심각한 기저질환 등으로 수술이 적당하지 않은 경우에는 어떠한 치료가 권장되는가?		
11-1. 전립선비대증 환자에서 심각한 기저질환 등으로 수술에 적당하지 않는 경우 간헐적 자가도뇨 또는 도뇨관 유치를 권장한다.	Strong	B
11-2. 전립선비대증 환자에서 심각한 기저질환 등으로 수술에 적당하지 않는 경우 TUNA 또는 TUMT를 고려할 수 있다. 그러나 장기적인 치료효과(재치료 및 증상개선정도)는 TURP에 비해 좋지않다.	Strong	A
11-3. 전립선비대증 환자에서 심각한 기저질환 등으로 수술에 적당하지 않는 경우 전립선 내 약물 주입이 시도되고 있으나 임상 적용은 권고하지 않는다.	Strong	A
12. 전립선비대증으로 진단 받은 환자의 추적관찰에 필요한 진단적 검사는 무엇이며, 추적관찰의 기간은 어떻게 설정하여야 하는가?		
12-1. 전립선비대증 치료 후 추적관찰 간격과 검사의 종류는 개별 환자의 중증도와 임상지표를 고려하여 임상의사의 경험이나 판단에 따른다.	Strong	C
12-2. 전립선비대증의 진행을 확인하기 위해서는 국제전립선증상점수, 직장수지검사, 혈청 전립선특이항원검사, 요속검사, 잔뇨량 측정 그리고 전립선초음파 등을 시행한다.	Strong	C
13. 전립선비대증으로 진단 받은 환자들 중에 반드시 비뇨기과 전문의에게 의뢰해야 하는 경우는 무엇인가?		
13-1. 전립선비대증 환자에서 하부요로증상이 1차 약물치료로 호전되지 않는 경우에는 비뇨기과 의사에게 의뢰해야 한다.	Strong	B
13-2. 전립선비대증 환자에서 요로감염, 혈뇨, 반복적인 요폐색과 같은 하부요로증상의 객관적인 이상이나 악화 소견이 동반될 때 비뇨기과 의사에게 의뢰하여야 한다.	Strong	A
13-3. 전립선비대증 환자에서 혈청 전립선특이항원검사가 정상범위를 벗어나거나 직장수지검사에서 이상소견이 관찰되는 경우 전립선암과의 감별을 위해 비뇨기과 의사에게 의뢰하여야 한다.	Strong	A

NA: Not Applicable

전립선비대증 진료권고안의 한계점

전립선비대증 진료권고안을 개발하면서 느낀 문제점은 양질의 국내 자료가 적고, 대부분의 양질의 자료는 역학적 특성이 다른 서양(북미와 유럽)의 자료라는 것이다. 국내 진료의 특성을 명확하게 반영하지 못하는 한계점이 있지만 근거중심방법론으로 수행된 의학적 근거를 존중하여야 한다. 현실에서 당연시 되는 진료방법이고 전문가동의가 이루어진 경우 근거부족을 이유로 일방적으로 제외하는 경우 또한 맹점이라고 생각된다. 향후 개정판에서는 그 내용과 근거를 보완하여 진료방법의 모호한 부분을 해소해 나가길 기대한다.

전립선비대증 진료권고안에서 권고하지 않는 부분은 진료 현장에서 피하길 바라지만 권고안에 없는 부분은 하지 말아야 된다는 규제를 의미하지 않는다. 우리의 의료보험제도와 진료현장의 실제 상황 사이의 갭을 줄여 나가는 데 도움이 되기를 바란다.

전립선비대증 진료권고안은 법적 지위 및 구속력을 가지지 않으며, 실제 임상에서 이루어 지는 환자의 치료결과에 대한 책임은 치료 담당자에게 직접 귀속되고 전립선비대증 진료권고안 개발위원회는 그 책임을 지지 않는다.

서 론

1. 목적

우리나라의 고령화 진행 속도는 세계에서 상위권에 진입하였고 그로 인한 노인 인구의 질환도 증가 일로에 있다. 남성의 대표적인 노화 질환인 전립선비대증은 급속한 고령화에 따라 유병률 또한 급속히 증가하고 있다. 하지만 우리나라에서 전문가에 의한 진료권고안의 개발은 매우 제한적으로 이루어졌고 그 또한 외국 진료권고안의 번역 수준에 머물러 있다.

이에 본 전립선비대증 진료권고안을 개발하여 전립선비대증 질환을 가지고 있는 환자의 진단 및 치료에 있어 근거중심의 진료를 위한 정보를 제공하고자 한다. 또한 진단에 필요한 검사에 대한 정보와 약물치료 및 수술 치료에 대한 기본적 정보를 제공하며 진단적 평가와 치료에 대한 효과성을 평가하고 정보를 제공하고자 한다.

본 진료권고안은 향후 전립선 질환의 진단 및 치료에 있어 근거기반치료를 확산시키는 데 일차적 도구로 활용될 수 있을 것으로 기대한다.

2. 진료지침을 적용할 대상집단

40대 이상 성인 남성 중 하부요로증상을 호소하는 경우

3. 진료지침의 이용자

본 진료권고안은 전립선비대증을 진료하는 데 종사하는 일차 및 이차 의료기관의 의사와 비뇨기과 전문의에게 양질의 진료를 제공하는 데 도움을 주는 근거중심의 진료선택을 하도록 하기 위해 만들게 되었다.

4. 진료지침의 범위

본 진료권고안은 전립선비대증의 진단, 치료에 대한 포괄적인 내용을 담고 있다. 실제 임상에서 적용이 가능한 내용 위주의 핵심질문을 통하여 도움을 주고자 하였다. 전립선비대증의 질환이 시작되는 40대 이상의 성인을 대상으로 진행한 연구를 근거로 하였다. 과학적 근거가 부족하거나 논란이 큰 부분은 본 진료권고안에서 제외하였으나, 일부 근거가 부족하더라도 임상적 의의가 있

고 전문가들의 의견이 일치되는 부분은 수정 델파이 기법(modified Delphi method)을 통한 합의 과정을 거쳐 권고안에 포함시켰다.

5. 진료지침 개발 및 검토자

본 진료권고안의 개발을 위해 대한비뇨기과학회, 대한가정의학회, 대한배뇨장애요실금학회, 대한예방의학회에서 개발을 위임하였다.

전립선비대증 진료권고안의 작성을 위하여 대한비뇨기과학회, 대한가정의학회, 대한배뇨장애요실금학회에서 추천한 전립선비대증 전문가로 구성된 전문가 그룹이 2014년 3월 6일 첫 회의를 가지면서 구체적인 개발위원회를 만들어 개발 작업을 진행하였다. 방법론 전문가로 대한예방의학회 권호장(단국대 예방의학교실), 메타분석 및 체계적 문헌고찰을 위해 김현정(고려대 예방의학교실)이 참여하였다.

개발위원회(가나다순, 17명)

김 광 택(가천대, 인천), 김 경 우(인제대 가정의학과, 서울), 김 명 기(전북대, 전주),
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조 원 진(조선대, 광주), 최 훈(고려대, 안산)

진료지침 검토자(가나다순, 7명)

진료지침 검토를 위해서 내과 전문의, 비뇨기과 개원의를 포함하여 구성하였다.

구 호 석(인제대 내과, 서울), 김 두 상(순천향대, 천안), 문 경 현(울산대, 울산),
박 현 준(부산대, 부산), 양 상 국(건국대, 충주), 우 승 효(을지대, 대전),
윤 동 희(타워비뇨기과, 개원의, 서울)

6. 진료지침 연구비 지원

본 진료권고안은 근거창출임상연구국가사업단의 임상진료지침개발사업 2013년 하반기 2차 과

제로 선정되어 개발되었고 인제대학교 산학협력단이 주관연구기관으로 진행하였다.

7. 진료지침의 갱신

본 진료권고안은 새로운 진단 방법 및 치료 약물의 개발, 새로운 수술법의 출현과 관련된 연구 결과의 축적에 따라 4–5년 주기로 개정되어야 한다.

8. 권고안 개발 방법

개발 방법에 대한 도움을 위해 임상진료지침 수용개작 매뉴얼 ver 2.0(한국보건의료연구원 2011)과 임상진료지침 개발 매뉴얼 ver 1.0(한국보건의료연구원 2011)을 참고하여 개발하였다. 자료검색 및 메타분석을 위해 관련 전문가에게 자문을 구하였다.

1) 핵심질문 도출

핵심질문의 도출을 위하여 population, intervention, comparison, outcome (PICO)의 원칙하에 임상질문에 필요한 필수요소를 포함시키고자 하였다. P (population)는 전립선비대증 환자 혹은 질병의 특징에 관한 사항으로 정의되고, I (intervention)는 진단법 혹은 치료법을 포함한 중재, C (comparison)는 특정 중재법과 비교가 되는 비교군, O (outcome)는 진단의 유용성 혹은 치료 결과로 정의되며 가급적 이 네 가지 요소를 최대한 포함시키고자 하였다. 본 진료권고안은 핵심질문 13개를 선정한 후 12개 핵심질문은 이미 개발되어 있는 외국 또는 국내의 다른 권고안을 바탕으로 수용개작을 하고 가장 활용도가 높을 약물치료에 관한 한 개의 핵심질문은 직접 개발하기로 하였다. 개발위원회의 회의를 거쳐 국내 진료 상황에 주요하며 활용도가 높은 핵심질문을 한 개 선정하였다.

2) 진료치침 검색

수용개발을 위해 기존의 진료권고안을 검색하였다. 검색을 위해 다양한 검색자료원을 활용하였는데 PubMed, Cochrane Library, National Guideline Clearing House, CMA Infobase, SIGN, NICE 그리고 국내 진료권고안 검색을 위해 KoreaMed, KmBase, RISS를 이용하였고 검색이 어려운 경우 대한비뇨기과학회의 자문을 받았다(부록 진료지침검색원). 검색 색인단어는 전립선비대증 관련 색인단어('benign prostate hyperplasia' OR 'lower urinary tract symptoms

disease')와 진료지침 관련 색인단어('guideline' OR 'guideline prostate hyperplasia' OR 'guideline adherence' OR 'practice guideline' OR 'practice guidelines as topic' OR 'clinical guideline' OR 'consensus' OR 'recommendation')의 조합으로 검색하였다. 주제별 혹은 형식별 검색을 통해 다섯 건의 외국 진료권고안과 한 건의 국내 진료권고안을 검토하였다. 출판일자의 범위를 2009년 1월 1일부터 2013년 12월 31일까지로 한정하였고, 영어 또는 한국어로 표기된 권고안만을 선택하였으며 개정판이 있는 경우 최신판을 선정하였다. 전문가 합의에 의한 지침(expert consensus), 단체 등을 대표하지 않고 한 명이 쓴 권고안을 제외하여 최종적으로 여섯 건의 권고안을 선정하였다.

3) 진료지침의 평가 및 선택

수용개발을 위해 검색 기준에 부합하는 진료권고안의 질 평가를 위하여 대한의학회 임상진료지침 전문위원회에서 배포한 K-AGREE 2.0 (AGREE 2.0의 한국형 버전) 평가 개발척도를 활용하여 진료권고안 질 평가를 하였다. 검색된 6개 권고안에 대하여 전문가 초빙 워크숍을 통해 평가 방법을 교육 받은 개발위원회 위원 12인이 평가하였고, 3점 이상 차이가 난 항목에 대하여 재평가를 실시하였다. 영역별 표준화 점수를 산출하고 각 영역의 점수를 비교하여 최종적으로 평가영역 3번 개발의 엄격성 표준화 점수가 50% 이상인 세 개의 지침을 선정하였다(부록 3. 진료지침평가표).

4) 권고안 결정 및 초안 작성

문헌고찰을 위한 근거의 검색은 PubMed (www.pubmed.gov)와 Embase (www.embase.com)를 사용하였고, 2000-2013년 사이에 인간을 대상으로 하고 영어로 출간된 논문 중 각각의 문항에 적합한 검색식을 만들어 근거를 검색하고 초록을 검토하여 각각의 문항과 관련 있는 근거문헌을 선정하였다. 2000년 이전 문헌 중 중요한 문헌은 평가를 통해 포함하도록 하였다. 최근에 출간된 체계적 고찰이나 메타분석이 있는 경우에는 그 이전에 출간된 낮은 근거수준의 문헌은 배제하였고 증례보고 등도 배제하였다. 각각의 검색식은 부록에 표기하였다(부록 6. 근거 검색식).

근거수준은 2011년도에 Oxford Centre for Evidence-Based Medicine (CEBM)에서 발표한 근거수준의 기준 중 진단, 예후 및 치료이익 분야에서의 근거수준 평가기준을 참고로 하여 세 단

계로 정의하였다. 권고수준은 델파이 합의안의 질문별 중위수 값에 따라 strong, weak 두 단계로 정의하였다.

표 1. 근거수준 및 권고수준의 정의

근거수준(Level of evidence)의 등급체계 정의

근거수준	정의
A	Level 1, 여러 개의 Level 2 연구
B	한 개의 Level 2 연구, 여러 개의 Level 3 연구
C	한 개의 Level 3 연구, Level 4, 5

Level of study 등급체계 정의

Level	진단	예후	치료이익
1	Systematic review, Meta-analysis	Systematic review, Meta-analysis	Systematic review, Meta-analysis
2	Individual cross sectional studies with consistently applied reference standard and blinding	Inception cohort studies	Randomized trial or observational study with dramatic effect
3	Non-consecutive studies, or studies without consistently applied reference standards**	Cohort study or control arm of randomized trial*	Non-randomized controlled cohort/follow-up study**
4	Case-control studies, or poor or non-independent reference standard**	Case series or case-control studies, or poor quality prognostic cohort study**	Case-series, case-control studies, or historically controlled studies**
5	Mechanism-based reasoning		Mechanism-based reasoning

* Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

** As always, a systematic review is generally better than an individual study.

권고수준의 정의

수준	정의
Strong (score 7–9)	Most or all individuals will be best served by the recommended course of action.
Weak (score 1–6)	Not all individuals will be best served by the recommended course of action. There is a need to consider more carefully than usual individual patient's circumstances, preferences, and values.

권고안 도출과 채택을 위해 델파이 방법을 사용하였다. 권고안 개발그룹의 대표성과 전문성을 담보하기 위하여 총 15인의 패널로 구성하였다. 초안을 바탕으로 한 평가지는 13개의 질문에 30개 문항이었다. 설문은 총 3회 실시하였고, 각 문항에 대한 권고안이 적절한가에 대한 응답척도는 9점 척도를 이용하였다. 1–3점은 '동의 안 함', 4–6점은 '불명확', 7–9점은 '동의함' 영역으로 정의하였고 각 영역에 응답한 패널리스트가 75% 이상이면 합의가 된 것으로 정의하였다. 델파이 합의를 위한 조사표에는 각 문항에 대해 수용하려고 선정한 타 권고안들의 권고등급, 검색한 근거문헌에 기초한 근거수준, 응답척도(9점 척도), 기타 의견 제시를 위한 공간으로 구성하였다. 다음 라운드에서는 합의에 이르지 못한 문항에 대해 전체 패널리스트들의 점수에 대한 중앙값과 질문지를 받는 패널리스트가 이전 라운드에서 응답했던 점수를 표시하였고 이전 라운드에서 합의된 문항은 제외하였다. 이전 라운드에서 합의에 실패한 문항에 대한 수정은 하지 않았고 패널리스트에 의해 제시된 기타 의견은 없었다. 총 30개의 문항 중 1차 설문에서 12개, 2차 설문에서 15개 그리고 3차 설문에서 나머지 3개의 문항에 대한 합의가 이루어졌다. 각 라운드의 응답률은 1차 88.2%, 2차 76.5%, 3차 100%였다. 델파이 합의 결과표는 부록에 표기하였다. 선정된 권고에 따라 진료권고안 초안을 집필하였다.

델파이 합의를 위한 패널(가나다순, 15명)

김 명 기(전북대, 전주),
김 재 헌(순천향대, 서울),
김 태 범(가천대, 인천),
김 형 지(단국대, 천안, 위원장),
노 준 화(광주기독병원, 광주),
배 재 현(고려대, 안산),
신 동 길(부산대, 부산),
양 승 옥(보훈병원, 서울),
오 철 영(한림대, 안양),
유 정 우(타워비뇨기과, 서울),
이 성 호(한림대, 동탄),
정 성 진(서울대, 분당),
조 영 삼(성균관대, 서울),
조 원 진(조선대, 광주),
최 훈(고려대, 안산)

5) 개발(De Novo)을 위한 체계적 문헌고찰 및 메타분석

개발을 결정한 핵심질문(8번 질문)에 대한 문헌고찰 및 메타분석을 위해 통계 전문가의 도움을 받아 시행하였다.

(1) 문헌검색

핵심질문에 따른 문헌검색은 Medline, Embase, Cochrane library, KoreaMed 등의 검색원을 이용하여 연구설계 및 언어의 제한 없이 검색하였다. 문헌검색에 사용한 주제어는 각 검색원에서 논문을 색인하기 위해 개발된 표준화된 의학용어(Medline:MeSH, Embase:emtree)와 자연어를 이용하여 검색하였다. 각 핵심질문은 PICO기법(Population or Patient problem, Intervention, Comparison, Outcome)을 이용하여 도출하였으며, 문헌검색의 과정, 근거표, 메타분석으로 제시하였다. 논문 제목과 초록을 통해 선정 기준에 부합하지 않는 문헌을 배제하였으며 필요한 경우에는 논문 전문을 검토하였다. 선택된 논문 전문을 자세히 검토한 후 핵심질문에 해당되는 자료를 추출하기 위해 표준화된 근거표와 메타분석표를 작성하였다.

(2) 메타분석

각 핵심질문은 각각의 근거표를 작성한 후, 메타분석을 하였다. 메타분석은 RevMan (version 5.3)을 이용하였다. 메타분석이 어려운 경우에는 각각의 연구 결과를 기술하는 방식으로 결과를 제시하였다.

(3) 개별 문헌의 평가

개별 문헌에 대한 평가는 연구설계에 따라 구분하여 각각의 도구를 이용하여 평가하였다. 무작위 배정실험연구의 경우 Cochrane 그룹에서 권고하는 비뚤림의 위험(risk of bias)의 다섯 가지 항목으로 평가하였다.

6) 외부 검토 및 승인

본 권고안은 근거창출임상연구국가사업단의 연구비 지원으로 개발되었으나 사업단 및 개발에 참여한 학회는 권고안의 개발에 영향을 주지 않았다. 진료권고안 개발위원회와 합의에 의해 채택된 권고안의 검증을 위한 검토위원회는 각각 독립적으로 활동하였다.

두 차례의 외부공청회를 개최하여 의견을 수렴하였고, 개발에 참여한 대한비뇨기과학회, 대한가정의학회, 대한배뇨장애요실금학회의 인증을 받았다. 대한의학회 임상진료지침 정보센터의 평가 시스템을 통해 동료평가를 받고 대한의학회의 인증을 받았으며 우수인증마크를 획득했다.

진 단

IPSS

배뇨일지

요속검사, 잔뇨량검사

DRE, 전립선초음파

PSA

KQ 1. 전립선비대증 환자를 처음 진료할 때 IPSS 설문지는 단순 병력 청취보다 진단에 도움을 주는가?

권고사항	권고수준	근거수준
1-1. 국제전립선증상점수(IPSS)는 치료에 대한 반응이나 추적관찰 중 증상악화를 판단하는 데 있어 중요한 요소이다. 따라서 치료를 시작하고자 하는 환자들에게 치료 전 IPSS를 작성하기를 권고한다.	Strong	B

전립선비대증 환자를 처음 진료 시 병력 청취와 함께 증상을 체크할 수 있는 검증된 설문지가 필요하다. 전립선비대증 환자가 치료를 원하는 것은 증상이 생활의 질을 변화시키기 때문이다. 따라서 증상의 수량화는 질환의 정도나 치료효과의 평가 및 관찰 시 증상의 진행 정도를 평가하는 데 중요하다. 주로 국제전립선증상점수(International Prostate Symptom Score: IPSS)가 추천되는데 이 설문지가 증상의 빈도나 정도를 판단하는 데 비체계적인 면담보다 유용하기 때문이다[1-7]. IPSS는 1992년에 미국비뇨기과학회의 주관으로 만들어졌으며 본래의 명칭은 미국비뇨기과학회 증상 설문(AUA-7)이다. IPSS는 1993년 세계보건기구가 주관한 전립선비대증 국제자문회의에서 기본적인 검사기준으로 채택되었고, 이후 한글을 포함한 각국의 언어로 번역되어 이를 이용하여 역학조사나 치료효과 판정 등에 대한 다양한 연구가 진행되고 있다[8]. IPSS는 총 8개로 이루어진 문항들(잔뇨감, 빈뇨, 간헐뇨, 요절박, 약뇨, 복압배뇨, 요주저, 야간뇨)에 대해 증상의 중증도에 따라 0-5점의 점수를 매겼으며, 증상과 관련된 일곱 항목을 이용하여 mild (0-7), moderate (8-19), severe (20-35)로 나눌 수 있다. 그리고 IPSS 생활만족도는 전립선비대증에 의한 삶의 질을 측정하는 것이다.

IPSS는 환자 스스로 작성이 가능하며 또한 진료현장에서 의료 제공자에 의해서도 작성이 가능하다. 아울러 치료의 효과를 판정하는 데에도 연속적으로 측정할 수 있다.

국제전립선증상점수와 다른 전립선비대증 검사의 심한 정도는 완전히 일치하는 것은 아니며 증상 점수만으로는 환자가 느끼는 문제의 정도를 전적으로 판단할 수 없다[9-11].

하부요로증상이 있는 모든 환자에게 IPSS 혹은 다른 종류의 타당성이 증명된 배뇨 설문지를

가능한 한 반드시 작성하여 환자의 기초 증상을 확인할 필요가 있다.

● 근거표

KQ 1	
Reference	1. Barry MJ, Fowler FJ, Jr., O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148:1549-57; discussion 64.
Study type	Case-control study
Patients	210 BPH patients and 108 control subjects
Purpose of Study	To invent and validate symptom index for BPH
Study Results	The final AUA symptom index includes 7 questions covering frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying and urgency. On revalidation, the index was internally consistent (Cronbach's alpha = 0.86) and the score generated had excellent test-retest reliability (r = 0.92). Scores were highly correlated with subjects' global ratings of the magnitude of their urinary problem (r = 0.65 to 0.72) and powerfully discriminated between BPH and control subjects (receiver operating characteristic area 0.85). Finally, the index was sensitive to change, with preoperative scores decreasing from a mean of 17.6 to 7.1 by 4 weeks after prostatectomy ($p < 0.001$). The AUA symptom index is clinically sensible, reliable, valid and responsive. It is practical for use in practice and for inclusion in research protocols
Level of Study	4
Reference	7. O'Leary MP, Wei JT, Roehrborn CG, Miner M; BPH Registry and Patient Survey Steering Committee. Correlation of the International Prostate Symptom Score bother question with the Benign Prostatic Hyperplasia Impact Index in a clinical practice setting. BJU Int 2008;101:1531-5.
Study type	Large, multicenter, longitudinal observational study
Patients	6,439
Purpose of Study	To evaluate the association between the International Prostate Symptom Score (IPSS) bother question (BQ) and a validated disease-specific quality-of-life questionnaire, the Benign Prostatic Hyperplasia (BPH) Impact Index (BPH-II), using the BPH Registry and Patient Survey database.
Study Results	The mean (sd) score of the IPSS BQ was 2.5 (1.4) and of the BPH-II was 2.8 (2.8). Based on responses to the BPH-II, at least half the men reported that their urinary symptoms were associated with physical discomfort, worry about their health, and bothersomeness. The IPSS BQ score was significantly correlated ($P < 0.001$) with the BPH-II (r = 0.68) and each of its four questions (physical discomfort, r = 0.52; worry about health, r = 0.53; bothersomeness of trouble with urination, r = 0.67; and time kept from usual activities, r = 0.44).
Level of Study	2

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KQ 2. 전립선비대증 환자를 진료할 때 배뇨일지는 단순 병력 청취보다 진단에 도움을 주는가?

권고사항	권고수준	근거수준
2-1. 배뇨일지가 병력 청취로부터 얻어진 정보를 명확히 하고 정확한 진단에 도움이 된다.	Strong	B

배뇨일지(voiding diary)는 환자의 객관적인 임상 정보를 제공한다[1,2]. 아직까지 공인된 표준 배뇨일지 형태는 없지만 3-7일간의 배뇨일지는 배뇨장애를 평가하는 데 유용한 도구이다. 배뇨일지로 24시간 요량, 배뇨횟수, 배뇨간격, 배뇨분포, 요실금이 일어나는 시간과 유발요소, 기능적 방광용적을 측정할 수 있다[3-6]. 배뇨일지에서 알 수 있는 빈뇨와 야간뇨의 정도는 국제전립선증상점수에 의해 알 수 있는 하부요로증상과 유의한 상관관계가 있다. 정확한 배뇨평가를 위해서는 환자의 일상생활 중에도 지속적으로 배뇨일지를 작성해야 한다[7,8].

배뇨일지를 통해서 24시간 동안 배뇨량을 파악하여 수분섭취량의 증가 여부를 확인할 수 있고, 배뇨량이 줄거나 각각의 배뇨량이 일정치 않은지를 확인하여 과민성 방광을 의심할 수도 있다[7].

수면 도중 배뇨량이 24시간 총배뇨량의 35% 이상을 의미하는 야간 다뇨(nocturnal polyuria)는 오로지 배뇨일지를 통해서만 진단될 수 있다[7].

빈뇨나 야간뇨 같은 저장증상의 주 원인은 요량의 증가나 기능적 방광용적의 감소이므로, 배뇨일지를 정확하게 기록하여 배뇨의 양과 횟수를 양적으로 측정함으로써 정확한 원인을 진단할 수 있다. 또한 배뇨일지는 시간제배뇨(timed voiding)와 방광훈련(bladder training) 같은 행동치료를 시행할 때 기초 자료가 된다.

저장증상을 호소하는 전립선비대증 환자의 초기검사로 24시간 배뇨일지의 기록은 기본검사이다. 배뇨일지는 비침습적이며, 비용이 저렴하고, 하부요로증상의 평가에 중요한 정보를 제공한다.

● 근거표

KQ 2	
Reference	3. Gisolf KW, et al. Analysis and reliability of data from 24-hour frequency-volume charts in men with lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2000;38:45-52.
Study type	Observational study
Patients	160 men with BPH
Purpose of Study	To analyse the data from frequency-volume charts and to study the reliability of these charts in men with LUTS due to BPH
Study Results	Another 28 patients who met all other criteria did not complete the frequency-volume charts correctly. Agreement exists between reported voided volumes in the literature and those found by us. We found a significant correlation ($p<0.001$) between nycturia and score on symptom question 7, and between diuria and score on symptom question 2 of the AUA symptom index. The difference between results obtained from frequency-volume charts completed during 24 h and those obtained from charts completed during three or more 24-hour periods was negligible with respect to the variation of data at an individual level. Frequency-volume charts are reliable in the investigation of patients with LUTS due to BPH. Reporting on frequency-volume charts during just 24 h is sufficient to gain insight into their voiding habits during normal daily life.
Level of Study	3
Reference	8. Groutz A, Blaivas JG, Chaikin DC, Resnick NM, Engleman K, Anzalone D, et al. Noninvasive outcome measures of urinary incontinence and lower urinary tract symptoms: a multicenter study of micturition diary and pad tests. J Urol 2000;164(3 Pt 1):698-701.
Study type	Prospective observational study
Patients	109
Purpose of Study	To assess the test-retest reliability of a 24, 48 and 72-hour micturition diary and pad test in patients referred for the evaluation of urinary incontinence and lower urinary tract symptoms
Study Results	The number of pads and total weight gain appeared to be reliable measures of the 24, 48 and 72-hour pad tests. For the 24-hour diary the total number of incontinence episodes was a reliable measure, while the total number of voiding episodes was marginally reliable (mean CCC 0.785 and 0. 689, respectively). For the 48-hour diary the number of incontinence episodes and total number of voiding episodes were reliable measures (mean CCC 0.78 and 0.83, respectively), while for the 72-hourdiary each parameter was highly reliable (CCC 0.86 and 0.826, respectively). However, an increased test period was associated with decreased patient compliance.
Level of Study	3

참고문헌

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3. Gisolf KW, van Venrooij GE, Eckhardt MD, Boon TA. Analysis and reliability of data from 24-hour frequency-volume charts in men with lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2000;38:45-52.
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5. Homma Y, Kawabe K, Tsukamoto T, Yamaguchi O, Okada K, Aso Y, et al. Estimate criteria for efficacy of treatment in benign prostatic hyperplasia. Int J Urol 1996;3:267-73.
6. Abrams P, Chapple C, Khoury S, Roehrborn C, de la Rosette J. Evaluation and treatment of lower urinary tract symptoms in older men. J Urol 2009;181:1779-87.
7. Weiss JP, van Kerrebroeck PE, Klein BM, Norgaard JP. Excessive nocturnal urine production is a major contributing factor to the etiology of nocturia. J Urol 2011;186:1358-63.
8. Groutz A, Blaivas JG, Chaikin DC, Resnick NM, Engleman K, Anzalone D, et al. Noninvasive outcome measures of urinary incontinence and lower urinary tract symptoms: a multicenter study of micturition diary and pad tests. J Urol 2000;164(3 Pt 1):698-701.

KQ 3. 전립선비대증 환자에서 요속검사 및 잔뇨량 측정은 치료법 결정에 도움을 주는가?

권고사항	권고수준	근거수준
3-1. 하부요로증상이 있는 전립선비대증 환자에게 선택적으로 요속검사를 시행한다.	Strong	C
3-2. 하부요로증상이 있는 전립선비대증 환자에게 선택적으로 잔뇨량검사를 시행한다.	Strong	C
3-3. 하부요로증상이 있는 전립선비대증 환자에서 전문의의 평가가 필요한 경우 요속검사와 잔뇨량 측정을 시행한다.	Strong	B

요속검사는 시간당 배뇨량을 측정하여 배뇨기능에 대한 유용한 정보를 제공하는 비침습적이고 간편한 검사이다. 요속검사에 이상 소견이 있을 경우 방광출구폐색이나 배뇨근기능이상을 의심할 수 있다. 하지만 요속검사와 잔뇨량 측정은 반복 측정에 대한 개연성이 떨어지는 타당성 문제가 존재한다. 환자는 평소의 배뇨처럼 편안한 환경에서 요의가 느껴질 때 자연스럽게 배뇨하도록 하며, 배뇨량이 150 ml 이상 되어야 의미 있는 결과를 얻을 수 있다. 정상최대요속은 일반적으로 20–25 ml/sec이며, 최대요속은 배뇨량에 따라 변하며 나이가 증가함에 따라 감소한다.

최대요속이 10 ml/sec 이하인 경우 압력요류검사(pressure–flow study)에서 알 수 있는 방광출구폐색일 경우가 비교적 높게 나타난다[1–4]. 이런 경우 수술 치료에 좋은 반응을 보일 확률이 높다. 하지만 방광근력저하와 방광출구폐색을 구분하지는 못하기 때문에 치료법 결정을 위한 보다 정확한 진단을 위해서는 압력요류검사가 필요하다.

잔뇨량 측정은 초음파를 이용하는 방법과 도뇨관을 이용하여 측정하는 방법이 있다. 초음파를 이용하는 경우는 비침습적인 장점이 있는 반면 도뇨관을 이용한 방법보다는 정확하지 못한 단점이 있다. 반면 도뇨관을 이용하여 측정하는 경우는 정확하지만 침습적 방법으로 환자에게 불편함을 주는 단점이 있다. 초음파를 이용한 잔뇨량 측정은 도뇨관을 이용하여 잔뇨량을 측정하는 경우와 정확도가 상당히 일치하기 때문에 잔뇨량이 많이 남을 거라고 의심되는 환자에서 시행해보는 것이 좋다[5,6].

요속검사와 잔뇨량 측정은 초기검사에서는 선택적으로 시행할 수 있지만, 방광출구폐색이 의심되는 환자에서 약물치료 실패 시 요속검사를 평가하여 다음 검사 또는 치료를 진행하고, 방광저장증상을 호소하는 환자에게 항콜린제를 투여하기 전에 잔뇨량 측정을 고려해야 한다[7].

전립선비대증 환자에서 요속검사 및 잔뇨량 측정이 배뇨장애의 패턴을 진단하는지 그 참고치에 대한 연구가 있었지만 실제로 치료법 결정에 도움이 되는지에 대한 연구는 아직까지 보고된 바가 없다.

● 근거표

KQ 3	
Reference	1. Oelke M, Hofner K, Jonas U, de la Rosette JJ, Ubbink DT, Wijkstra H. Diagnostic accuracy of noninvasive tests to evaluate bladder outlet obstruction in men: detrusor wall thickness, uroflowmetry, postvoid residual urine, and prostate volume. European Urology 2007;52:827-34.
Study type	Prospective study
Patients	160 patients
Purpose of Study	The aim of this prospective study was to compare the diagnostic accuracy of detrusor wall thickness (DWT), free uroflowmetry, postvoid residual urine, and prostate volume (index tests) with pressure-flow studies (reference standard) to detect bladder outlet obstruction (BOO) in men.
Study Results	One hundred sixty men between 40-89 yr of age (median: 62 yr) were included in the study; 75 patients (46.9%) had BOO according to pressure-flow studies. The results of all investigated index tests differed significantly between obstructed and non-obstructed men. DWT was the most accurate test to determine BOO: the positive predictive value was 94%, specificity 95%, and the area under the curve of ROC analysis 0.93. There was an agreement of 89% between the results of DWT measurement and pressure-flow studies.
Level of Study	3
Reference	2. Poulsen AL, Schou J, Puggaard L, Torp-Pedersen S, Nordling J. Prostatic enlargement, symptomatology and pressure/flow evaluation: Interrelations in patients with symptomatic BPH. Scandinavian Journal of Urology and Nephrology Supplementum 1994;157:67-73.
Study type	Prospective study
Patients	188 patients
Purpose of Study	Benign prostatic hyperplasia (BPH) is the most common pathologic condition to afflict the aging male. Many patients with symptomatic BPH undergo prostatectomy without rigorous evaluation. Three concepts should be considered before any treatment of a patient with symptomatic BPH; Prostatic enlargement, symptomatology and bladder outflow obstruction.

Study Results	Neither uroflowmetry, symptomatology nor prostate size correlated well with bladder outlet obstruction. The positive predictive value for infravesical obstruction was 88% if a maximum flow rate under 10 ml/s was used. Symptomatology could not be used to differentiate between patients with bladder outlet obstruction and patients without obstruction. The positive predictive value for infravesical obstruction was 76% if a prostate volume over 40 ml was chosen.
Level of Study	3
Reference	3. Reynard JM, Peters TJ, Lim C, Abrams P. The value of multiple free-flow studies in men with lower urinary tract symptoms. British Journal of Urology 1996;77:813-8.
Study type	Prospective study
Patients	165 patients
Purpose of Study	To assess the variability of free-flow studies in men presenting with lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction (BPO) and to determine the sensitivity, specificity and predictive values of consecutive measurements of maximum flow rate for the presence of bladder outlet obstruction (BOO) at several threshold values.
Study Results	The mean Qmax on void 1 was 10.2 mL/s and the mean maximum value for Qmax between voids 1 and 2 was 12.5 mL/s. For voids 1, 2 and 3, the mean maximum Qmax was 13.9 mL/s and for voids 1 to 4 it was 15.2 mL/s. There were no significant changes in PVR among any of these voids. There was a statistically significant, although small, decrease in voided volume between voids 1 to 3 and voids 1 to 4. The specificity and PPV of Qmax for BOO increased with each subsequent void, such that using a threshold value for Qmax of 10 mL/s on the fourth void, the specificity and PPV for BOO were 96% and 93%, respectively.
Level of Study	3
Reference	4. Reynard JM, Yang Q, Donovan JL, Peters TJ, Schafer W, De la Rosette JJMC, et al. The ICS-'BPH' Study: Uroflowmetry, lower urinary tract symptoms and bladder outlet obstruction. British Journal of Urology 1998;82:619-23.
Study type	Prospective study
Patients	1,271 patients
Purpose of Study	To explore the relationship between uroflow variables and lower urinary tract symptoms (LUTS): to define performance statistics (sensitivity, specificity, positive and negative predictive values) for maximum urinary flow rate (Qmax) with respect to bladder outlet obstruction (BOO) at various threshold values; and to investigate the diagnostic value of low-volume voids.
Study Results	The relationship between symptoms and uroflow variables was poor. The mean difference between home-recorded and clinic-recorded voided volumes was -48 mL. Qmax was significantly lower in those with BOO (9.7 mL/s for void 1) than in those with no obstruction (12.6mL/s; $P<0.001$) and Qmax was negatively correlated with obstruction grade (Spearman's correlation coefficient -0.3, $P<0.001$), even when controlling for the negative correlation between age and Qmax

Study Results	(Spearman's partial correlation coefficient -0.29, P<0.001). A threshold value of Qmax of 10 mL/s had a specificity of 70%, a positive predictive value (PPV) of 70% and a sensitivity of 47% for BOO. The specificity using a threshold Qmax of 15 mL/s was 38%, the PPV 67% and the sensitivity 82%. Those voiding <150 mL (n=225) had a 72% chance of BOO (overall prevalence of BOO 60%). In those voiding >150 mL the likelihood of BOO was 56%. The addition of a specific threshold of 10 mL/s to these higher volume voiders improved the PPV for BOO to 69%.
Level of Study	3
Reference	5. D'Silva KA, Dahm P, Wong CL. Does this man with lower urinary tract symptoms have bladder outlet obstruction?: The Rational Clinical Examination: a systematic review. JAMA 2014;312:535-42.
Study type	systematic review
Patients	
Purpose of Study	To systematically review the evidence on (1) the diagnostic accuracy of office-based tests for bladder outlet obstruction in men with lower urinary tract symptoms; and (2) the accuracy of the bladder scan as a measure of urine volume because management decisions rely on measuring postvoid bladder residual volumes.
Study Results	Among males with lower urinary tract symptoms, the likelihood ratios (LRs) of individual symptoms and questionnaires for diagnosing bladder outlet obstruction from the highest quality studies had 95% CIs that included 1.0, suggesting they are not significantly associated with one another. An International Prostate Symptom Score cutoff of 20 or greater increased the likelihood of bladder outlet obstruction (positive LR, 1.5; 95% CI, 1.1-2.0), whereas scores of less than 20 had an LR that included 1.0 in the 95% CI (negative LR, 0.82; 95% CI, 0.67-1.00). We found no data on the accuracy of physical examination findings to predict bladder outlet obstruction. Urine volumes measured by a bladder scanner correlated highly with urine volumes measured by bladder catheterization (summary correlation coefficient, 0.93; 95% CI, 0.91-0.95). In patients with lower urinary tract symptoms, the symptoms alone are not enough to adequately diagnose bladder outlet obstruction. A bladder scan for urine volume should be performed to assess patients with suspected large postvoid residual volumes.
Level of Study	1

● 참고문헌

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2. Poulsen AL, Schou J, Puggaard L, Torp-Pedersen S, Nordling J. Prostatic enlargement, symptomatology and pressure/flow evaluation: Interrelations in patients with symptomatic BPH. Scandinavian Journal of Urology and Nephrology Supplementum 1994;157:67-73.

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KQ 4. 전립선비대증의 해부학적인 평가를 위해서 직장수지검사보다 초음파검사가 더 정확한 평가를 할 수 있는가?

권고사항	권고수준	근거수준
4-1. 정확한 전립선의 해부학적인 평가를 위해서는 직장수지검사 외에 전립선초음파가 필요하다.	Strong	B

직장수지검사는 전립선비대증 초기 평가에 있어서 필수적인 검사이다. 초진 방문 시에 하복부와 외부생식기 관찰 등의 신체검사의 일환으로 진행되어야 한다. 직장수지검사를 통해 결절이 만져지거나 딱딱하게 만져지는 부분이 있으면 조직검사를 고려해야 한다. 전립선초음파검사는 전립선비대증에 있어서 초기 평가에 필수적인 검사는 아니지만 사정관 폐쇄 유무, 정낭의 병변을 확인하기 위하여 필요하다. 또한 전립선 석회화, 전립선 실질 내 고반향 및 저반향 에코, 전립선 주위 정맥총 확장, 전립선 피막의 불규칙성, 전립선 요도 주위부의 불규칙성 같은 이상소견을 관찰할 수 있다.

전립선비대증 진단에 있어 전립선 크기의 측정은 중요하다. 그 이유는 전립선 크기가 전립선 비대증의 임상적 경과와 치료에 대한 반응에 영향을 주기 때문이다[1,2]. 전립선초음파를 시행하여 얻을 수 있는 또 하나의 장점은 방광 내 전립선 돌출 정도를 알 수 있다는 것이다. 방광 내 전립선 돌출 정도는 5 mm 미만, 5 mm 이상 그리고 10 mm 미만, 10 mm 이상으로 나눌 수 있으며 이 돌출 정도는 요역동학검사상의 방광출구폐색 정도와 유의한 상관관계를 보였다[3-5].

전립선 크기를 측정하는 데 있어서 전립선초음파의 정확도는 직장수지검사에 비해 타당성이 인정되고 있다. 실제로 전립선암으로 전립선적출술을 시행한 대규모 지역사회 연구에서 전립선초음파 및 직장수지검사의 정확도를 전립선 실제 크기와 비교하였을 때 직장수지검사의 정확도가 많이 떨어지며 특히 전립선 크기가 작은 경우에는 정확도가 더 떨어진다고 보고되었다[6].

직장수지검사로 전립선 크기를 측정하는 것은 실제로 사이즈가 40 cc 이상으로 큰 경우에는 전립선초음파에 비해 전립선 크기를 과소 평가하는 경우가 많으며[7] 단순 직장수지검사만으로는 전립선 크기를 정확히 알아 내기가 쉽지 않고 3D 모델화를 하는 등 별도의 노력이 있어야 정확한 크

기의 측정이 가능하다[8].

● 근거표

KQ 4	
Reference	6. Loeb S, Han M, Roehl KA, Antenor JA, Catalona WJ. Accuracy of prostate weight estimation by digital rectal examination versus transrectal ultrasonography. J Urol 2005;173:63-5.
Study type	Cross-sectional study
Patients	2,238
Purpose of Study	To evaluated the relative accuracy of these weight estimates by comparing them to prostate weight following radical retropubic prostatectomy
Study Results	DRE estimates of prostate weight by multiple examiners correlated poorly with RRP specimen weight (r = 0.2743). However, TRUS estimates correlated moderately well (r = 0.6493). TRUS provided more accurate estimates of prostate weight for smaller glands, although it generally underestimated gland weight compared to the weight of the surgical specimen.In a large, community based prostate cancer screening study prostate weight estimated by DRE was shown to correlate poorly with actual prostate weight. Compared with DRE, TRUS provides a better estimate of prostate weight. In addition, TRUS measurements were more accurate in smaller prostate glands.
Level of Study	3
Reference	7. Roehrborn CG, Girman CJ, Rhodes T, Hanson KA, Collins GN, Sech SM, et al. Correlation between prostate size estimated by digital rectal examination and measured by transrectal ultrasound. Urology 1997;49:548-57.
Study type	Cross-sectional study
Patients	397
Purpose of Study	To correlate prostate size estimates performed by single or multiple examiners through digital rectal examination (DRE) with volume measured by transrectal ultrasound (TRUS) and to propose measures for predicting prostatevolume using DRE estimates in clinical settings
Study Results	DRE estimates and TRUS volumes were significantly correlated (r = 0.4 to 0.9), but prostate size was underestimated by 25% to 55% for men with a prostate volume over 40 mL..According to receiver operating characteristic curves, surface area (SA) showed a 70% and 76% chance of correctly identifying men with prostate volume greater than 30 or 40 mL, respectively; those with larger prostates were best distinguished by SA greater than 7 cm2 (sensitivity greater than 0.74, specificity greater than 0.50).
Level of Study	3

Reference	8. Roehrborn CG, Sech S, Montoya J, Rhodes T, Girman CJ. Interexaminer reliability and validity of a three-dimensional model to assess prostate volume by digital rectal examination. Urology 2001;57:1087-92.
Study type	Cross-sectional study
Patients	121
Purpose of Study	To evaluate the interexaminer reliability and accuracy compared with transrectal ultrasound (TRUS) of a three-dimensional (3D) model and other scales to improve the estimation of prostate volume by digital rectal examination (DRE).
Study Results	DRE size estimates and TRUS volume were moderately to highly correlated in men without prostate cancer. A 3D sizing model showed comparable reliability and correlation with TRUS. Although the DRE estimates generally tend to underestimate the TRUS-measured prostate volume, these tools may be useful in identifying men with enlarged prostate glands.
Level of Study	3

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KQ 5. 전립선비대증 환자에서 전립선특이항원 수치는 반드시 측정해야 하는가?

권고사항	권고수준	근거수준
5-1. 40세 이상의 하부요로증상을 호소하는 전립선비대증 환자에서 전립선특이항원검사를 해야 한다.	Strong	A

〈PSA의 정의 및 PSA 수치에 미치는 여러 인자〉

전립선특이항원(prostate specific antigen, PSA)은 prostate gland cell에서 생산되는 단백질이며, 혈액에서 측정할 수 있다. PSA는 human kallikrein family의 한 member이고 전립선의 ductal epithelium으로부터 분비된다. 정상적인 생리 환경에서, prostatic duct의 epithelial basement membrane은 PSA가 전신 순환(systemic circulation)으로 들어가는 것을 방지하는 방어막 역할을 한다[1].

일반적으로 혈액에서 PSA 수치가 낮게 유지되는 것이 정상이지만, 전립선암(prostate cancer) 또는 다른 양성 전립선 질환으로 PSA 수치가 상승할 수 있다. 나이가 들수록 양성 전립선 질환과 전립선암이 더 흔하게 발생하는데, 가장 흔한 양성 전립선 질환은 만성 전립선염(chronic prostatitis, also known chronic pelvic pain syndrome)과 전립선비대증(benign prostatic hyperplasia, BPH)이다. 그 외 요로감염(urinary tract infection)과 관련된 전립선 염증(prostatic inflammation)과 요폐(urinary retention), 도뇨(urethral catheterization)와 관련된 trauma 등이 PSA 수치를 상승시킬 수 있다[1]. 이와는 반대로, 항안드로젠(anti-androgen) 또는 5α환원효소억제제(5-alpha reductase inhibitor)는 PSA 수치를 50% 정도 낮출 수 있다[2-6].

〈전립선암 선별검사로서의 역할〉

PSA 수치의 상승은 전립선암의 가능성이 있음을 의미하기 때문에[7-9], 전립선비대증이 의심되어 내원한 환자들에게 전립선암을 감별할 필요가 있는 경우 PSA 검사를 시행해야 한다.

PSA 검사는 기대 여명(life expectancy)이 10년 이상이고 전립선암의 진단이 환자의 치료 방향을 변화시킬 수 있을 때 해야 한다[7]. PSA 검사에 따른 위양성과 위음성의 결과뿐만 아니라, 전립

선조직검사 후 생길 수 있는 합병증 등을 포함하는 PSA 검사의 이익(benefit)과 위험(risk)에 대해 환자와 충분히 상의하여야 한다[7]. 전립선암의 진단과 관련된 불확실성 때문에, 특정한 PSA 수치에 따라 어떤 환자에게 전립선초음파를 이용한 전립선조직검사를 시행할지 여부를 임상적으로 잘 판단해야 한다[7].

기대 여명이 10년 미만이거나, 전립선암 치료의 적응증이 아닌 환자는 일반적으로 PSA 수치의 측정은 권장되지 않는다. 하지만, 적어도 10년 이상의 기대 여명을 가지고 있는 환자, 그리고 전립선암을 진단함으로써 치료를 변화시킬 수 있고 PSA 수치의 측정이 전립선 크기 등을 추정하여 하부요로증상(LUTS)에 대한 치료를 변화시킬 수 있는 경우 PSA 검사를 시행하여야 한다[10]. 전립선암이 없는 환자에서의 PSA 수치는 전립선 크기를 짐작할 수 있는 유용한 지표가 될 수 있으며, 전립선비대증 진행(BPH progression)의 위험도를 예측할 수 있다[11].

〈전립선 크기 예측〉

지금까지 많은 연구에서 혈중 PSA 수치가 전립선 크기와 관련이 있으며[12-14], 전립선비대를 유용하게 예측할 수 있다고 보고하고 있다[15]. 우리나라에서 시행된 대규모 다기관연구[16]에서도, 전립선 크기와 혈중 PSA 수치는 연령 의존형(age-dependent) 로그선형관계를 보였으며, 또한 PSA는 전립선의 다양한 크기의 기준값(30, 40 and 50 mL)을 잘 예측하는 인자였다[16]. 이 연구에서 한국인에서의 PSA와 전립선 크기와의 관계는 백인(Caucasian)과 비슷하였으나, 한국인은 백인(Caucasian)에 비해 낮은 PSA 수치와 작은 전립선 크기를 가졌다[16]. 또한 전립선 크기가 40 mL 이상임을 예측할 수 있는 PSA 수치의 age-specific criteria는 60대, 70대, 80대에 각각 > 1.3 ng/mL, >1.7 ng/mL, >2.0 ng/mL이었다[16]. 이처럼 혈중 PSA 검사는 하부요로증상을 동반한 환자에서 전립선 크기의 예측인자이며, 임상적 결정을 내리는 데 도움이 된다[7].

〈질환 진행 예측〉

PSA 수치를 측정한 사람과 측정하지 않은 사람 간의 하부요로증상의 치료 효과를 직접적으로 비교한 근거는 아직까지 없다. 또한 PSA 수치가 증상 진행(progression)을 예측하는 예측 인자임을 제시하는 data 역시 아직까지는 일관적이지 않으며, PSA 수치가 전립선비대증의 진행 예측과 관련하여 임상적으로 의미가 없다는 보고도 있다[17,18]. 하지만, 혈중 PSA 기저치와 질환의 진행과의 관련성에 대해 회귀분석(regression analysis)을 시행한 많은 연구에서 혈중 PSA 수치가 전

립선비대증의 진행을 예측하였다. Roehrborn 등[19]은 혈중 PSA 수치와 전립선 크기는 향후 질환의 진행을 예측할 수 있음을 보고하였다. 여러 연구에서 혈중 PSA 기저치가 높을수록 전립선비대증 진행(overall BPH progression) 가능성과 수술과 같은 침습적 치료(invasive therapy)를 받게 되는 발생률(incidence rate)이 높았다[20-23]. 혈중 PSA 기저치가 대조군(placebo군)에서 증상 악화를 예측하는 인자이고, 대조군과 비교하여 Finasteride 5 mg 치료군의 유의한 증상 호전을 예측할 수 있었다[24]. 삶의 질의 변화와 치료 전 PSA 수치가 유의한 음의 상관관계가 있다고 보고하였다[25]. 국제전립선증상점수(IPSS) >7의 Odds ratio (95% CI)가 PSA 수치에 따라 PSA≤2: 1.0, PSA>2-4: 1.62(1.2-2.2), PSA>4-10: 2.64 (1.5-4.7), PSA >10: 4.28 (1.8-10.3)인 것으로 보고하였다[26].

결론적으로 40세 이상의 전립선비대증 환자에서 혈중 PSA 수치의 측정은 전립선암과의 감별, 전립선 크기 예측, 질환의 진행 예측 그리고 치료법 결정을 위해 필요하다.

● 근거표

KQ 5	
Reference	20. Crawford ED, Wilson SS, McConnell JD, Slawin KM, Lieber MC, Smith JA, et al. Baseline factors as predictors of clinical progression of benign prostatic hyperplasia in men treated with placebo. J Urol 2006;175:1422-6.
Study type	Longitudinal follow up of the placebo arm of an RCT with 4 years follow up
Patients	- Men with BPH and moderate to severe symptom (AUASS) mean 17 (range of 8- 20). - The average age was 62 years. (N=737)
Purpose of Study	Analysis of data from the placebo arm of the MTOPS trial to determine clinical predictors of BPH progression
Study Results	Baseline PSA level was associated with symptom progression. At 4 years, the cumulative probability and incidence rate of overall BPH progression was significantly higher in the baseline high PSA group (p<0.001). Incidence rate of ≥ 4 points increase in AUASS was significantly higher in the high PSA group (4.5 vs. 2.8 events/100 person year). The incidence rate of acute urinary retention and invasive therapy was also significantly higher in the group with higher baseline PSA.
Level of Study	2
Reference	21. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr., Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387-98.

Study type	RCT double blinded (4 arms)
Patients	- N: 3047 out of 4391 screened, - Mean age: 62.6 ± 7.3
Purpose of Study	To know the long-term effect of these drugs, singly or combined, on the risk of clinical progression
Study Results	Prognosis value of PSA, based on placebo arm [Data from Crawford 2006] - Overall BPH progression was defines as the first occurrence of an increase of at least 4 points in the AUASS, AUR, urinary incontinence or renal insufficiency or recurrent UTI - Cumulative probability of BPH progression (4 year follow up) PSA≥1.6 ng/ml: 24% PSA<1.6 ng/ml: 13.5% P<0.001 (values read from graph) - Incidence rate of overall BPH progression (events/100 person year) PSA≥1.6 ng/ml: 5.9 PSA<1.6 ng/ml: 3.1 P=0.0002 - Incidence rate of ≥4 points increase in AUASS (events/100 person year) PSA≥1.6 ng/ml: 4.5 PSA<1.6 ng/ml: 2.8 P=0.028 - Incidence rate of AUR (events/100 person year) PSA≥1.6 ng/ml: 1.0 PSA<1.6 ng/ml: 0.3 P=0.0029 - Incidence rate of invasive therapy (events/100 person year) PSA≥1.6 ng/ml: 1.8 PSA<1.6 ng/ml: 0.8 P=0.018
Level of Study	2
Reference	24. Roehrborn CG, Boyle P, Bergner D, Gray T, Gittelman M, Shown T, et al. Serum prostatespecific antigen and prostate volume predict long-term changes in symptoms and flow rate: results of a four-year, randomized trial comparing finasteride versus placebo. PLESS Study Group. Urology 1999;54:662-9.
Study type	RCT with follow up of 4 years.
Patients	- Men with clinical BPH, moderate to severe symptoms - Serum PSA 4 -9.9 ng/mL with negative biopsy - N: 3040 (Drop outs: 1157) - Group 1 Finasteride 5mg/day - Group 2 Placebo Notes: Baseline PSA was divided into 3 tertiles: First (0.2 - 1.3) Second (1.4 – 3.2) Third (3.3 – 12.0)
Purpose of Study	To determine whether baseline prostate-specific antigen (PSA), in addition to prostate volume, is associated with long-term changes in symptoms and urinary flow rate.
Study Results	- Baseline PSA predicts deterioration of symptoms in untreated patients. Baseline PSA predicts improvement of symptoms for those patients treated with finasteride relative to placebo Baseline PSA does not predict improvement of symptoms in the finasteride treatment group alone. - Mean Change in Quasi-AUA Symptom Score (± SE) over time (years 1-4) for each PSA tertile in placebo patients (group 2): 1st tertile had a significantly better long-term symptom improvement than those in other tertiles p < 0.001 There was no significant difference between long term symptom improvement between 2nd and 3rd tertiles p=0.65 - Mean Change in Quasi-AUA Symptom Score (± SE) over time (years 1-4) for each PSA tertile group 1 vs. group 2: 1st tertile Not sig. 2nd tertile (p=0.004) 3rd tertile (p=0.001)

Level of Study	2
Reference	25. Laguna MP, Kiemeney LA, Debruyne FM, de la Rosette JJ. Baseline prostatic specific antigen does not predict the outcome of high energy transurethral microwave thermotherapy. J Urol 2002;167:1727-30.
Study type	Cohort
Patients	- N: 404 - Age (mean, range): 66.3 (44.8-89.7)
Purpose of Study	To assessed the prognostic value of baseline prostate specific antigen (PSA) for outcome after high energy transurethral thermotherapy in patients with lower urinary tract symptoms.
Study Results	Linear regression: Change in QoL vs. pretreatment PSA Spearman r: -0.135 "linear regression coefficient": -0.04 P value: 0.01
Level of Study	2
Reference	26. Tubaro A, La Vecchia C. The relation of lower urinary tract symptoms with life-style factors and objective measures of benign prostatic enlargement and obstruction: An italian survey. Eur Urol 2004;45:767-72.
Study type	Cross sectional, observational
Patients	- Age: 50-80 years - N: 866 - Drop outs: 64/866, 802 analysed - Age (mean, range): 64 (50-80)
Purpose of Study	The association between the severity of LUTS and prostate volume, prostate-related variables and general life-style factors was investigated in a large number of patients with persistent LUTS suggestive of BPH (LUTS/BPH).
Study Results	Multiple logistic regressions: IPSS >7 vs. PSA (ng/ml), IPSS<7 is the reference Odds ratio (95%CI) PSA≤2: 1.0 PSA>2-4: 1.62 (1.2-2.2) PSA>4-10: 2.64 (1.5-4.7) PSA>10: 4.28 (1.8-10.3)
Level of Study	2

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26. Tubaro A, La Vecchia C. The relation of lower urinary tract symptoms with life-style factors and objective measures of benign prostatic enlargement and obstruction: An italian survey. Eur Urol 2004;45:767-72.

치 료

생활습관 개선, 대기요법

약물치료

알파차단제
5α환원효소억제제
항콜린제

약물치료-병합요법

알파차단제와 5α환원효소억제제
알파차단제와 항콜린제
알파차단제와 PDE5억제제

급성요폐와 도뇨관 치료

경요도전립선절제술

경요도수술
최소침습술

추적관찰

전문진료 의뢰사항

KQ 6. 전립선비대증 환자에서 생활습관 개선은 증상 호전에 도움이 되는가?

권고사항	권고수준	근거수준
6-1. 경증의 전립선비대증 환자는 대기요법이 적절하다.	Strong	B
6-2. 하부요로증상을 가진 환자에게 약물 치료 전 또는 약물 치료와 동시에 생활습관 개선에 대한 교육을 시행하여야 한다.	Strong	B

〈대기요법〉

하부요로증상을 지닌 환자 중 많은 경우는 증상이 심하지 않아 약물치료나 수술적 치료와 같은 적극적인 치료가 필요하지 않다. 국제전립선증상점수표의 증상점수가 7점 이하인 경도의 하부요로증상을 가진 환자는 치료하지 않고 경과를 지켜보는 대기요법의 대상이 될 수 있다. 또한 국제전립선증상점수표의 증상점수가 8점에서 19점 사이인 중등도의 환자도 하부요로증상에 따른 불편함이 없다면 대기요법의 대상이 될 수 있다. 대기요법 시행 후 일부 증상은 자연적으로 호전이 되기도 하고, 수년간 증상의 변화 없이 유지될 수 있다[1].

중등도의 하부요로증상을 호소하는 환자들에서 대기요법과 경요도전립선절제술의 효과를 비교한 대규모 무작위 배정 연구 결과, 대기요법군의 36%는 5년 안에 결국 수술을 받았으며 나머지 64%는 대기요법을 유지하였다. 수술을 받은 군을 분석하였을 때, 수술 전 불편함의 정도가 컸던 환자일수록 수술 결과가 좋았다[2]. 또 다른 대규모 연구에서는 대기요법을 시행한 결과 1년째 85%가 증상의 변화가 없었으나, 5년째는 65%가 병의 진행을 보였다[3,4].

〈교육, 생활습관 개선〉

대기요법을 시작할 때 교육 및 행동요법의 효과를 비교한 연구에서 세 차례의 행동요법 교육을 받은 군은 교육이 없었던 군에 비해 3, 6, 12개월째 국제전립선증상점수표의 증상점수가 각각 5.7점, 6.5점, 5.2점 더 낮았으며, 이후 약물 또는 수술 치료를 받게 되는 경우는 각각 10% (vs 42%), 27% (vs 57%), 32% (vs 64%)로 적었다[5]. 그러나 대기요법과 생활습관 개선이 하부요로증상에 미치는 영향에 대한 연구는 아직 많지 않으며, 위와 같은 결과 차이의 원인에 대해서는 아직 명확

히 밝혀진 것은 없다.

국제전립선증상점수 중등도 이상의 환자에서 대기요법을 고려할 경우 증상 불편 정도를 반드시 확인하고 대기요법 중 병의 진행 위험이 있음을 염두해 두어야 한다. 대기요법 중 급성 요폐색이나 신장기능부전, 결석과 같은 합병증이 드물게 발생할 수 있다[6,7]. 따라서 이에 대해 환자에게 교육하고 추적관찰을 할 수 있도록 하며, 주기적인 검사를 통해 환자의 하부요로증상을 재평가하는 것이 중요하다. 대기요법 환자에게 다음과 같은 교육 및 생활습관 개선을 권장한다[1,4,8,9].

- 현재 환자의 하부요로증상에 대해 교육하고 이해시킨다.
- 하부요로증상의 원인이 암으로 인한 것이 아님을 확인하고 이해시킨다.
- 주기적인 추적관찰을 받도록 한다.
- 빈뇨와 야간뇨로 불편한 경우 특정 시간대의 수분 섭취량을 줄이도록 한다. 특히 야간뇨가 문제인 경우 늦은 오후와 저녁 시간의 수분 섭취를 제한하도록 권장한다.
- 이뇨작용과 방광자극효과가 있어 빈뇨, 급박뇨, 야간뇨를 일으킬 수 있는 카페인과 알코올 섭취를 줄이거나 피하도록 한다.
- 긴장을 푼 편안한 상태에서 소변을 나누어 보는 이중배뇨(double voiding technique)를 시도해본다.
- 배뇨 후 소변이 몇 방울 흘러나오는 점적이 문제인 경우 회음부부터 요도를 훑어내는 방법(urethral milking)을 시도해본다.
- 저장증상의 개선을 위해 방광 용적이나 배뇨 간격을 늘릴 필요가 있을 경우 소변이 마려운 느낌이 들 때 소변을 참아보는 방광 훈련을 시도해본다.
- 복용 중인 약물들을 확인하고 배뇨에 영향을 주는 약(예, 이뇨제)의 복용 시간을 조정하거나 가급적 배뇨에 영향이 적은 약으로 교체한다.
- 배뇨를 악화시킬 수 있는 변비를 치료하도록 한다.

● 근거표

KQ 6	
Reference	1. Isaacs JT. Importance of the natural history of benign prostatic hyperplasia in the evaluation of pharmacologic intervention. Prostate 1990;3(Suppl):1-7.
Study type	Review

Patients	
Purpose of Study	To summarize Importance of the natural history of benign prostatic hyperplasia in the evaluation of pharmacologic intervention.
Study Results	These comparisons demonstrate that 1) placebo treatment does not affect the natural history of the disease; 2) spontaneous improvement usually occurs within the first 6 months of initial presentation of symptoms, if it is to occur at all; and 3) 3-6 months of follow-up are needed to determine if a patient is going to get worse. Thus, to evaluate accurately the potential benefit of any medical intervention for symptomatic BPH, placebo-controlled clinical trials will be required and should be of at least 6 month's duration.
Level of Study	5
Reference	2. Flanigan RC, Reda DJ, Wasson JH, et al. 5-year outcome of surgical resection and watchful waiting for men with moderately symptomatic BPH: a Department of Veterans Affairs cooperative study. J Urol 1998;160:12-6.
Study type	Control arm of randomized trial
Patients	280: TURP 276: Watchful waiting 5 year follow-up
Purpose of Study	To know the outcomes after 5 years of follow-up for men who were randomized to receive TURP or watchful waiting for moderate symptoms of BPH.
Study Results	Treatment failure rates were 10% for TURP versus 21% for watchful waiting ($p = 0.0004$). The crossover rate at 5 years was 36% and was positively associated with the degree of bother.
Level of Study	3
Reference	3. Wasson JH, Reda DJ, Bruskewitz RC, et al. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. New Engl J Med 1995;332:75-9.
Study type	Control arm of randomized trial
Patients	280: TURP 276: Watchful waiting 3 year follow-up
Purpose of Study	To know the outcomes after 3 years of follow-up for men who were randomized to receive TURP or watchful waiting for moderate symptoms of BPH.
Study Results	Of the men assigned to the watchful-waiting group, 65 (24 percent) underwent surgery within three years after the assignment. Surgery was associated with improvement in symptoms and in scores for urinary difficulties and interference with activities of daily living ($P<0.001$ for all comparisons).
Level of Study	3
Reference	4. Netto NR, de Lima ML, Netto MR, et al. Evaluation of patients with bladder outlet obstruction and mild international prostate symptom score followed up by watchful waiting. Urol 1999;53:314-6.

Study type	Study without consistently applied reference standards / Cohort study
Patients	479 patients 50 to 81 years old (mean age 63) with lower urinary tract symptoms attributed to BPH.
Purpose of Study	To know the variability of bladder outlet obstruction and mild lower urinary tract symptoms in patients with benign prostatic hyperplasia (BPH) followed up by watchful waiting.
Study Results	Of 50 patients with mild symptoms, 16 (32%) had bladder outlet obstruction. After a period of 9 to 22 months (mean 17) of watchful waiting, these 16 patients were reviewed. Twelve (75%) of the 16 had bladder outlet obstruction reconfirmed by pressure-flow studies, and 3 (18.8%) of 16 had increased symptoms (moderate symptomatic) and underwent treatment. A total of 4 (25%) of 16 patients still had mild voiding disturbances. The remaining 34 patients with no obstruction had annual routine follow-up and had persistent mild symptom scores and normal uroflowmetric results.
Level of Study	4
Reference	5. Brown CT, Yap T, Cromwell DA, et al. Self-management for men with lower urinary tract symptoms – a randomized controlled trial. BMJ 2007;334:25.
Study type	Control arm of randomized trial
Patients	- 140 men (mean age 63 (SD 10.7) years), referred by general practitioners to urological outpatient departments with uncomplicated lower urinary tract symptoms. - Self management and standard care (n=73) or standard care alone (n=67). 12 months follow-up
Purpose of Study	To evaluate the effectiveness of self management as a first line intervention for men with lower urinary tract symptoms
Study Results	At three months, treatment failure had occurred in 7 (10%) of the self management group and in 27 (42%) of the standard care group (difference=32%, 95% confidence interval 18% to 46%). Corresponding differences in the frequency of treatment failure were 42% (27% to 57%) at six months and 48% (32% to 64%) at 12 months. At three months, the mean international prostate symptom score was 10.7 in the self management group and 16.4 in the standard care group (difference=5.7, 3.7 to 7.7). Corresponding differences in score were 6.5 (4.3 to 8.7) at six months and 5.1 (2.7 to 7.6) at 12 months.
Level of Study	3
Reference	6. Ball AJ, Feneley RC, Abrams PH. The natural history of untreated 'prostatism'. Br J Urol 1981;53:613-6.
Study type	Study without consistently applied reference standards / Cohort study
Patients	107 patients with symptoms of prostatic obstruction in whom prostatectomy was not clinically indicated. 5 year follow-up
Purpose of Study	To evaluate the natural history of patients with symptoms of prostatic obstruction
Study Results	Ten had subsequently required surgery and 97 remained untreated. In the majority, symptoms did not worsen and only 2 developed acute retention.

Level of Study	4
Reference	7. Kirby RS. The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology 2000;56(5 Suppl 1):3-6.
Study type	Review
Patients	
Purpose of Study	To summarize our current understanding of the natural history of benign prostatic hyperplasia
Study Results	Age is a strong independent risk factor for the development of AUR. Transurethral resection of the prostate was more effective than watchful waiting in preventing AUR, as shown in the Veteran's Affairs Cooperative Study. Data from the Olmsted County study revealed that urinary flow decreases and prostate size increases with advanced age.
Level of Study	5
Reference	8. Yap TL, Brown C, Cromwell DA, et al. The impact of self-management of lower urinary tract symptoms on frequency-volume chart measures. BJU Int 2009;104:1104-8.
Study type	Control arm of randomized trial
Patients	140 men with uncomplicated lower urinary tract symptoms. 12 months follow-up
Purpose of Study	To assess the effect of a self-management programme (SMP) on actual voiding behaviour using frequency-volume chart (FVC) data.
Study Results	Of the 140 patients, 104 completed the FVC data at baseline; at 3, 6 and 12 months charts were received from 99, 95 and 70, respectively. Baseline FVC variables were equivalent between the randomized groups. At 3 months the mean voided volume had increased in the SMP group and differed from the control group by a mean (95% confidence interval, CI) of 57 (33-83) mL. The total number of voids and episodes of nocturia were also lower in the SMP group, with a mean (95% CI) decrease of 2.6 (-3.6 to -1.5) and 0.7 (-1.1 to -0.3) episodes, respectively. These changes were maintained at 6 and 12 months.
Level of Study	3
Reference	9. Brown CT, van der Meulen J, Mundy AR, et al. Defining the components of self-management programme in men with lower urinary tract symptoms: a consensus approach. Eur Urol 2004;46:254-63.
Study type	multidisciplinary panel rating
Patients	An eight member multidisciplinary panel rated 94 items
Purpose of Study	To define the components of a self-management programme of lifestyle and behavioural interventions for symptom control in men with uncomplicated LUTS.

Study Results	The panel agreed that 57 of the original 94 items were appropriate to be incorporated in the self-management programme. These interventions were contained within the following categories: patient assessment prior to starting a self-management programme (6), education and reassurance (4), fluid management (6), caffeine (4), alcohol (2), concurrent medication (2), types of toileting (2), bladder re-training (15), miscellaneous (1), and implementation of a self-management programme (15).
Level of Study	4

● 참고문헌

1. Isaacs JT. Importance of the natural history of benign prostatic hyperplasia in the evaluation of pharmacologic intervention. Prostate 1990;3(Suppl):1-7.
2. Flanigan RC, Reda DJ, Wasson JH, et al. 5-year outcome of surgical resection and watchful waiting for men with moderately symptomatic BPH: a Department of Veterans Affairs cooperative study. J Urol 1998;160:12-6.
3. Wasson JH, Reda DJ, Bruskewitz RC, et al. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. New Engl J Med 1995;332:75-9.
4. Netto NR, de Lima ML, Netto MR, et al. Evaluation of patients with bladder outlet obstruction and mild international prostate symptom score followed up by watchful waiting. Urol 1999;53:314-6.
5. Brown CT, Yap T, Cromwell DA, et al. Self-management for men with lower urinary tract symptoms – a randomized controlled trial. BMJ 2007;334:25.
6. Ball AJ, Feneley RC, Abrams PH. The natural history of untreated 'prostatism'. Br J Urol 1981;53:613-6.
7. Kirby RS. The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology 2000;56(5 Suppl 1):3-6.
8. Yap TL, Brown C, Cromwell DA, et al. The impact of self-management of lower urinary tract symptoms on frequency-volume chart measures. BJU Int 2009;104:1104-8.
9. Brown CT, van der Meulen J, Mundy AR, et al. Defining the components of self-management programme in men with lower urinary tract symptoms: a consensus approach. Eur Urol 2004;46:254-63.

KQ 7. 전립선비대증 환자에서 일차치료법으로 약물치료법이 수술적 치료보다 우선적으로 고려되어야 하는가?

권고사항	권고수준	근거수준
7-1. 전립선비대증으로 인해 중등도 이상의 증상을 보이는 경우는 약물치료가 일차적으로 권장된다. 그러나, 방광돌이 있는 경우, 방광기능장애를 동반한 방광게실이 있는 경우, 상부요로의 확장으로 인한 신기능부전이 동반된 경우, 약물치료에도 불구하고 요폐, 요로감염, 혈뇨가 반복되거나 배뇨증상, 배뇨 후 잔뇨량의 호전이 없는 경우에는 수술치료가 고려되어야 한다.	Strong	B
7-2. 5α환원효소억제제는 중등도 이상의 하부요로증상을 호소하는 환자에서 직장수지검사 또는 전립선초음파검사에서 전립선 크기가 크거나 혈청 전립선특이항원 검사에서 전립선비대증의 진행 가능성이 보이는 경우 장기간 처방을 고려해야 하는 치료약물이다.	Strong	A
7-3. 항콜린제는 중등도 이상의 하부요로증상을 보이는 환자 중 방광자극증상을 주로 호소하는 환자에서 고려될 수 있으며, 방광출구폐색이 심하거나 배뇨 후 잔뇨량이 많은 경우 신중한 사용이 필요하다.	Strong	A
7-4. 알파차단제는 중등도 이상의 하부요로증상을 보이는 전립선비대증 환자에게 우선적으로 고려되어야 하는 치료약물이다.	Strong	A

전립선비대증 치료방법의 선택은 각종 관련검사의 결과뿐만 아니라 환자의 선호도나 치료방침의 기대효과, 부작용이나 합병증, 비용 등을 감안하여야 한다.

7-1. 알파차단제

현재 국내에서 전립선비대증 약물치료에 사용 가능한 알파차단제에는 terazosin, doxazosin, alfuzosin, tamsulosin, silodosin, naftopidil이 있다.

약제 간 비교에 의하면 언급한 알파차단제들은 적절한 용량에서 비슷한 효능을 나타내는 것으로 알려져 있다[1]. 여러 무작위 위약-대조군 연구에서 밝혀진 바에 따르면, 알파차단제는 보통 국제전립선증상점수를 약 35-40% 감소시켜주고 최대요속을 약 20-25% 증가시켜준다[2-13]. 일부

open-label 연구에서는 국제전립선증상점수가 50%까지 감소하고 최대요속은 40%까지 증가하는 것으로 나타났다[1,14].

1년 미만의 경과관찰에서는 전립선 크기가 알파차단제 효능에 영향을 끼치지 않았지만, 1년 이상에서는 40 mL 미만의 작은 전립선을 가진 환자에서 더 우수한 약물효능을 보였다[14]. 장기간 관찰연구에서 알파차단제는 전립선 크기를 감소시켜주지 않으며 급성요폐를 막지 못하는 것으로 나타났다[2].

가장 흔한 부작용은 무기력, 어지러움, 기립성저혈압이다. 혈압감소가 고혈압 환자에게는 이득이 될지 모르나 일부 무기력 및 어지러움은 혈압감소에 의한 증상으로 볼 수 있다. 혈관확장효과는 doxazosin, terazosin에서 가장 두드러지며 alfuzosin, tamsulosin에서는 훨씬 적다[15]. 따라서 doxazosin, terazosin은 치료를 시작할 때 용량적정(dose titration)이 필요하다. 심혈관계 질환을 갖고 있거나 혈관에 작용하는 약물(각종 항고혈압제제, 발기부전에 사용되는 PDE5억제제)을 복용 중인 환자는 알파차단제에 의한 혈관확장에 더욱 민감할 수 있다[16].

알파차단제가 오랫동안 광범위하게 사용되어 왔지만 2005년에 이르러서야 처음으로 수술 중 홍채이완증후군(intraoperative floppy iris syndrome)이 보고되었다[17]. 대부분의 보고는 tamsulosin과 관련된 것이었는데, 다른 알파차단제에 비해 tamsulosin이 높은 위험도를 보이는 것인지 또는 tamsulosin이 타 약제에 비해 광범위하게 사용되었기 때문인지는 명확하지 않다[18]. 백내장 수술 전 알파차단제를 처방하지 않도록 주의하는 것은 물론 알파차단제를 복용 중인 환자에서도 백내장 수술이 계획된 경우라면 약물을 중지해야 한다.

배뇨증상과 발기부전이 동반된 경우 알파차단제 치료가 성기능을 더욱 악화시키지는 않는다. 알파차단제가 성욕을 저해시키지 않으며 발기능에 약간의 이득이 있는 것으로 평가되나 종종 비정상적 사정을 일으킨다는 문제점을 갖고 있다[19]. 보통 비정상적 사정은 역행성 사정일 것으로 판단되나 최근 자료에서는 젊은 연령에서 비정상적 사정을 보이는 경우 상대적인 무사정증에 기인하는 것으로도 보고하고 있다. 비정상적 사정은 앞서 언급한 다른 약물보다 tamsulosin에서 더 빈번하고, silodosin과 같이 알파1A수용체에 더욱 선택적인 약물에서 비정상적 사정에 대한 위험이 더 큰 것으로 나타났다[19,20].

문헌고찰에 따르면, silodosin, naftopidil은 아직 관련 연구가 많지는 않으나 저용량의 tamsulosin에 준하는 증상 호전을 보이는 것으로 나타났다[21,22].

7-2. 5α환원효소억제제

5α환원효소억제제의 종류에는 dutasteride와 finasteride가 있다. Dutasteride는 5α환원효소

1유형과 2유형을 모두 저해하고, finasteride는 5α환원효소 2유형만을 저해하는 약제이다. 상기 약제들은 전립선상피세포의 세포사멸(apoptosis)을 조장하여 전립선 크기가 줄어들면서 효과를 나타낸다[23].

위약에 비해 임상적으로 효과를 나타내는 시기는 적어도 6-12개월의 치료기간이 경과한 이후이다. 전립선비대로 하부요로증상을 호소하는 환자가 5α환원효소억제제를 복용한 지 2-4년이 지나면 국제전립선증상점수가 약 15-30% 감소하고 전립선 크기도 약 18-28% 감소하며 최대요속은 약 1.5-2.0 mL/s 증가하는 것으로 나타났다[24-33]. 또한, 5α환원효소억제제는 급성요폐 및 수술 필요성에 대한 장기간(1년 이상)의 위험을 감소시켜주는 것으로 보고되었다[28,30,34,35].

Finasteride에 의한 증상 호전은 치료 전 전립선 크기에 따라 다른데, 전립선이 40 mL보다 작은 경우나 PSA 1.4 ng/ml 이하인 경우 위약군에 비해 별로 효과적이지 않을 것으로 여겨진다[36,37]. 한편, dutasteride는 치료 전 전립선 크기가 30-40 mL인 경우에도 최대요속을 상승시키는 것으로 나타났다[38,39]. 두 약제는 몇몇 연구 간 간접 비교를 통해 살펴봤을 때, 하부요로증상의 치료에 거의 동등한 효능을 보이는 것으로 보고되었다[40].

한국인의 평균 전립선 크기는 50대 이상 모든 연령대에서 서양인의 평균 전립선 크기에 비해 5-10 mL 작은 것으로 나타났다[41]. 평균 전립선 크기가 큰 서양인을 대상으로 진행된 연구들을 근거로 얻어진 외국의 진료지침권고를 그대로 받아들이는 것은 적합하지 않다. 서양인 기준의 연구에 근거한 전립선 용적 30 ml 또는 PSA 1.4 ng/ml 이상인 경우 5α환원효소억제제 사용 권고는 한국 성인 남성의 전립선 용적 기준에 맞추어 조정되어야 한다. 이에 대한 명확한 근거를 제시하기 위한 국내 연구가 필요하다.

5α환원효소억제제를 복용한 지 6-12개월이 경과한 후에는 전립선특이항원 수치가 약 50% 감소하므로[40], 전립선특이항원 수치의 해석에 유의하여야 한다.

5α환원효소억제제의 성기능 관련 부작용으로는 성욕감소, 발기부전, 역행성 사정과 같은 사정장애, 사정실패, 정액량 감소가 있으며[30,33,40], 여성형 유방도 환자의 1-2%에서 보고된다.

7-3. 항콜린제

현재 국내에서 사용 가능한 주요 항콜린제에는 tolterodine, trospium, solifenacin, fesoterodine, propiverine, oxybutynin Imidafenacin이 있다. 과민성 방광에서 주로 처방되는 약으로 전립선비대증에서는 자극증상을 호소할 때 고려해 볼 수 있는 약제들이다.

Tolterodine은 open-label 연구에서 12-25주 복용 후 주간빈뇨, 야간뇨, 절박요실금, 국제전립선증상점수가 복용 전에 비해 유의하게 호전되는 것으로 나타났다[42,43]. 한편, 무작위 위약-대조군 연구에서는 tolterodine 복용군의 경우 위약군에 비해 절박요실금, 주간 및 24시간 빈뇨가 유의하게 줄어드는 것으로 나타났다. 야간뇨, 절박뇨, 국제전립선증상점수도 대부분 줄어들었으나 통계적으로 유의하지는 않았다[44-46].

항콜린제는 배뇨 후 잔뇨량 증가와 요폐에 대한 위험 때문에 방광출구폐색이 심한 전립선비대증 환자에서는 일반적으로 권장되지 않는다. 중등도 이하의 방광출구폐색이 있는 환자에서는 tolterodine을 사용하였을 때 위약군에 비해 배뇨 후 잔뇨량은 유의하게 증가하였지만, 급성 요폐 발생에는 차이가 없었다[47].

Tolterdine의 가장 흔한 부작용은 입마름이며, 7-24%의 빈도로 발생한다[41,45,46]. 대규모의 무작위 연구들에 따르면 tolterodine 복용군에서 요폐, 변비, 설사, 졸림과 같은 부작용은 대조군과 비슷한 빈도를 보였다[48,49].

방광자극증상을 보이는 전립선비대증 환자에 관한 연구는 대부분 tolterodine과 일부 fesoterodine에서 수행되기는 했지만, 대개 다른 항콜린제에서도 효과나 부작용은 비슷할 것으로 받아들여진다.

7-4. 일차치료법으로서 약물치료와 수술치료의 비교

일차치료법으로서 약물치료와 수술치료의 임상결과를 직접적으로 비교한 연구는 확인되지 않았다. 다만, 치료비용 기준으로 살펴봤을 때 중등도 증상인 환자에서는 약물치료가, 심한 증상인 환자에서는 수술치료가 비용 대비 효과적인 것으로 나타났다[49].

두 치료 간의 직접적인 비교연구는 없지만, 주요 진료지침들에서는 수술을 고려해야 하는 경우에 대해 다음과 같이 권장하고 있다.

EAU (2012)	전립선비대로 인해 재발성 또는 치료불응성인 요폐, 범람성 요실금, 재발성 요로감염, 방광돌이나 방광게실, 치료저항성 육안적 혈뇨, 상부요로의 확장(± 신기능부전)이 발생했을 경우 수술치료를 필요로 한다(절대적 적응증). 또한, 보존적 치료나 약물치료에도 불구하고 하부요로증상이나 배뇨 후 잔뇨량의 호전이 불충분한 경우 수술을 고려할 수 있다(상대적 적응증).

AUA (2010)	전립선비대로 인한 신기능부전, 재발성 요로감염, 방광돌, 육안적 혈뇨가 있거나 다른 치료에 불응성인 하부요로증상을 보이는 경우 수술치료가 권장된다. 방광게실은 반복성 요로감염이나 진행성의 방광기능장애가 동반되지 않으면 수술의 절대적 적응증이 아니다.
NCGC (2010)	배뇨증상이 심각한 경우, 보존적 치료나 약물치료가 실패한 경우 또는 적절하지 않은 경우 수술을 권장한다. 경증 또는 중등도의 증상인 환자에게는 수술치료 전에 다른 치료법을 시도해야 한다.

이를 토대로 미루어 보았을 때, 수술의 적응증이 동반된 상황에서는 처음부터 수술을 권장할 수 있으나 중등도 이하의 증상을 보이는 환자에서는 약물치료가 일차적으로 고려되어야 하는 것이 적절하다고 판단된다. 또한, 수술여부는 수술에 따른 합병증 위험, 수술비용 등을 치료이득과 비교하여 환자의 입장에서 결정하여야 한다. 전립선비대에 따른 수술방법은 다음과 같은 것들이 있으며, 경요도적전립선절제술(TURP)이 아직까지는 수술치료의 기준으로 받아들여지고 있다.

- Transurethral resection of the prostate (TURP)
- Transurethral incision of the prostate (TUIP)
- Transurethral vaporization of the prostate (TUVP)
- Photoselective vaporization of the prostate (PVP)
- Transurethral holmium laser ablation of the prostate (HoLAP)
- Holmium laser resection of the prostate (HoLRP)
- Transurethral holmium laser enucleation of the prostate (HoLEP)
- Open prostatectomy
- Laparoscopic and robotic prostatectomy (considered investigational)

● 근거표

KQ 7	
Reference	1. Djavan B, Chapple C, Milani S, et al. State of the art on the efficacy and tolerability of alpha1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. Urology 2004;64:1081-8.

Study type	Systematic review
Patients	33 studies, 22,562 patients
Purpose of Study	To aim in the present report to update the analysis published in 1999 to assess whether these α1-AR antagonists can be distinguished with regard to efficacy and/or tolerability
Study Results	All α1-AR antagonists have comparable efficacy in improving symptoms and Qmax when administered at their full therapeutic dose. α1-AR antagonists that require dose titration and are initiated at subtherapeutic doses (eg, terazosin) have a slower onset of action than α1-AR antagonists that can be initiated at their full therapeutic dose (eg, tamsulosin). The main difference between α1-AR antagonists relates to their tolerability profile, with alfuzosin (especially the XL formulation) and tamsulosin (especially the 0.4 mg o.d. dose) better tolerated than doxazosin (including the GITS formulation) and terazosin. As demonstrated in the direct-comparative studies, tamsulosin tends to interfere less with blood pressure regulation and induces slightly less vasodilatory AEs than alfuzosin. This seems particularly to be the case in the elderly and patients with cardiovascular disease and/or comedication. Abnormal ejaculation has mainly been reported in placebo-controlled trials with tamsulosin. In direct-comparative trials, its incidence with tamsulosin was comparable or slightly greater than that with alfuzosin and greater than that with terazosin. However, it seems that patients with LUTS/BPH are more likely to discontinue α1-AR antagonist therapy because of vasodilatory AEs such as dizziness than abnormal ejaculation and that over-all sexual function is improved with all α1-AR antagonists, including tamsulosin. Vasodilatory AEs may lead to falls, fractures, and institutionalization, in particular in the elderly or very elderly and/or in those with concomitant cardiovascular comorbidity/co-medication.
Level of Study	1
Reference	2. McConnell JD, Roehrborn CG, Bautista O, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387-98.
Study type	Randomized, placebo-controlled trial
Patients	3,047 patients
Purpose of Study	To compare the effects of placebo, doxazosin, finasteride, and combination therapy on measures of the clinical progression of benign prostatic hyperplasia
Study Results	The risk of overall clinical progression-defined as an increase above base line of at least 4 points in the American Urological Association symptom score, acute urinary retention, urinary incontinence, renal insufficiency, or recurrent urinary tract infection-was significantly reduced by doxazosin (39 percent risk reduction, P<0.001) and finasteride (34 percent risk reduction, P=0.002), as compared with placebo. The reduction in risk associated with combination therapy (66 percent for the comparison with placebo, P<0.001) was significantly greater than that associated with doxazosin (P<0.001) or finasteride (P<0.001) alone. The risks of acute urinary retention and the need for invasive therapy were significantly reduced by combination therapy (P<0.001) and finasteride (P<0.001) but not by doxazosin. Doxazosin (P<0.001), finasteride (P=0.001), and combination therapy (P<0.001) each resulted in significant improvement in symptom scores, with combination therapy being superior to both doxazosin (P=0.006) and finasteride (P<0.001) alone.
Level of Study	2

Reference	3. Jardin A, Bensadoun H, Delauche-Cavallier MC, et al. Alfuzosin for treatment of benign prostatic hypertrophy. The BPH-ALF Group. Lancet 1991;337:1457-61.
Study type	Randomized, placebo-controlled trial
Patients	518 patients
Purpose of Study	To assess the long-term efficacy and safety of alfuzosin, a selective alpha 1-adrenergic antagonist
Study Results	Obstructive and irritative symptoms, assessed according to the Boyarsky scale, significantly improved in the alfuzosin group compared with the placebo group (p = 0.0004). Fewer patients in the alfuzosin group than in the placebo group dropped out due to lack of efficacy (6.8% vs 14.6%, p = 0.004) and the prevalence of spontaneous acute urine retention was lower in the alfuzosin group (0.4% vs 2.6%, p = 0.04). By 6 months, mean urinary flow rates had increased (p less than 0.05) and residual volume had decreased (p = 0.017) in the alfuzosin group, although the two groups were broadly similar with respect to increase in peak flow rate. The overall incidence of adverse events was similar in the two groups, which led to the withdrawal of 10.8% and 9.0% of patients, respectively.
Level of Study	2
Reference	4. Buzelin JM, Roth S, Geffriaud-Ricouard C, et al. Efficacy and safety of sustained-release alfuzosin 5 mg in patients with benign prostatic hyperplasia. ALGEBI Study Group. Eur Urol 1997;31:190-8.
Study type	Randomized, placebo-controlled trial
Patients	390 patients
Purpose of Study	To assess the efficacy and safety of a sustained-release (SR) formulation of alfuzosin, a selective alpha(1)-blocker, in patients with symptomatic benign prostatic hyperplasia (BPH)
Study Results	SR-alfuzosin significantly improved urinary symptoms versus placebo assessed using the I-PSS (-31 vs. -18%, p = 0.007) and Boyarsky (-30 vs. -16%, p < 0.001) scores, with a direct correlation between both scores. Maximum flow rate increased significantly with SR-alfuzosin (+2.4 ml/s, i.e. +29%) compared with placebo (+1.1 ml/s, i.e. +14%, p = 0.006). Residual urine was also significantly reduced with SR-alfuzosin. Overall, SR-alfuzosin was as well tolerated as placebo. Nine patients dropped out for adverse events with SR-alfuzosin (4.6%) and 14 (7.1%) with placebo. The incidence of vasodilation-related events (dizziness, postural symptoms, headache) with SR-alfuzosin (3.1%) was similar to that of placebo (3.6%). No first-dose effect was observed compared with placebo. The reduction in supine blood pressure with SR-alfuzosin was minor (< or = 5 mmHg), both in normotensive and hypertensive patients.
Level of Study	2
Reference	5. van Kerrebroeck P, Jardin A, Laval KU, et al. Efficacy and safety of a new prolonged release formulation of alfuzosin 10 mg once daily versus alfuzosin 2.5 mg thrice daily and placebo in patients with symptomatic benign prostatic hyperplasia. ALFORTI Study Group. Eur Urol 2000;37:306-13.

Study type	Randomized, placebo-controlled trial
Patients	447 patients
Purpose of Study	To assess the efficacy and safety of a new prolonged release formulation of the uroselective alpha (1)-blocker alfuzosin for a once-daily dosing regimen in patients with lower urinary tract symptoms (LUTS) suggestive of symptomatic benign prostatic hyperplasia (BPH)
Study Results	Both alfuzosin formulations significantly improved urinary symptoms versus placebo assessed using the International Prostate Symptom Score (alfuzosin 10 mg once daily: -6.9; alfuzosin 2.5 mg thrice daily: -6.4; placebo: -4.9, p = 0.005). Peak flow rate increased significantly with alfuzosin 10 mg once daily (+2.3 ml/s, p = 0.03 vs. placebo) and with alfuzosin 2.5 mg thrice daily (+3.2 ml/s, p<0.0001 vs. placebo) compared to placebo (+1.4 ml/s). Overall both formulations of alfuzosin were well tolerated in comparison with placebo. In addition, vasodilatory adverse events appeared to be less frequent with the once daily than the thrice daily formulation (6.3 vs. 9.4%, respectively). No first-day effect was reported with alfuzosin once daily and the effect on blood pressure did not differ from those observed in placebo, both in normotensive and hypertensive patients. No specific sexual dysfunction including ejaculation disorder was reported in the alfuzosin 10 mg once-daily group.
Level of Study	2
Reference	6. MacDonald R, Wilt TJ. Alfuzosin for treatment of lower urinary tract symptoms compatible with benign prostatic hyperplasia: a systematic review of efficacy and adverse effects. Urology 2005;66:780-8.
Study type	Systematic review
Patients	11 studies, 3,901 patients
Purpose of Study	To evaluate the efficacy and adverse effects of alfuzosin for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia (BPH)
Study Results	The search strategy identified 11 trials involving 3,901 men with a mean age of 64 years. Eight trials were placebo-controlled studies, two were alfuzosin versus alternative alpha-blockers, and one was alfuzosin versus finasteride and combination alfuzosin/finasteride therapy. The study durations were short term, 4 to 26 weeks. The mean baseline symptom scores and peak urinary flow rates were indicative of moderate BPH. Alfuzosin (7.5 or 10 mg) improved lower urinary tract symptoms assessed by the International Prostate Symptom Score compared with placebo. The mean absolute change from baseline was -5.4 points for alfuzosin compared with -3.6 points for placebo, a weighted mean difference of 1.8 points (three studies). Alfuzosin increased the peak urinary flow more than did placebo, although the improvement varied across the eight studies. Symptom and flow improvements were generally comparable to that with combination therapy and with other alpha1-blockers. Alfuzosin had good short-term tolerability, and the numbers of study withdrawals were comparable to those with placebo and controls. Efficacy and short-term safety were similar across the various (immediate-release, sustained, and once-daily) formulations.
Level of Study	1
Reference	7. Kirby RS, Andersen M, Gratzke P, et al. A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. BJU Int 2001;87:192-200.

Study type	Randomized, placebo-controlled trial
Patients	795 patients
Purpose of Study	To report an integrated analysis of two previous studies fully characterizing the clinical utility of the controlled-release gastrointestinal therapeutic system (GITS) formulation of doxazosin in the treatment of benign prostatic hyperplasia (BPH)
Study Results	Both doxazosin GITS and doxazosin-S significantly improved the symptoms of BPH, as shown by a 45% reduction for each in total IPSS from baseline to final visit, compared with a 34% reduction in patients on placebo. Doxazosin GITS and doxazosin-S produced comparable improvements in Qmax that were significantly greater than with placebo, with a greater improvement sooner after treatment with doxazosin GITS than with doxazosin-S. Nearly half of the patients on doxazosin GITS had symptom relief at the 4-mg starting dose. A similar number of patients in both doxazosin groups were titrated to the maximum dose. Secondary outcomes were consistent with the primary effects. Both doxazosin GITS and doxazosin-S produced significant improvements in sexual function according to IIEF scores among those with dysfunction at baseline. The overall incidence of adverse events was similar among patients treated with doxazosin GITS and placebo, and slightly lower than those on doxazosin-S. There was no apparent difference in the type of adverse events reported for the two formulations of doxazosin, although most adverse events were reported at a lower frequency with doxazosin GITS.
Level of Study	2
Reference	8. Chapple CR, Wyndaele JJ, Nordling J, et al. Tamsulosin, the first prostate-selective alpha 1A-adrenoceptor antagonist. A meta-analysis of two randomised, placebo-controlled, multicentre studies in patients with benign prostatic obstruction (symptomatic BPH). European Tamsulosin Study Group. Eur Urol 1996;29:155-67.
Study type	Meta-analysis
Patients	2 studies, 575 patients
Purpose of Study	To evaluate the efficacy and safety of modified-release tamsulosin 0.4 mg once daily compared with placebo in patients with benign prostatic enlargement, lower urinary tract symptoms and prostatic obstruction (symptomatic BPH)
Study Results	Maximum urinary flow rate improved to a greater extent in the tamsulosin group (1.6 ml/s, 16%) than the placebo group (0.6 ml/s, 6%) ($p = 0.002$). Total Boyarsky symptom score also improved to a greater extent in the tamsulosin group (3.3 points, 35.1% reduction) than the placebo group (2.4 points, 25.5% reduction) ($p = 0.002$). Significantly more tamsulosin patients (66%) than placebo patients (49%) had a > or = 25% decrease in total symptom score at endpoint ($p < 0.001$). Twelve weeks of treatment with tamsulosin also produced significant improvements in average urinary flow rate ($p = 0.005$) and voiding or "obstructive" ($p = 0.008$) and storage or "irritative' ($p = 0.017$) symptom scores. The incidence of drug-related adverse events was comparable for the tamsulosin and placebo groups (13 and 12% respectively, $p = 0.802$). The same applies to the incidence of adverse events commonly attributed to alpha 1-adrenoceptor antagonists, such as dizziness, headache, postural hypotension, syncope, asthenia, somnolence and rhinitis. There were no clinically significant changes in blood pressure or pulse rate in tamsulosin patients compared with placebo patients both in hypertensive and normotensive BPH patients.
Level of Study	1
Reference	9. Lepor H. Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. Tamsulosin Investigator Group. Urology 1998;51:892-900.

Study type	Randomized, placebo-controlled trial
Patients	756 patients
Purpose of Study	To evaluate the efficacy and safety of two once-daily doses of tamsulosin, the first selective alpha1A-antagonist studied in clinical trials
Study Results	Statistically significant improvements in all efficacy parameters were observed in tamsulosin-treated compared with placebo-treated patients. Additionally, the 0.4-mg/day dose demonstrated a rapid onset of action (4 to 8 hours) based on Qmax after the first dose of double-blind medication. A review of the safety parameters demonstrated excellent tolerance at 1 week after the initial 0.4-mg/day dose and continued tolerance during the additional 12 weeks of 0.4- and 0.8-mg/day dosing. The incidence of positive orthostatic test results in the tamsulosin groups was comparable to that observed in the placebo group. Adverse events were comparable in the 0.4-mg/day tamsulosin and placebo groups and were somewhat higher in the 0.8-mg/day tamsulosin group.
Level of Study	2
Reference	10. Wilt TJ, Mac Donold R, Rutks I. Tamsulosin for benign prostatic hyperplasia. Cochrane Database Syst Rev 2003;(1):CD002081.
Study type	Systematic review
Patients	14 studies, 4,122 patients
Purpose of Study	To assesse the effects of tamsulosin in the treatment of lower urinary tract symptoms (LUTS) compatible with BPH
Study Results	Fourteen studies involving 4,122 subjects met inclusion criteria. Study duration ranged from 4-26 weeks, and no placebo-controlled study lasted longer than 13 weeks. The mean age of subjects was 64 years. Baseline symptom scores and urine flow rates demonstrated that men had moderate LUTS. Tamsulosin improved symptoms and peak urine flow relative to placebo. The weighted mean differences (WMD) for mean change from baseline for the Boyarsky symptom score for 0.4 mg and 0.8 mg doses of tamsulosin relative to placebo were -1.1 points (95% CI = -1.49, -0.72; 12% improvement) and -1.6 points (95% CI = -2.3, -1.0; 16% improvement), respectively. The WMD for mean change from baseline in peak urine flow were 1.1 mL/sec (95% CI = 0.59, 1.51) and 1.1 mL/sec (95% CI= 0.65, 1.48) for 0.4 mg and 0.8 mg, respectively. Tamsulosin (0.2 mg-0.4 mg) was as effective as other alpha antagonists and the phytotherapeutic agent Permixon in improving symptoms and flow rates though the doses of all alpha-antagonists studied may not have been optimal. Discontinuations from treatment for any reason and discontinuations "due to adverse events" were similar in the low dose tamsulosin (0.2 mg) and placebo groups but increased to 16% in trials utilizing a 0.8 mg dose of tamsulosin. Low dose tamsulosin was generally well tolerated although not all the trials reported specific adverse events. The most frequently reported adverse events that were significantly greater than placebo included dizziness, rhinitis and abnormal ejaculation. Adverse effects increased markedly as tamsulosin dosing increased, and were reported in 75% of men receiving the 0.8 mg dose. Men receiving a 0.2 mg dose tamsulosin were less likely to discontinue treatment compared to men receiving terazosin.
Level of Study	1

Reference	11. Brawer MK, Adams G, Epstein H. Terazosin in the treatment of benign prostatic hyperplasia. Terazosin Benign Prostatic Hyperplasia Study Group. Arch Fam Med 1993;2:929-35.
Study type	Randomized, placebo-controlled trial
Patients	160 patients
Purpose of Study	To evaluate the efficacy and tolerability of terazosin, a long-acting selective alpha 1-receptor antagonist, in patients with benign prostatic hyperplasia
Study Results	Terazosin-treated patients had decreases in Boyarsky obstructive, irritative, and total scores of 3.3 (52%), 1.3 (29%), and 4.6 (42%), respectively, compared with decreases of 0.7 (12%), 0.4 (9%), and 1.1 (11%), respectively, in the placebo group (P < .05). Peak urine flow increased by a mean of 2.6 mL/s (30%) in terazosin-treated patients and 1.2 mL/s (14%) in placebo-treated patients (P < or = .05). Adverse events that differed significantly in the two groups were dizziness (19% in the terazosin group vs 5% in the placebo group) and urinary tract infection (1% in the terazosin group vs 10% in the placebo group).
Level of Study	2
Reference	12. Roehrborn CG, Oesterling JE, Auerbach S, et al. The Hytrin Community Assessment Trial study: a one-year study of terazosin versus placebo in the treatment of men with symptomatic benign prostatic hyperplasia. HYCAT Investigator Group. Urology 1996;47:159-68.
Study type	Randomized, placebo-controlled trial
Patients	2,084 patients
Purpose of Study	To determine the clinical effectiveness and safety of alpha (1)-blockade therapy versus placebo in the treatment of men with moderate to severe symptoms of prostatism in a community-based population under usual care conditions
Study Results	AUA-SS (0 to 35 point scale) improved from a baseline mean of 20.1 points by 37.8% during terazosin (n=976) and by 18.4% during placebo (n=973) treatment (P<0.001). Similarly, statistically superior improvements were observed in regard to the AUA-BS, BII, and the QQL score in the terazosin-treated patients. Peak urinary flow rate improved from a baseline of 9.6 mL/s (both regional treatment groups) by 2.2 mL/s in the terazosin group (n=137) and by 0.7 mL/s in the placebo group (n=140) (P< or = 0.05). Treatment failure occurred in 11.2% of terazosin- and 25.4% of placebo-treated patients (P<0.001; Kaplan-Meier adjusted withdrawal rates of 365 days). Withdrawal from study drug treatment due to adverse events occurred in 19.7% of terazosin- and 15.2% of placebo-treated patients (P<0.001).
Level of Study	2
Reference	13. Wilt TJ, Howe RW, Rutks I, et al. Terazosin for benign prostatic hyperplasia. Cochrane Database Syst Rev 2002;(4):CD003851.
Study type	Systematic review
Patients	17 studies, 5,151 patients

Purpose of Study	To evaluate the effectiveness and adverse effects of the alpha-blocker, terazosin, for treatment of urinary symptoms associated with BPO
Study Results	17 studies involving 5,151 subjects met inclusion criteria (placebo-controlled (10); alpha-blockers (7); finasteride alone or in combination with terazosin as well as placebo (1); microwave therapy (TUMT) (1). Study duration ranged from 4-52 weeks. Mean age was 65 years and 82% of men were white. Baseline urologic symptom scale scores and flow rates demonstrated that men had moderate BPO. Efficacy outcomes were rarely reported in a fashion that allowed for data pooling but indicated that terazosin improved symptom scores and flow rates more than placebo or finasteride and similarly to other alpha antagonists. The pooled mean percentage improvements for the Boyarsky symptom score was 37% for terazosin versus 15% for placebo (n=4 studies). The mean percentage improvement for the American Urological Association symptom score (AUA) was 38% compared to 17% and 20% for placebo and finasteride, respectively (n = 2 studies). The pooled mean improvement in the International Prostate Symptom Score (IPSS) (40%) was similar to tamsulosin (43%). Peak urine flow rates improved greater with terazosin (22%), than placebo (11%) and finasteride (15%) but did not differ significantly from the other alpha-blockers. The percentage of men discontinuing terazosin was comparable to men receiving placebo and finasteride but was greater then with other alpha-antagonists. Adverse effects were greater than placebo and included dizziness, asthenia, headache and postural hypotension.
Level of Study	1
Reference	14. Michel MC, Mehlburger L, Bressel HU, et al. Comparison of tamsulosin efficacy in subgroups of patients with lower urinary tract symptoms. Prostate Cancer Prost Dis 1998;1:332-5.
Study type	Open-label, observational study (no control group)
Patients	19,365 patients
Purpose of Study	To compare treatment efficacy in subgroups of patients with the a1-blocker tamsulosin
Study Results	In a comparison of patients aged <61, 61±70 and >70 y thepretreatment IPSS increased with age in both studies (Table 1). However, the treatment-associated reduction of the IPSS was very similar in all three age groups with a mean reduction of _9 points corresponding to _50% (Table 1). The pretreatment Qmax decreased with age in both studies (Table 1). While the tamsulosin-induced absolute increases of Qmax were slightly smaller in the oldest compared to the youngest age group (4.3_0.2 vs 5.1_0.2 ml/s and 4.3_0.1 vs 4.8_0.1 ml/s in studies 1 and 2, respectively; P<0.05), the relative increases of Qmax were similar in all age groups, that is _40% (Table 1). To study treatment effects in relation to disease severity, patients were stratified according to their pretreatment IPSS (0±7, 8±19 and 20±35, Table 2), Qmax (<10, 10± 15 and >15 ml/s, Table 2) and post-voiding residual urine (<100 and _100 ml, Table 2). Patients with the most severe symptoms benefited at least as much from tamsulosin treatment as those with mild or moderate symptoms and, if anything, had even greater improvements (Table 2). Even more importantly 42% and 50% of patients had an IPSS _20 and a Qmax<10 ml/s prior to treatment, but only 5% and 15%, respectively, remained in that category after four weeks of tamsulosin treatment (Figure 1). Among patients with _100 ml residual urine before treatment only 15% remained in that group after four weeks of treatment, while all others dropped to <100 ml residual urine, and 41% of patients had values of <50 ml.
Level of Study	3

Reference	15. Nickel JC, Sander S, Moon TD. A meta-analysis of the vascular-related safety profile and efficacy of a-adrenergic blockers for symptoms related to benign prostatic hyperplasia. Int J Clin Pract 2008;62:1547-59.
Study type	Meta-analysis
Patients	30 studies, 1,053 patients
Purpose of Study	To evaluate the safety profile and efficacy of alpha1-adrenergic receptor blockers (A1Bs) currently prescribed for benign prostatic hyperplasia (BPH)
Study Results	Of 2389 potential citations, 25 were usable for evaluation of safety data, 26 for efficacy. A1B use was associated with a statistically significant increase in the odds of developing a vascular-related event [odds ratio (OR) 2.54; 95% confidence interval (CI): 2.00-3.24; $p < 0.0001$]. The odds of developing a vascular-related adverse event were: alfuzosin, OR 1.66, 95% CI: 1.17-2.36; terazosin, OR 3.71, 95% CI: 2.48-5.53; doxazosin, OR 3.32, 95% CI: 2.10-5.23 and tamsulosin, OR 1.42, 95% CI: 0.99-2.05. A1Bs increased Q(max) by 1.32 ml/min (95% CI: 1.07-1.57) compared with placebo. Difference from placebo in American Urological Association symptom index/ International Prostate Symptom Score was -1.92 points (95% CI: -2.71 to -1.14).
Level of Study	1
Reference	16. Barendrecht MM, Koopmans RP, de la Rosette JJ, et al. Treatment for lower urinary tract symptoms suggestive of benign prostatic hyperplasia: the cardiovascular system. BJU Int 2005;95(Suppl.4):19-28.
Study type	Systematic review
Patients	Not specified in detail
Purpose of Study	review the physiological basis of cardiovascular side-effects of α1-AR antagonists, identify risk factors for these side-effects, and describe their interaction with specific drugs
Study Results	α1-AR antagonists are a reasonably well-tolerated drug class, but cardiovascular side-effects can occur, and these can lead to serious morbidity such as falls and fractures. Although the available data are not conclusive, it appears that patients with cardiovascular comorbidities and those concomitantly using antihypertensives and/or PDE-5 inhibitors might be particularly at risk. The safety of tamsulosin in such risk groups is better documented than that of other α1-AR antagonists, and this should affect drug choice in patients with LUTS/BPH belonging to any of these risk groups.
Level of Study	1
Reference	17. Chang DF, Campbell JR. Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg 2005;31:664-73.
Study type	Consecutive retrospective study/Prospective cohort study
Patients	511 patients/741 patients
Purpose of Study	To assess the incidence and possible causative factors of a newly recognized syndrome, the intraoperative floppy iris (IFIS)

Study Results	Three percent (16/511) of the patients in the retrospective study, representing 3.0% (25/706) of the total eyes, were taking tamsulosin (Flomax) for benign prostatic hypertrophy. The overall prevalence of IFIS was 2.0% (10/511 patients). The syndrome was noted intraoperatively in 63.0% (10/16) of the tamsulosin patients but in none of the 11 patients on other systemic alpha-1 blockers. In the prospective study of 900 consecutive cataract surgeries, the prevalence of IFIS was 2.2% (16/741 patients). Ninety-four percent (15/16) of the IFIS patients were taking or had taken systemic tamsulosin. Twenty-six patients (36 eyes) in the 2 studies had IFIS associated with systemic tamsulosin. Sphincterotomies and mechanical pupil stretching were ineffective in maintaining adequate pupil dilation in this surgical population.
Level of Study	2
Reference	18. Michel MC, Okutsu H, Noguchi Y, et al. In vivo studies on the effects of a1-adrenoceptor antagonists on pupil diameter and urethral tone in rabbits. Naunyn-Schmiedeberg's Arch Pharmacol 2006;372:346-53.
Study type	Animal study
Patients	
Purpose of Study	In study I we compared the potential of various α1-adrenoceptor antagonists to inhibit the mydriatic effects of phenylephrine in pentobarbital-anaesthetised rabbits. In study II we established effective doses of these drugs for antagonising the effects of phenylephrine on intraurethral pressure (IUP) in order to establish ratios for ocular effects vs. those for the desired effects in the lower urinary tract. In study III we determined the potential of these α1-adrenoceptor antagonists to affect pupil diameter in conscious rabbits.
Study Results	Study I: The mean basal pupil diameter in the vehicle group was 7.15±0.11 mm, and similar basal values were observed in all groups receiving the α1-adrenoceptor antagonists (no significant differences among all groups in a one-way ANOVA, data not shown). The first phenylephrine injection (30 μg/kg i.v.) transiently (for about 20 s) increased pupil diameter in the vehicle group by 0.96±0.13 mm, and similar dilatations were observed in all groups receiving the α1 adrenoceptor antagonists (no significant differences among all groups in a one-way ANOVA, data not shown). Four additional consecutive phenylephrine injections caused roughly similar pupil dilatation . On the other hand, alfuzosin (30 –1,000 μg/kg), doxazosin (30 –1,000 μg/kg), naftopidil (300 –10,000 μg/kg), prazosin (10 –300 μg/kg), tamsulosin (1–30 μg/kg) and terazosin (30 –1,000 μg/kg) dose-dependently inhibited phenylephrine-induced pupil dilatation without affecting the duration of the mydriatic response in a relevant manner. study II: The mean basal IUP in the vehicle group was 21.9±2.8 cmH2O, and similar basal values were observed in all groups receiving the α1-adrenoceptor antagonists (no significant differences among all groups in a one-way ANOVA, data not shown). The first phenylephrine injection (30 μg/kg i.v.) transiently (for about 70 s) increased IUP in the vehicle group by 43.1±5.7 cm H2O, and similar elevations were observed in all groups receiving the α1-adrenoceptor antagonists (no significant differences among all groups in a one-way ANOVA, data not shown). Three additional consecutive phenylephrine injections caused roughly similar IUP elevation. On the other hand, alfuzosin (30 –300 μg/kg), doxazosin (30 –300 μg/kg), naftopidil (300–3,000 μg/kg), prazosin (10–100 μg/kg), tamsulosin (1–10 μg/kg) and terazosin (30–300 μg/kg) dosedependently inhibited phenylephrine-induced IUP elevation without affecting the duration of the response in a relevant manner. A comparison of the ED50 values for inhibition of pupil dilatation and IUP elevation demonstrated that each antagonist required similar doses for inhibition of the two responses.

	Study III: The mean basal pupil diameter in the vehicle group was 6.73±0.27 mm, and similar basal values were observed in all groups receiving the α1-adrenoceptor antagonists (no significant differences among all groups in a one-way ANOVA, data not shown). The pupil size remained relatively stable over the entire 8-h observation period in the vehicle-treated group. All α1-adrenoceptor antagonists tested dose-dependently reduced pupil size with maximum miotic effects after 15 min, except for terazosin where maximum effects were observed after 30 min. Of note, the lowest tested antagonist doses in this study corresponded to or even exceeded the doses that caused almost maximum inhibition of phenylephrineinduced pupil dilatation except for naftopidil ;nevertheless, these doses failed to cause statistically significant miosis except for terazosin, and for most drugs only 30- to 100-fold higher doses (3-fold higher for naftopidil) caused detectable miosis.
Level of Study	4
Reference	19. van Dijk MM, de la Rosette JJ, Michel MC. Effects of a1-adrenoceptor antagonists on male sexual function. Drugs 2006;66:287-301.
Study type	Systematic review
Patients	Not specified in detail
Purpose of Study	To consider methodological issues in the analysis of adverse effects on sexual function associated with the use of α-blockers, and then summarize the effects of individual α-blockers
Study Results	Numerous studies have reported on possible adverse effects of α-blocker treatment on sexual function. Adverse α-blocker effects on sexual desire, erectile function, ejaculatory function and global sexual function occur in few patients only, and in some cases even improved functions have been reported. In this regard, it should be considered that the overwhelming majority of findings come from BPH patients, that is a condition with major effects on quality of life. When α-blockers improve BPH symptoms, associated improvements of sexual function may reflect a generally improved perception of wellbeing. Therefore, caution needs to be applied when extrapolating findings from BPH to, for example, hypertensive patients, who have not been studied extensively in this regard. There appears to be little difference between α-blockers with regard to effects on sexual function. A notable exception the effect of tamsulosin on ejaculatory function, now proposed to be (relative) anejaculation rather than retrograde ejaculation. While adverse effects of tamsulosin on ejaculatory function have been well documented, the magnitude of differences with other α-blockers is insufficient to be detectable as statistically significant unless very large patient numbers are compared, and the incidence of abnormal ejaculations in OLS is low. Therefore, the possibility of abnormal ejaculation with tamsulosin must be weighed against the unparalleled cardiovascular safety record of this agent when choosing the most appropriate α-blocker for an individual patient.
Level of Study	1
Reference	20. Kawabe K, Yoshida M, Homma Y; Silodosin Clinical Study Group. Silodosin, a new a1A-adrenoceptorselective antagonist for treating benign prostatic hyperplasia: a results of a phase III randomised, placebo-controlled, double-blind study in Japanese men. BJU Int 2006;98:1019-24.
Study type	Randomized, placebo-controlled trial

Patients	457 patients
Purpose of Study	To verify the efficacy and safety of the new alpha1A-adrenoceptor-selective antagonist silodosin compared with tamsulosin and placebo in patients with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH)
Study Results	In all, 457 patients were randomized (silodosin 176, tamsulosin 192 and placebo 89). The change in the total IPSS from baseline in the silodosin, tamsulosin and placebo groups was -8.3, -6.8 and -5.3, respectively. There was a significant decrease in the IPSS vs placebo in the silodosin group from 1 week. In the early-stage comparison, silodosin showed a significant decrease in IPSS vs tamsulosin at 2 weeks. The change in QoL from baseline was -1.7, -1.4 and -1.1 in the silodosin, tamsulosin and placebo groups, respectively; silodosin showed a significant improvement in the QoL score vs placebo. In the subgroup of patients with severe symptoms (IPSS > or = 20) silodosin also gave a significantly better improvement than placebo (-12.4 vs -8.7). The incidence rates of adverse events and drug-related adverse events were, respectively, 88.6%, 82.3% and 71.6% and 69.7%, 47.4% and 36.4%, respectively. The most common adverse event in the silodosin group was abnormal ejaculation, which occurred more often in the silodosin than in the tamsulosin group (22.3% vs 1.6%). However, only five men (2.9%) discontinued treatment for abnormal ejaculation.
Level of Study	2
Reference	21. Garimella PS, Fink HA, Macdonald R, et al. Naftopidil for the treatment of lower urinary tract symptoms compatible with benign prostatic hyperplasia. Cochrane Database Syst Rev 2009;(4):CD007360.
Study type	Systematic review
Patients	8 studies, 744 patients
Purpose of Study	To evaluate the efficacy and adverse effects of naftopidil, a selective alpha-1d oral alpha-blocking agent for the treatment of LUTS associated with BPH
Study Results	Eight trials were eligible (N = 744 participants). All trials were conducted in Japan. Study duration ranged from 4 to 17 weeks. The mean age of participants was 68 years; pretreatment mean IPSS = 17.8 and mean peak urine flow (Qmax) = 9.5 mL/s (milliliters/second). No trials compared naftopidil to placebo. In 5 trials (N = 419), naftopidil in doses of 25 to 75 mg/d (milligrams/day) showed a mean IPSS improvement similar to low-dose tamsulosin (0.2 mg/d) (8.4 versus 8.9 points). Compared to a phytotherapy preparation (eviprostat), naftopidil significantly improved total IPSS (-5.9 versus 0.4; P < 0.0002). In one trial, the addition of anticholinergic drugs (oxybutynin or propiverine hydrochloride) to naftopidil did not offer any significant improvement for IPSS or Qmax in comparison to treatment with naftopidil alone. Although IPSS did not significantly differ between high- (75 mg/d) and low-dose (25 mg/d) naftopidil, high dose significantly improved Qmax compared to low dose (1.2 mL/s versus 0.2 mL/s). Adverse events reported were few, mild and similar to those seen with 0.2 mg/d tamsulosin.
Level of Study	1
Reference	22. Ding H, Du W, Hou ZZ, et al. Silodosin is effective for treatment of LUTS in men with BPH: a systematic review. Asian J Androl 2013;15:121-8.

Study type	Systematic review and Meta-analysis
Patients	4 studies, 2,504 patients
Purpose of Study	To review the evidence on the efficacy and safety of silodosin treatments on lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH) from randomized controlled trials
Study Results	At the follow-up end points, the pooled results showed that the change from baseline for the silodosin group was significantly higher than the placebo group for the IPSS, QoL score and Q(max)(mean difference (MD)=-2.78, P<0.00001; MD=-0.42, P=0.004; MD=1.17, P<0.00001, respectively) and patients felt more satisfied with QoL related to urinary symptoms in the silodosin group than the placebo group. Ejaculation disorder was the most commonly reported adverse effect. The pooled results also showed that the silodosin group was superior to the 0.2 mg tamsulosin group with respect to the IPSS and QoL score (IPSS: MD=-1.14, P=0.02; QoL score: MD=-0.26, P=0.02) and inferior to the 0.2 mg tamsulosin group with respect to Q(max) (MD=-0.85, P=0.01). In contrast, there was no significant difference in the incidence of ejaculation disorder and dizziness between the silodosin and 0.2 mg tamsulosin groups. The current meta-analysis suggested that silodosin is an effective therapy for LUTS in men with BPH and is not inferior to 0.2 mg tamsulosin.
Level of Study	1
Reference	23. Rittmaster RS, Norman RW, Thomas LN, et al. Evidence for atrophy and apoptosis in the prostates of men given finasteride. J Clin Endocrinol Metab 1996;81:814-9.
Study type	Randomized, placebo-controlled trial
Patients	26 patients
Purpose of Study	To determine the mechanism by which finasteride reduces prostate size
Study Results	The mean epithelial cell width in control prostates (mean +/- SEM, 21 +/- 0.7 microns) decreased with duration of treatment to 19 +/- 1 microns in group 1, 15 +/- 2 microns in group 2, and 8 +/- 0.3 microns in group 3. Mean duct width decreased from 135 +/- 6 microns in the control prostates to 128 +/- 10 microns in group 1, 103 +/- 3 microns in group 2, and 63 +/- 6 microns in group 3. To assess whether prostate cell death was occurring, sections were in situ end labeled for DNA breaks and immunostained for tissue transglutaminase (tTG), a marker of apoptosis (programmed cell death). The percentage of epithelial cells staining for DNA breaks was 0.4 +/- 0.2 in control prostates, 2.8 +/- 0.9 in group 1, 1.7 +/- 0.5 in group 2, and 0.7 +/- 0.3 microns in group 3. Anti-tTG staining of epithelial cells was graded on a scale of 0-4. In control prostates, 3 +/- 1% of the ducts were grade 3 or 4 (> 50% of epithelial cells staining). In finasteride-treated prostates, 2 +/- 2% of the prostates in group 1, 13 +/- 4% of the prostates in group 2, and 0.5 +/- 0.5% of the prostates in group 3 were grade 3-4. These results indicate that a progressive decrease in epithelial cell size and function occurs during the first several months in the prostates of men treated with finasteride.
Level of Study	2
Reference	24. Lepor H, Williford WO, Barry MJ, et al. The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. N Engl J Med 1996;335:533-9.

Study type	Randomized, placebo-controlled trial
Patients	1,229 patients
Purpose of Study	To compare the safety and efficacy of placebo, terazosin (10 mg daily), finasteride (5 mg daily), and the combination of both drugs in men with BPH
Study Results	The mean changes from base line in the symptom scores in the placebo, finasteride, terazosin, and combination-therapy groups at one year were decreases of 2.6, 3.2, 6.1, and 6.2 points, respectively (P<0.001 for the comparisons of both terazosin and combination therapy with finasteride and with placebo). The mean changes at one year in the peak urinary-flow rates were increases of 1.4, 1.6, 2.7, and 3.2 ml per second, respectively (P<0.001 for the comparisons of both terazosin and combination therapy with finasteride and with placebo). Finasteride had no more effect on either measure than placebo. In the placebo group, 1.6 percent of the men discontinued the study because of adverse effects, as did 4.8 to 7.8 percent of the men in the other three groups.
Level of Study	2
Reference	25. Kirby R, Roehrborn CG, Boyle P, et al; Prospective European Doxazosin and Combination Therapy Study Investigators. Efficacy and tolerability of doxazosin and finasteride, alone or in combination, in treatment of symptomatic benign prostatic hyperplasia: the Prospective European Doxazosin and Combination Therapy (PREDICT) trial. Urology 2003;61:119-26.
Study type	Randomized, placebo-controlled trial
Patients	1,095 patients
Purpose of Study	To evaluate the efficacy and tolerability of the selective alpha(1)-adrenergic antagonist doxazosin and the 5-alpha-reductase inhibitor finasteride, alone and in combination, for the symptomatic treatment of benign prostatic hyperplasia
Study Results	An intent-to-treat analysis of 1007 men showed doxazosin and doxazosin plus finasteride combination therapy produced statistically significant improvements in total IPSS and Qmax compared with placebo and finasteride alone (P<0.05). Finasteride alone was not significantly different statistically from placebo with respect to total IPSS and Qmax. All treatments were generally well tolerated.
Level of Study	2
Reference	26. Andersen JT, Ekman P, Wolf H, et al. Can finasteride reverse the progress of benign prostatic hyperplasia? A two-year placebo-controlled study. The Scandinavian BPH Study Group. Urology 1995;46:631-7.
Study type	Randomized, placebo-controlled trial
Patients	707 patients
Purpose of Study	To study if placebo-induced improvement in men with symptomatic benign prostatic hyperplasia (BPH) is maintained over 2 years, and to study the efficacy and safety from intervention with finasteride 5 mg for 24 months

Study Results	In finasteride-treated patients the total symptom score improved throughout the study, with a significant difference between the two groups at 24 months (P < or = 0.01), whereas in placebo-treated patients, there was an initial improvement in the symptom score but no change from baseline at 24 months. The maximum urinary flow rate decreased in the placebo group, but improved in the finasteride group, resulting in a between-group difference of 1.8 mL/s at 24 months (P < or = 0.01). The mean change in prostate volume was +12% in the placebo group versus -19% in the finasteride-treated group (P < 0.01). Finasteride was generally well tolerated throughout the 2-year study period.
Level of Study	2
Reference	27. Nickel JC, Fradet Y, Boake RC, et al. Efficacy and safety of finasteride therapy for benign prostatic hyperplasia: results of a 2-year randomised controlled trial (the PROSPECT study). PROscar Safety Plus Efficacy Canadian Two year Study. CMAJ 1996;155:1251-9.
Study type	Randomized, placebo-controlled trial
Patients	613 patients
Purpose of Study	To evaluate the efficacy and safety of 2 years' treatment of moderate benign prostatic hyperplasia (BPH) with finasteride
Study Results	In the efficacy analyses the mean BPH symptom scores decreased 2.1 points (from 15.8 to 13.7) in the finasteride group, as compared with a decrease of 0.7 points (from 16.6 to 15.9) in the placebo group (P < or = 0.01). The maximum urinary flow rate increased by a mean of 1.4 mL/s (from 11.1 to 12.5 mL/s) in the finasteride group, as compared with an increase of 0.3 mL/s (from 10.9 to 11.2 mL/s) in the placebo group (p < or = 0.01). The mean prostate volume decreased by 21% (from a mean volume of 44.1 cm3 at baseline) in the treatment group; it increased by 8.4% (from a mean volume of 45.8 cm3 at baseline) in the placebo group (p < or = 0.01). In the safety analysis, the proportion of patients who experienced any adverse event was similar in the two groups (81.0% in the treatment group and 81.2% in the placebo group). However, the incidence of adverse events related to sexual dysfunction were significantly higher in the finasteride group than in the placebo group (ejaculation disorder 7.7% v. 1.7% and impotence 15.8% v. 6.3%; p < or = 0.01 for both parameters).
Level of Study	2
Reference	28. McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. N Engl J Med 1998;338:557-63.
Study type	Randomized, placebo-controlled trial
Patients	3,040 patients
Purpose of Study	To evaluate the extent to which the benefit is sustained and whether finasteride reduces the incidence of related events, including the need for surgery and the development of acute urinary retention

Study Results	During the four-year study period, 152 of the 1,503 men in the placebo group (10 percent) and 69 of the 1,513 men in the finasteride group (5 percent) underwent surgery for benign prostatic hyperplasia (reduction in risk with finasteride, 55 percent; 95 percent confidence interval, 41 to 65 percent). Acute urinary retention developed in 99 men (7 percent) in the placebo group and 42 men (3 percent) in the finasteride group (reduction in risk with finasteride, 57 percent; 95 percent confidence interval, 40 to 69 percent). Among the men who completed the study, the mean decreases in the symptom score were 3.3 in the finasteride group and 1.3 in the placebo group (P<0.001). Treatment with finasteride also significantly improved urinary flow rates and reduced prostate volume (P<0.001).
Level of Study	2
Reference	29. Marberger MJ, on behalf of the PROWESS Study Group. Long-term effects of finasteride in patients with benign prostatic hyperplasia: a double-blind, placebo-controlled, multicenter study. Urology 1998;51:677-86.
Study type	Randomized, placebo-controlled trial
Patients	3,270 patients
Purpose of Study	To compare the long-term effects of finasteride (5 mg/day) and placebo in patients with moderate symptoms of benign prostatic hyperplasia (BPH)
Study Results	Of the 3,270 men enrolled, 3,168 contributed data to the safety analysis, and 2,902 to the efficacy evaluation. Significantly greater improvement with finasteride compared to placebo was observed at 12 and 24 months for total symptom score (mean -2.9 versus -1.9 at 12 months, P < or =0.001; -3.2 versus -1.5 at 24 months, P < or =0.001), obstructive symptom score (mean -1.9 versus -1.3 at 12 months, P < or =0.001; -2.1 versus -1.1 at 24 months, P < or =0.001), maximal urinary flow rate (mean +1.2 versus +0.6 mL/s at 12 months, P = 0.010; +1.5 versus +0.7 mL/s at 24 months, P = 0.002), and prostate volume (mean -14.2 versus +5.4% at 12 months, P < or =0.01; -15.3 versus +8.9% at 24 months, P < or =0.001). Greater improvements in placebo-adjusted total symptom score occurred in men with large prostates than in men with small prostates (mean -2.4 versus -1.1 at 12 months; -3.2 versus -1.3 at 24 months, placebo-adjusted data, P = 0.053). Fifteen of 1,450 men (1.0%) in the finasteride group experienced an acute urinary retention event, compared with 37 of 1,452 (2.5%) in the placebo group, and the corresponding figures for surgery were 51 of 1,450 (3.5%) and 86 of 1,452 (5.9%), respectively. The hazard rate for occurrence, computed using the log-rank statistic, decreased by 57% for acute urinary retention and by 40% for surgery accompanied by finasteride therapy compared to placebo.
Level of Study	2
Reference	30. McConnell JD, Roehrborn CG, Bautista O, et al; Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387-98.
Study type	Randomized, placebo-controlled trial
Patients	3,047 patients
Purpose of Study	Benign prostatic hyperplasia is commonly treated with alpha-adrenergic-receptor antagonists (alpha-blockers) or 5alpha-reductase inhibitors. The long-term effect of these drugs, singly or combined, on the risk of clinical progression is unknown.

Study Results	The risk of overall clinical progression--defined as an increase above base line of at least 4 points in the American Urological Association symptom score, acute urinary retention, urinary incontinence, renal insufficiency, or recurrent urinary tract infection--was significantly reduced by doxazosin (39 percent risk reduction, P<0.001) and finasteride (34 percent risk reduction, P=0.002), as compared with placebo. The reduction in risk associated with combination therapy (66 percent for the comparison with placebo, P<0.001) was significantly greater than that associated with doxazosin (P<0.001) or finasteride (P<0.001) alone. The risks of acute urinary retention and the need for invasive therapy were significantly reduced by combination therapy (P<0.001) and finasteride (P<0.001) but not by doxazosin. Doxazosin (P<0.001), finasteride (P=0.001), and combination therapy (P<0.001) each resulted in significant improvement in symptom scores, with combination therapy being superior to both doxazosin (P=0.006) and finasteride (P<0.001) alone.
Level of Study	2
Reference	31. Roehrborn CG, Boyle P, Nickel JC, et al; ARIA3001 ARIA3002 and ARIA3003 Study Investigators. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. Urology 2002;60:434-41.
Study type	Randomized, placebo-controlled trial
Patients	4,325 patients
Purpose of Study	To study the efficacy and safety of dutasteride, a dual inhibitor of the 5-alpha-reductase isoenzymes types I and II
Study Results	At 24 months, serum dihydrotestosterone was reduced from baseline by a mean of 90.2% (median -93.7%; P<0.001), and the total prostate and transition zone volumes were reduced by a mean of 25.7% and 20.4%, respectively (P<0.001). The symptom score was improved by as early as 3 months, with pooled significance from 6 months onward (P<0.001) and a reduction of 4.5 points (21.4%) at 24 months (P<0.001). The maximal flow rate improved significantly from 1 month (P<0.01), with an increase of 2.2 mL/s reported at 24 months (P<0.001). Hence, the risk reduction of acute urinary retention was 57% and the risk reduction of benign prostatic hyperplasia-related surgical intervention was 48% compared with placebo. The drug was well tolerated.
Level of Study	2
Reference	32. Roehrborn CG, Siami P, Barkin J, et al; CombAT Study Group. The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. J Urol 2008;179:616-21.
Study type	Randomized, parallel group trial
Patients	4,844 patients
Purpose of Study	To investigate whether combination therapy with dutasteride and tamsulosin is more effective than either monotherapy alone for improving symptoms and long-term outcomes in men with moderate to severe lower urinary tract symptoms and prostatic enlargement (30 cc or greater) (Preplanned 2-year analyses)

Study Results	Combination therapy resulted in significantly greater improvements in symptoms vs dutasteride from month 3 and tamsulosin from month 9, and in benign prostatic hyperplasia related health status from months 3 and 12, respectively. There was a significantly greater improvement from baseline in peak urinary flow for combination therapy vs dutasteride and tamsulosin monotherapies from month 6. There was a significant increase in drug related adverse events with combination therapy vs monotherapies, although most did not result in the cessation of therapy.
Level of Study	2
Reference	33. Roehrborn CG, Siami P, Barkin J, et al; CombAT Study Group. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombATstudy. Eur Urol 2010;57:123-31.
Study type	Randomized, parallel group trial
Patients	4,844 patients
Purpose of Study	To investigate whether combination therapy is more effective than either monotherapy in reducing the relative risk for acute urinary retention (AUR), BPH-related surgery, and BPH clinical progression over 4 yr in men at increased risk of progression
Study Results	Combination therapy was significantly superior to tamsulosin monotherapy but not dutasteride monotherapy at reducing the relative risk of AUR or BPH-related surgery. Combination therapy was also significantly superior to both monotherapies at reducing the relative risk of BPH clinical progression. Combination therapy provided significantly greater symptom benefit than either monotherapy at 4 yr. Safety and tolerability of combination therapy was consistent with previous experience with dutasteride and tamsulosin monotherapies, with the exception of an imbalance in the composite term of cardiac failure among the three study arms. The lack of placebo control is a study limitation.
Level of Study	2
Reference	34. Roehrborn CG, Siami P, Barkin J, et al; CombAT Study Group. The influence of baseline parameters on changes in International Prostate Symptom Score with dutasteride, tamsulosin, and combination therapy among men with symptomatic benign prostatic hyperplasia and enlarged prostate: 2-year data from the CombAT Study. Eur Urol 2009;55:461-71.
Study type	Randomized, parallel group trial
Patients	4,844 patients
Purpose of Study	To examine the influence of baseline parameters on changes in International Prostate Symptom Score (IPSS) and maximum urinary flow rate (Q(max)) in men with BPH receiving dutasteride, tamsulosin, or a combination of the two using 2-yr Combination of Avodart and Tamsulosin (CombAT) study data
Study Results	Combination therapy was more effective than either monotherapy after 24 mo in improving IPSS in all baseline subgroups, with benefit onset varying by baseline prostate volume. Combination therapy was also more effective in improving Q(max) versus tamsulosin in all subgroups and versus dutasteride in 10 of 18 subgroups. At 24 mo, dutasteride monotherapy resulted in significantly greater IPSS improvements versus tamsulosin in men with lower age, worse symptoms, worse QoL, less bother, higher BMI, greater Q(max), higher prostate volume, and higher PSA at baseline. Post hoc analyses, the lack of placebo control, and the exclusion of men with unsuccessful medical BPH treatment are study limitations.

Level of Study	2
Reference	35. Roehrborn CG. BPH progression: concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. BJU Int 2008;101(Suppl.3):17-21.
Study type	Systematic review
Patients	4 studies, 15,929 patients
Purpose of Study	To know effects of alpha-blocker, 5ARI and combination therapy on BPH progression
Study Results	In selected patients, combination of an alpha(1)-blocker and a 5alpha-reductase inhibitor is the most effective form of BPH medical therapy to reduce the risk of clinical progression and relieve LUTS. Monotherapy also significantly reduces the risk of BPH clinical progression, mainly through a reduction of LUTS deterioration for alpha(1)-blockers while 5alpha-reductase inhibitors also reduce the risk of AUR and need for BPH-related surgery. Enlarged prostate and high serum prostate-specific antigen levels have been consistently found to be good clinical predictors of AUR and BPH-related surgery in longitudinal population-based studies and placebo arms of controlled studies. High post-void residual urine (PVR) is also associated with an increased risk of LUTS deterioration and should thus be reconsidered in practice as a predictor of BPH progression. Conversely, baseline LUTS severity and low peak flow rate, initially identified as predictors of unfavourable outcomes in community setting, behave paradoxically in controlled trials, probably as a consequence of strict inclusion criteria and subsequent regression to the mean and glass ceiling effects. Lastly, there is increasing evidence that dynamic variables, such as LUTS and PVR worsening, and lack of symptomatic improvement with alpha(1)-blockers are important predictors of future LUTS/BPH-related events, allowing better identification and management of patients at risk of BPH progression.
Level of Study	1
Reference	36. Boyle P, Gould AL, Roehrborn CG. Prostate volume predicts outcome of treatment of benign prostatic hyperplasia with finasteride: meta-analysis of randomised clinical trials. Urology 1996;48:398-405.
Study type	Meta-analysis
Patients	6 studies, 2,601 patients
Purpose of Study	Six randomized clinical trials have compared at least 1 year of 5 mg finasteride to placebo in the treatment of clinical benign prostatic hyperplasia (BPH). The findings for the 2601 men in these trials provide an opportunity to investigate the heterogeneity of the effects seen in the individual studies and to identify pretreatment predictors of outcomes as expressed by symptoms or peak urinary flow rates.
Study Results	The effect of finasteride treatment on improvements in total symptom severity, frequency score, and peak urinary flow rate was consistent across all six trials and similar among men with similar prostate volumes at baseline. Symptom severity improved by 1.8 points (95% confidence interval [CI], 0.7 to 2.9) in men with prostate volumes less than 20 cc (n = 72), while the improvement was 2.8 points (95% CI, 2.1 to 3.5) for men with volumes greater than 60 cc (n = 272) on the Quasi-IPSS Scale (range 0 to 30). Similarly, improvements in peak urinary flow rate ranged from 0.89 mL/s (95% CI, -0.05 to 1.83) for men with prostate volumes less than 20 cc to 1.84 mL/s (95% CI, 1.37 to 2.30) in men with volumes greater than 60 cc. The difference in the magnitude of improvement between finasteride and placebo becomes significant (that is,

Study Results	no overlap in 95% CI) for men with a baseline prostate volume assessed by either transrectal ultrasonography or magnetic resonance imaging of greater than 40 cc, which encompasses approximately 50% of the entire population. Baseline prostate volume is a key predictor of treatment outcomes: approximately 80% of the variation in the treatment effects noted between studies could be attributed to differences in mean prostate volumes at baseline. Variation in entry criteria results in large differences in baseline symptom severity status, prostate volume, and consequently apparent inconsistencies in the overall outcomes of these trials.
Level of Study	1
Reference	37. Roehrborn CG, Boyle P, Bergner D, et al. Serum prostate-specific antigen and prostate volume predict long-term changes in symptoms and flow rate: results of a four-year, randomized trial comparing finasteride versus placebo. PLESS Study Group. Urol 1999;54:662-9.
Study type	Non-randomized controlled cohort/follow-up study
Patients	3,040 patients
Purpose of Study	To determine whether baseline prostate-specific antigen (PSA), in addition to prostate volume, is associated with long-term changes in symptoms and urinary flow rate.
Study Results	Baseline PSA and prostate volume are good predictors of long-term symptomatic and flow rate changes. Baseline PSA levels of 1.4 ng/mL or greater and enlarged prostate glands predict the best long-term response to finasteride compared with placebo.
Level of Study	3
Reference	38. Roehrborn CG, Lukkarinen O, Mark S, et al. Long-term sustained improvement in symptoms of benign protatic hyperplasia with the dual 5a-reductase inhibitor dutasteride: results of 4-year studies. BJU Int 2005;96:572-7.
Study type	Randomized, placebo-controlled trial
Patients	4,325 patients
Purpose of Study	To report additional analyses of efficacy over the initial 2 years and during a 2-year open-label extension of the three pivotal phase 3 studies in which dutasteride, a dual inhibitor of type 1 and 2 5alpha-reductase, was shown to be effective and well tolerated
Study Results	There was a clinically meaningful improvement in AUA-SI in patients on dutasteride in the double-blind phase, but not in those on placebo. At 48 months, patients on dutasteride in both study phases had greater improvements in AUA-SI score and individual question scores than those on dutasteride in the open-label phase only. The proportion of patients with severe symptoms declined in both study groups, although these changes were more profound in those receiving dutasteride for the 4-year duration of the study. In men with symptomatic benign prostatic hyperplasia, long-term (4-year) treatment with the dual isozyme 5alpha-reductase inhibitor dutasteride resulted in sustained and continued improvements in symptoms and flow rate. For 4 vs 2 years, longer dutasteride therapy resulted in greater symptom improvement.
Level of Study	2

Reference	39. Gittelman M, Ramsdell J, Young J, et al. Dutasteride improves objective and subjective disease measures in men with benign prostatic hyperplasia and modest or severe prostateenlargement. J Urol 2006;176:1045-50.
Study type	Randomized, placebo-controlled trial
Patients	4,325 patients
Purpose of Study	To determine whether the effect of dutasteride for benign prostatic hyperplasia is influenced by baseline prostate volume using data from 3 phase III clinical trials
Study Results	In patients treated with dutasteride throughout the study (dutasteride/dutasteride group) the mean reduction in prostate volume from baseline to month 48 was 30.3% in those with a baseline prostate volume of 30 to less than 40 cc and 26.2% in those with a prostate volume of 40 cc or greater. Mean improvements in peak urinary flow from baseline to month 48 were 2.7 ml per second regardless of baseline prostate volume. Improvements in the American Urological Association symptom index score were 6.3 in men with a prostate volume of 30 to less than 40 cc and 6.5 in those with a prostate volume of 40 cc or greater. No significant relationships between treatment effect and baseline prostate volume were observed for these parameters. In dutasteride/dutasteride treated patients the risk of acute urinary retention was decreased by 60% in those with a prostate volume of 30 to less than 40 cc and 55% in those with a prostate volume of 40 cc or greater vs values in placebo/dutasteride treated patients ($p = 0.036$ and <0.001, respectively). The corresponding values for benign prostatic hyperplasia related surgery were 27% and 48% ($p = 0.35$ and <0.001, respectively).
Level of Study	2
Reference	40. Naslund MJ, Miner M. A review of the clinical efficacy and safety of 5α-reductase inhibitors for the enlarged prostate. Clin Ther 2007;29:17-25.
Study type	Systematic review
Patients	Not specified in detail
Purpose of Study	To review the natural history of enlarged prostate and the data supporting management of this condition with alpha-blocker and 5ARI therapy, either as monotherapy or combination therapy, for symptomatic relief and a reduction in long-term disease progression
Study Results	Clinical trials of alpha-blockers in men with enlarged prostate have reported improvements in total symptom scores of 10% to 20% compared with placebo; however, these agents were not shown to reduce the risk of long-term complications or disease progression. Studies of the 5ARIs have reported significant reductions compared with placebo in the relative risk for AUR and enlarged prostate-related surgery, slowing of disease progression, and relief of symptoms. In studies of dutasteride, improvements in symptom scores were greater after 4 years of therapy compared with 2 years (-6.4 vs -4.3 points, respectively) and flow rates were better (2.6 vs 2.3 mL/sec). Six-year data for finasteride showed maintenance of the decreased risk for AUR and enlarged prostate-related surgery. Use of combination therapy with an alpha-blocker and a 5ARI may be of benefit in patients who require immediate relief of symptoms, with discontinuation of the alpha-blocker after several months of therapy. 5ARIs were generally well tolerated, with sexual dysfunction the most frequently reported adverse effect, although in only a small proportion of men (1-8%).
Level of Study	1

Reference	41. Chung BH, Hong SJ, Cho JS, Seong DH. Relationship between serum prostate-specific antigen and prostate volume in Korean men with benign prostatic hyperplasia: a multicentre study. BJU Int 2006;97:742-6.
Study type	Non-randomized controlled cohort/follow-up study
Patients	5,716 patients
Purpose of Study	To evaluate the relationship between prostate specific antigen (PSA) and prostate volume (PV) in Korean men, as PV is a key predictor of both disease progression and response to medical therapy in patients with benign prostatic hyperplasia (BPH), and PSA has been suggested as a proxy marker to estimate the total PV, mainly in Caucasians.
Study Results	The PSA-PV relationship in Korean men is similar to that in Caucasians, but Korean men have a slightly lower PSA level and a smaller PV than Caucasians. The approximate age-specific criteria for detecting Korean men with a PV of >40 mL were a PSA level of >1.3 ng/mL, >1.7 ng/mL and >2.0 ng/mL for men with BPH in their sixth, seventh and eighth decade, respectively.
Level of Study	3
Reference	42. Kaplan SA, Walmsley K, Te AE. Tolterodine extended release attenuates lower urinary tract symptoms in men with benign prostatic hyperplasia. J Urol 2005;174:2273-5.
Study type	Open label, prospective study
Patients	43 patients
Purpose of Study	To determine the efficacy and tolerability of tolterodine extended release (ER) in men with benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) in whom previous alpha-blocker therapy had failed
Study Results	A total of 39 men (91%) with a mean age of 61 years completed the 6-month trial. Mean 24-hour micturition frequency decreased from 9.8 to 6.3 voids and nocturia decreased from 4.1 to 2.9 episodes nightly. Significant changes in mean American Urological Association symptom scores (-6.1), the peak urinary flow rate (1.9 ml per second) and post-void residual volume (-22 ml) were also observed. Of the men 27 (63%) were potent at baseline and 29 (67%) were potent after 6 months of tolterodine ER treatment. Mean International Index of Erectile Function erectile function domain scores increased (6.9). Four men (9%) discontinued therapy because of intolerable dry mouth. There were no reports of urinary retention.
Level of Study	2
Reference	43. Höfner K, Burkart M, Jacob G, et al. Safety and efficacy of tolertodine extended release in men with overactive bladder symptoms and presumed non-obstructive benign prostatic hyperplasia. World J Urol 2007;25:627-33.
Study type	Prospective, observational non-interventional study
Patients	741 patients
Purpose of Study	To generate real-life efficacy and safety data in patients with presumed non-obstructive BPH (Q (max)>or= 15 ml/s) treated with tolterodine ER 4 mg/day for OAB symptoms, alone or added to unsuccessful alpha-blocker treatment of >or=6 weeks duration

Study Results	Mean PVR did not increase (25.4 +/- 26.5 vs. 29.3 +/- 30.9 ml at baseline). AUR requiring catheterization occurred in two patients, acute UTI in four patients. Median IPSS total scores decreased from 17 to 10, IPSS QoL scores from 4 to 2, OAB-q symptom bother scores from 50.0 to 22.5 and OAB-q HRQL scores increased from 59.2 to 81.6. In men with OAB symptoms and presumed non-obstructive BPH, tolterodine ER provided considerable symptomatic and QoL improvements with a low risk of AUR, acute UTI, or increased PVR.
Level of Study	2
Reference	44. Kaplan SA, Roehrborn CG, Chancellor M, et al. Extended-release tolterodine with or without tamsulosin in men with lower urinary tract symptoms and overactive bladder: effects on urinary symptoms assessed by the International Prostate Symptom Score. BJU Int 2008;102:1133-9.
Study type	Randomized, placebo-controlled trial
Patients	851 patients
Purpose of Study	To evaluate the efficacy of tolterodine extended-release (ER) plus tamsulosin on lower urinary tract symptoms (LUTS) as assessed by changes in the International Prostate Symptom Score (IPSS) in men who met symptom entry criteria for both overactive bladder (OAB) and benign prostatic hyperplasia (BPH) trials
Study Results	Patients receiving tolterodine ER + tamsulosin had significantly greater improvements than those taking placebo on IPSS storage subscale scores and scores for all three individual storage items included on the IPSS (urinary frequency, urgency, and nocturnal micturitions) by 12 weeks. Storage subscale and urgency scores were significantly improved vs placebo at 1 and 6 weeks, whereas frequency scores were significantly improved at 6 weeks. Changes in IPSS storage subscale and individual storage item scores in the tolterodine ER and tamsulosin monotherapy groups were not significantly different from placebo at most time points. IPSS voiding subscale scores and scores for three of four individual voiding items (sensation of incomplete emptying, intermittency, and weak stream) were significantly improved by 12 weeks for patients receiving tamsulosin monotherapy vs placebo. Voiding subscale and intermittency scores were significantly improved vs placebo at 1 week; weak stream scores were significantly improved at 1 and 6 weeks. The IPSS voiding subscale and individual voiding item scores in the tolterodine ER + tamsulosin and tolterodine ER groups were not significantly different from placebo at most time points.
Level of Study	2
Reference	45. Kaplan SA, Roehrborn CG, Dmochowski R, et al. Tolterodine extended release improves overactive bladder symptoms in men with overactive bladder and nocturia. Urology 2006;68:328-32.
Study type	Post-hoc analysis of data from randomized, placebo-controlled trial
Patients	745 patients
Purpose of Study	To evaluate the efficacy and safety of nighttime dosing with tolterodine extended release (TER) in men with overactive bladder (OAB) and nocturia

Study Results	A total of 745 men (mean age 64 years) were randomized to placebo (n = 374) or TER (n = 371). Of the 745 men, 73% reported no incontinence episodes in a 7-day diary at baseline. At week 12, the weekly values for nighttime severe OAB micturitions and 24-hour and daytime total, OAB, and severe OAB micturitions were significantly reduced in the TER group versus the placebo group. The TER-treated men also reported a significant reduction in the mean urgency rating versus placebo. Adverse events associated with TER were low and comparable to those in the placebo group, with the exception of dry mouth (11% versus 4%). Withdrawals because of adverse events were infrequent (3% TER, 4% placebo). Five men were withdrawn for symptoms suggestive of urinary retention (3 TER, 2 placebo).
Level of Study	3
Reference	46. Dmochowski R, Abrams P, Marschall-Kehrel D, et al. Efficacy and tolerability of tolterodine extended release in male and female patients with overactive bladder. Eur Urol 2007;51:1054-64.
Study type	Post-hoc analysis of data from randomized, placebo-controlled trial
Patients	1,698 patients
Purpose of Study	To evaluate the efficacy and tolerability of tolterodine extended release (ER) in men and women with overactive bladder (OAB)
Study Results	At baseline, 73% (547 of 745) of men and 57% (539 of 953) of women were continent. By week 12, tolterodine ER (n=848) reduced OAB and severe OAB micturitions during 24-h, daytime, and nocturnal intervals in both sexes compared with placebo (n=850). Adverse event rates were low and similar across treatment and gender.
Level of Study	3
Reference	47. Abrams P, Kaplan S, De Koning Gans HJ, et al. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction. J Urol 2006;175:999-1004.
Study type	Randomized, placebo-controlled trial
Patients	222 patients
Purpose of Study	To evaluate the safety of tolterodine vs placebo in men with OAB and BOO
Study Results	Median treatment differences in Qmax (-0.7 ml per second, 95% CI -1.6 to 0.4) and pdetQmax (-7 cm H2O, 95% CI -3 to 11) were comparable. Tolterodine significantly reduced the BOOI vs placebo (-9 vs 0, $p < 0.02$). There were significant treatment differences in volume to first detrusor contraction (+59 ml, 95% CI 19-100) and maximum cystometric capacity (+67 ml, 95% CI 35-103), favoring tolterodine over placebo ($p < 0.003$). Change in PVR was significantly greater among patients treated with tolterodine (+25 ml) than placebo (0 ml, $p < 0.004$). There were no significant between-group differences in the incidence of adverse events. Urinary retention was reported by 1 patient treated with placebo.
Level of Study	2
Reference	48. Kaplan SA, Roehrborn CG, Rovner ES, et al. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. JAMA 2006;296: 2319-28.

Study type	Randomized, placebo-controlled trial
Patients	879 patients
Purpose of Study	To evaluate the efficacy and safety of tolterodine extended release (ER), tamsulosin, or both in men who met research criteria for both overactive bladder and benign prostatic hyperplasia
Study Results	A total of 172 men (80%) receiving tolterodine ER plus tamsulosin reported treatment benefit by week 12 compared with 132 patients (62%) receiving placebo (P<.001), 146 (71%) receiving tamsulosin (P=.06 vs placebo), or 135 (65%) receiving tolterodine ER (P=.48 vs placebo). Patients receiving tolterodine ER plus tamsulosin compared with placebo experienced significant reductions in urgency urinary incontinence (-0.88 vs -0.31, P=.005), urgency episodes without incontinence (-3.33 vs -2.54, P=.03), micturitions per 24 hours (-2.54 vs -1.41, P<.001), and micturitions per night (-0.59 vs -0.39, P.02). Patients receiving tolterodine ER plus tamsulosin demonstrated significant improvements on the total International Prostate Symptom Score (-8.02 vs placebo, -6.19, P=.003) and QOL item (-1.61 vs -1.17, P=.003). All interventions were well tolerated. The incidence of acute urinary retention requiring catheterization was low (tolterodine ER plus tamsulosin, 0.4%; tolterodine ER, 0.5%; tamsulosin, 0%; and placebo, 0%).
Level of Study	2
Reference	49. Disantostefano RL, Biddle AK, Lavelle JP. An evaluation of the economic costs and patient-related consequences of treatments for benign prostatic hyperplasia. BJU Int 2006;97:1007-16.
Study type	Decision analysis using published data including systematic reviews
Patients	Not specified in detail
Purpose of Study	To compare the costs and effectiveness of treatments for benign prostatic hyperplasia (BPH), including watchful waiting, pharmaceuticals (alpha-blockers, 5-alpha-reductase inhibitors, combined therapy), transurethral microwave thermotherapy (TUMT), and transurethral resection of the prostate (TURP)
Study Results	What is the 'best' treatment depends on the value that an individual and society place on costs and consequences. Alpha-blockers are less expensive than the alternatives, and are effective at relieving patient-reported symptoms. Unfortunately, they have little effect on clinical outcomes and have the highest BPH progression rate. Other treatments have lower disease progression and better clinical outcomes, but are more expensive and entail more invasive treatments, and/or more uncertainty. Treatment decisions are made using a variety of information, including the cost and consequences of treatment. The best treatment depends on the patient's preference and the outcome considered most important. alpha-Blockers are very effective at treating urinary symptoms but do not improve clinical outcomes, including disease progression, relative to other treatments. TURP remains the 'gold standard' for surgical procedures. The desire to avoid TURP or the 2 weeks of catheterization associated with TUMT might affect a patient's treatment decision when symptoms are severe. Therefore, more information about patient preferences and risk aversion is needed to inform treatment decision-making for BPH.
Level of Study	2

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KQ 8. 전립선비대증 환자에서 병용요법이 알파차단제 단독사용보다 치료효과를 높일 수 있는가?

권고사항	권고수준	근거수준
8-1. 전립선비대증 환자에서 알파차단제와 5α환원효소억제제 병용요법은 알파차단제 단독요법보다 하부요로증상 완화에 효과적인 치료방법이다.	Strong	A
8-2. 알파차단제와 항콜린제 병용요법은 중등도 이상의 하부요로증상을 가진 환자에서 알파차단제 단독요법의 효과가 불충분할 경우에 시행한다.	Strong	A
8-3 알파차단제와 항콜린제 병용요법은 배뇨 후 잔뇨량이 많고 방광출구폐색이 의심되는 남성에서는 신중하게 시행한다.	Strong	A
8-4. PDE5 억제제와 알파차단제의 병용 투여는 중등도 이상의 하부요로증상을 감소시키는 데 있어 알파차단제 단독요법보다 효과적이다.	Weak	A

8-1. 5α환원효소억제제 병용요법

전립선비대증 환자에서 알파차단제와 5α환원효소억제제의 병용요법은 전립선비대의 성장을 억제하는 5α환원효소억제제의 효과와 방광경부와 전립선요도의 평활근을 이완하는 알파차단제의 효과를 이중으로 얻을 수 있는 이상적인 치료법이다. 알파차단제(terazosin doxazosin, alfuzosin, tamsulosin, silodosin, naftopidil)는 수시간에서 수일 내에 하부요로증상 완화 효과를 나타내고, 5α환원효소억제제(finasteride, dutasteride)는 의미 있는 임상효과를 나타내는 데 수개월이 필요하다. 두 약물의 병용요법에 대한 장기추적 연구에서는 병용요법이 알파차단제 단독요법이나 5α환원효소억제제 단독요법보다 증상 감소 및 최고요속 개선에 있어서 효과적이었고, 급성요폐 및 수술의 필요성 감소에서는 알파차단제 단독요법보다 우월하였다.

Finasteride와 알파차단제의 병용요법의 효과를 알아보기 위한 MTOPS (medical therapy of prostatic symptoms)연구에서 전립선비대증의 임상적 진행에 대한 위약, doxazosin, finasteride 단독요법, 병용요법의 효과를 비교하기 위하여 남성 3,047명을 대상으로 장기 이중맹검 연구를 하였다. 전반적인 전립선비대증 진행 가능성은 위약에 비해 66% 감소하여 doxazosin (39% 감

소)과 finasteride (34% 감소)에 비해 유의하게 감소하였다. 급성요폐 발생과 수술적 치료의 빈도는 병용요법과 finasteride 단독요법에서는 유의하게 감소하였다. CombAT (Combination of Avodart® and Tamsulosin) 연구는 병용요법이 증상 개선 및 Qmax 관점에서 치료 시작 9개월째부터 각각의 단독요법보다 우월하고 급성요폐 및 수술의 필요성 감소 측면에선 8개월째부터 알파차단제보다 우월함을 보였다[1,2].

병용요법은 전체 임상적 진행(적어도 4점 이상의 IPSS 증가, 급성요폐, 요로감염, 요실금, 또는 기저치 대비 50% 이상의 혈청 크레아티닌의 증가)을 억제하는 데 있어 MTOPS 및 CombAT 연구에서 단독요법보다 우월하였다. 5α환원효소억제제와 알파차단제 병용요법은 최소한 1년 이상의 기간을 유지해야 효과가 나타날 수 있고 규칙적인 전립선특이항원 확인이 필요하였다.

SMART-1 연구(Symptom Management after Reducing Therapy Study)는 24주간 dutasteride와 tamsulosin 병용요법 후 tamsulosin을 중단하였을 때 증상 개선 효과가 유지될 수 있는지 알아보기 위해 진행되었다. 주관적 증상은 30주째에서 병용요법군의 9%, 단독요법군의 23%에서 악화되었고, 36주째에는 각각 4%, 7%에서 악화되어, 알파차단제를 중단한 후에는 증상이 악화될 수 있으나 장기간 사용하면 개선될 수 있다고 보고하였다[3].

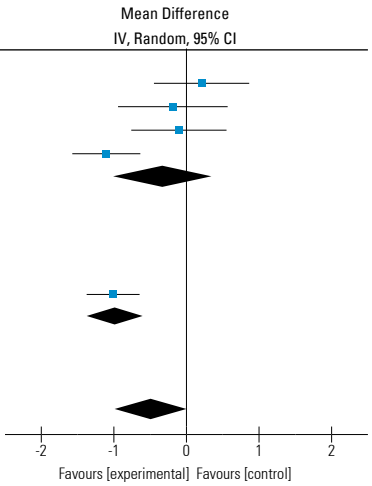
알파차단제 단독요법과 알파차단제와 5α환원효소억제제의 병용요법의 메타분석비교를 보면 단독요법에 대한 병용요법의 mean difference가 IPSS는 −0.49 (95% 신뢰구간 −1.01 − 0.02)로 단독요법보다 병용요법이 증상 개선에 효과적이었으나 통계적인 유의성은 없었고, 최고요속(Q-max)의 mean difference는 0.88 (95% 신뢰구간 0.40 − 1.35)로 최고요속의 개선폭이 단독요법보다 병용요법이 더 컸으며 통계적 유의성도 확인하였다.

문헌고찰과 메타분석 결과를 토대로 보았을 때, 알파차단제와 5α환원효소억제제의 병용요법은 단독요법에 비하여 전립선비대증의 진행을 효과적으로 예방하며 증상 개선에 나은 효능을 보였다.

그림 8-1. 알파차단제 단독요법군과 알파차단제와 5α 환원효소억제제의 병용요법군에서 효과에 대한 숲 그림 (forest plot)

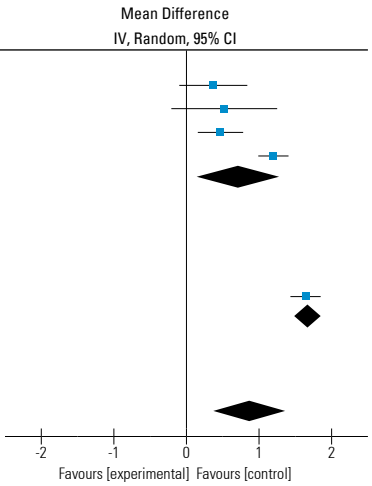
(A) IPSS

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 finasteride								
Debruyne FM 1998	-6.1	4.4	358	-6.3	4.4	349	18.7%	0.20 [-0.45, 0.85]
Kirby R 2003a	-8.6	4.4	265	-8.4	4.1	250	17.2%	-0.20 [-0.93, 0.53]
Lepor H 1996	-6.2	4.2	309	-6.1	4.1	305	18.5%	-0.10 [-0.76, 0.56]
McConnell JD 2003a	-7	4.5	786	-5.9	4.5	756	22.1%	-1.10 [-1.55, -0.65]
Subtotal (95% CI)			**1718**			**1660**	**76.5%**	**-0.33 [-0.98, 0.31]**
Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 13.38$, df = 3 (P = 0.004); $I^2 = 78\%$								
Test for overall effect: Z = 1.00 (P = 0.32)								
2.1.2 dutasteride								
Roehrborn CG 2010a	-6.3	5.4	1610	-5.3	5	1611	23.5%	-1.00 [-1.36, -0.64]
Subtotal (95% CI)			**1610**			**1611**	**23.5%**	**-1.00 [-1.36, -0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.45 (P < 0.00001)								
Total (95% CI)			**3328**			**3271**	**100.0%**	**-0.49 [-1.01, 0.02]**
Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 18.10$, df = 4 (P = 0.001); $I^2 = 78\%$								
Test for overall effect: Z = 1.88 (P = 0.06)								
Test for subgroup differences: $Chi^2 = 3.15$. df = 1 (P = 0.08). $I^2 = 68.2\%$								



(B) Q-max

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 finasteride								
Debruyne FM 1998	2.2	3.4	358	1.8	2.7	349	18.9%	0.40 [-0.05, 0.85]
Kirby R 2003a	4.1	3.7	265	3.6	3.6	250	16.3%	0.50 [-0.13, 1.13]
Lepor H 1996	3.2	2	309	2.7	2.1	305	20.6%	0.50 [0.18, 0.82]
McConnell JD 2003a	3.7	1.9	786	2.5	2	756	22.0%	1.20 [1.01, 1.39]
Subtotal (95% CI)			**1718**			**1660**	**77.9%**	**0.68 [0.20, 1.16]**
Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 21.15$, df = 3 (P < 0.0001); $I^2 = 86\%$								
Test for overall effect: Z = 2.79 (P = 0.005)								
2.2.2 dutasteride								
Roehrborn CG 2010a	2.4	2.6	1610	0.8	2.6	1611	22.1%	1.60 [1.42, 1.78]
Subtotal (95% CI)			**1610**			**1611**	**22.1%**	**1.60 [1.42, 1.78]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 17.46 (P < 0.00001)								
Total (95% CI)			**3328**			**3271**	**100.0%**	**0.88 [0.40, 1.35]**
Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 53.71$, df = 4 (P < 0.00001); $I^2 = 93\%$								
Test for overall effect: Z = 3.62 (P = 0.0003)								
Test for subgroup differences: $Chi^2 = 12.50$. df = 1 (P = 0.0004). $I^2 = 92.0\%$								



Debruyne FM 1998[5], Kirby R 2003a[6], Lepor H 1996[4], McConnell JD 2003a[1], Roehrborn CG 2010a[2]

● 근거표

KQ 8-1						
Reference	**Study type**	**Treatment (daily dose)**	**Patients (n)**	**Change in symptoms (% IPSS)**	**Change in Qmax (mL/s)**	**Level of Study**
Lepor et al. (1996)	randomized controlled trial	Placebo Terazocin Finasteride Terazocin 1 x 10mg + Finasteride 1 x 5mg	305 305 310 309	-16.5a -37.7a,b,d -19.8a -39a, b ,d	+1.4 +2.7b,d +1.6 +3.2b,d	2
Debruyne et al. (1998)	randomized controlled trial	Alfuzosin 2 x 5 mg Finasteride 1 x 5 mg Alfuzosin 2 x 5 mg + finasteride 1 x 5 mg	358 344 349	-41.2d -33.5 -39.1d	+1.8 +1.8 +2.3	2
Kirby et al. (2003)	randomized controlled trial	Placebo Doxazosin 1 x 1-8 mg Finasteride 1 x 5 mg Doxazosin 1 x 1-8 mg + finasteride 1 x 5 mg	253 250 239 265	-33.1 -49.1b,d -38.6 -49.7b,d	+1.4 +3.6b,d +1.8 +3.8d	2
McConnell et al. (2003)	randomized controlled trial	Placebo Doxazosin 1 x 1-8 mg Finasteride 1 x 5 mg Doxazosin 1 x 1-8 mg + finasteride 1 x 5 mg	737 756 768 786	-23.8a -35.3a,b,d -28.4a,b -41.7a,b,c,d	+1.4a +2.5a,b +2.2a,b +3.7a,b,c,d	2
Roehrborn et al. (2008)	randomized controlled trial	Tamsulosin 1 x 0.4 mg Dutasteride 1 x 0.5 mg Tamsulosin 1 x 0.4 mg + dutasteride 1 x 0.5 mg	1611 1623 1610	-27.4 -30.5 -39.2c,d	+0.9 +1.9 +2.4c,d	2
Roehrborn et al. (2010)	randomized controlled trial	Tamsulosin 1 x 0.4 mg Dutasteride 1 x 0.5 mg Tamsulosin 1 x 0.4 mg + dutasteride 1 x 0.5 mg	1611 1623 1610	-23.2 -32.3 -38c,d	+0.7 +2.0 +2.4c	2

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8-2. 항콜린제 병용요법

전립선비대증 환자는 일반적으로 많은 비율에서 과민성방광 증상을 동반하게 된다. 전립선비대증으로 인한 폐색이 존재하는 경우 50-75%에서 과민성방광이 동반되며, 폐색을 치료한 후에도 과민성방광이 38% 정도에서 보이는 것으로 알려져 있다[1]. 일반적으로 연령이 증가할수록 전립선비대에 의한 폐색의 발생률이 증가하고 과민성방광이 동반되는 경우도 증가하게 되는데 전립선비대증으로 인한 하부요로폐색이 심할수록 과민성방광의 발생률도 비례하여 증가한다. 실제로 환자에게 빈뇨, 요절박과 같은 자극증상이 폐색증상보다 더 큰 괴로움을 준다고 알려져 있고, 치료 시 이러한 점들을 충분히 감안하여야 한다.

과민성방광을 동반한 전립선비대증의 경우 알파차단제만으로는 증상 개선에 한계가 있으며 이러한 과민성방광으로 인한 자극증상을 치료하기 위하여 항콜린제(anti-cholinergic agent)를 사용할 수 있다.

항콜린제는 불수의적 방광수축을 보이는 환자에서 방광수축이 일어날 때 최초 방광 용적을 증가시키고, 수축력을 감소시키며, 최대방광용량을 증가시킨다. 그러므로 요절박, 절박성요실금 등의 증상을 보이는 과민성방광의 치료에 항콜린제가 주로 사용되고 있으며, 현재 임상적으로 그 약효가 증명된 항콜린제는 darifencacin, fesoterodine, Imidafenacin, oxybutynin, propiverine, solifenacin, tolterodine 그리고 trospium chloride이다.

전립선비대증에서 알파차단제와 항콜린제의 병용요법은 주로 알파차단제를 사용한 환자에서 지속적으로 남아있는 자극증상의 호전을 위해 선택적으로 사용되는 경우가 많았다. 이러한 병용요법은 알파차단제 또는 위약 단독요법과 비교하여 절박뇨뿐만 아니라 절박성요실금 에피소드를 유의하게 감소시키며, 삶의 질을 증가시켰다[2].

여러 임상시험에서 알파차단제로 치료하는 동안 하부요로증상이 지속되는 환자를 대상으로 기존의 알파차단제에 항콜린제를 추가하여 병용요법의 효능을 평가하였다. 병용요법군에서 전반

적인 증상개선 정도는 혈청 전립선특이항원 농도에 관계없이 위약군보다 유의하게 높은 반면, tolterodine 단독요법은 전립선특이항원 농도가 1.3 ng/mL 미만인 환자에서 주로 증상을 개선하였다[3]. 또한 관련된 임상시험에서 지속되는 대부분 하부요로증상이 배뇨근 과활동과 관련된 경우에 있어서 항콜린제의 추가에 의해서 의미 있게 감소될 수 있음을 보여주었다[4–6].

Medline, EMbase, Cochrane, KoreaMed에서 검색식을 적용하여 검색하였을 때, 총 573개의 문헌이 검색되고, 중복배제 후 기간을 1990년 1월 1일부터 2014년 7월 1일로 제한하였을 때, 430개의 문헌이 추출되었고, 이 중 관련 논문인 총 13개의 문헌을 근거로 사용하였다.

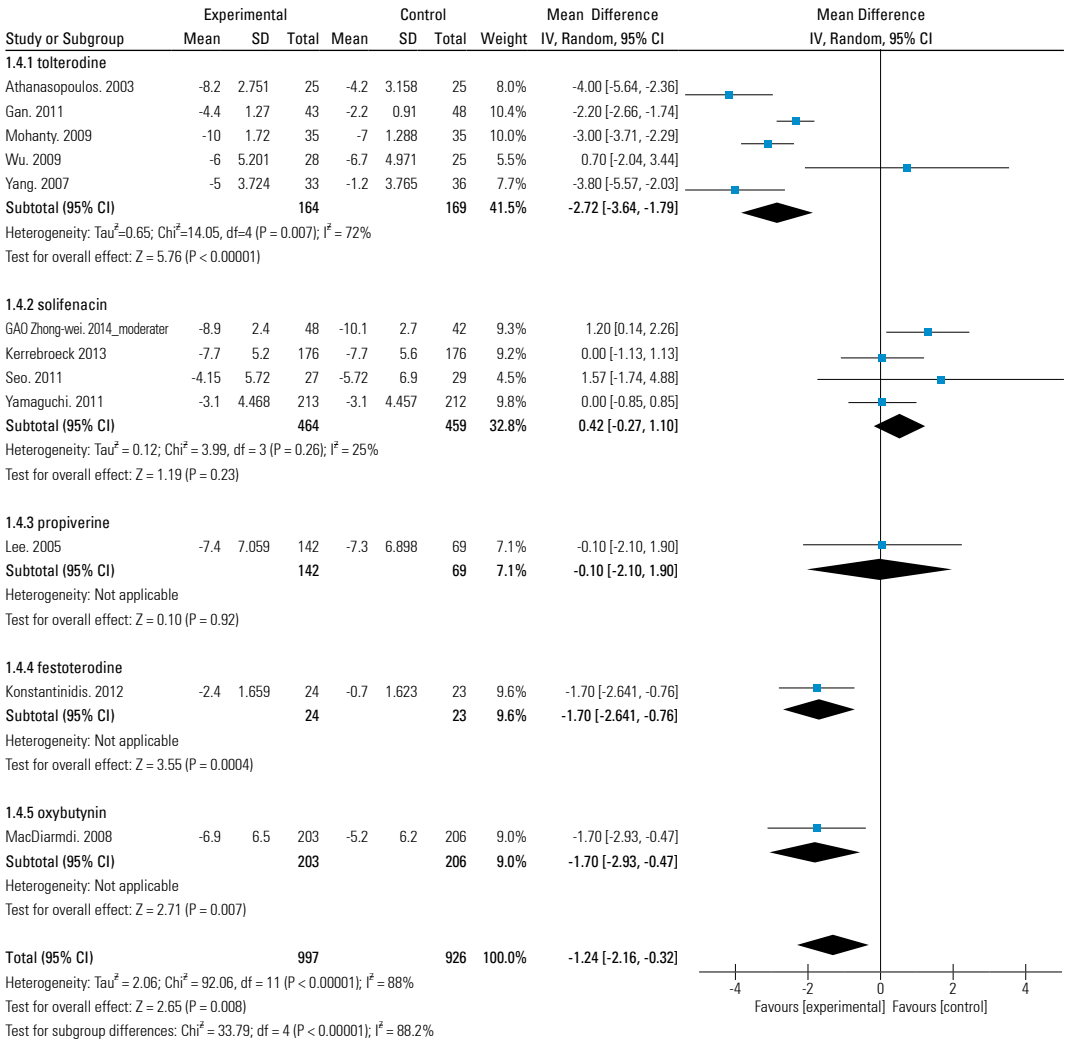
단독요법과 병용요법의 증상 개선 비교 결과를 보면 병용요법의 mean difference가 IPSS는 −1.24 (95% 신뢰구간 −2.16 – −0.32) 정도로 증상 개선에 좀 더 효과적이었으며 통계적으로 유의하였다. 최대요속은 병용요법군이 알파차단제 단독요법군에 비해 mean difference −0.26 (95% 신뢰구간 −0.60 – 0.09)로 수치상 감소된 효과를 보이지만 통계적으로 유의하지는 않았다. 각 군에 포함된 연구결과의 이질성은 없어 보이며 또한 약제에 따라 일부 효과의 차이가 있어 보이지만 약제 각각에 포함된 연구의 수가 많지 않아 약제에 따른 약효의 차이를 결론 내리기는 어려웠다.

문헌고찰과 메타분석 결과를 토대로 보았을 때, 알파차단제와 항콜린제의 병용요법은 임상적으로 알파차단제 요법에 비하여 미비하게 최고요속을 감소시킬 수 있으나 의미있는 감소는 아니며 증상 개선 측면에서 유의한 우위를 보여주었다.

결론적으로 임상적으로 중등도 이상에서, 특히 자극증상을 주로 호소하는 환자의 경우 병용요법의 유효성과 안정성이 증명되었다. 다만 남성에서 방광출구폐색이 있는 경우에는 항콜린제로 인한 요폐색의 합병증을 증가시킬 수 있으므로 주의가 필요하다[7].

그림 8-2. 알파차단제 단독요법군과 알파차단제와 항콜린제의 병용요법군에서 효과에 대한 숲 그림 (forest plot)

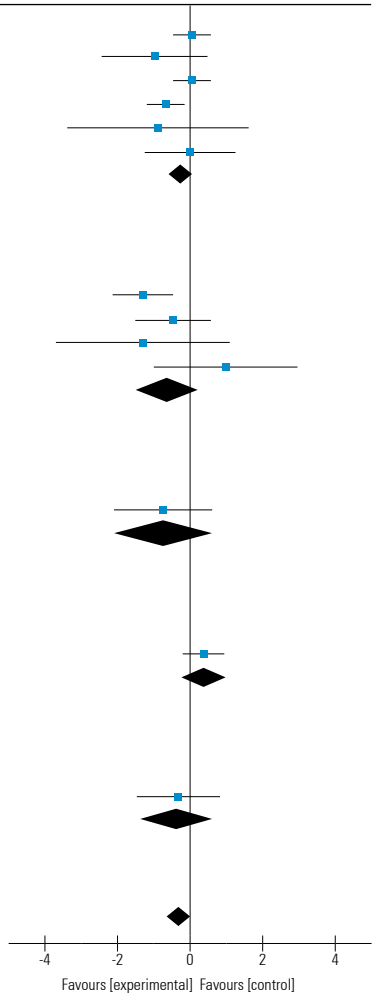
(A) IPSS



Athanasopoulos. 2003[4], Gan. 2011[15], Mohanty. 2009[11], Wu. 2009[12], Yang. 2007[6], GAO Zhong-wei. 2014_moderater[18], Kerrebroeck 2013[17], Seo. 2011[14], Yamaguchi. 2011[13], Lee. 2005[8], Konstantinidis. 2012[16], MacDiarmdi. 2008[10]

(B) Q–max

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 tolterodine								
Athanasopoulos. 2003	1.32	0.862	25	1.16	0.769	25	14.6%	0.16 [-0.29, 0.61]
Chapple. 2008	-0.2	8.5	289	0.8	8.53	293	4.7%	-1.00 [-2.38, 0.38]
Gan. 2011	3	1.16	43	2.9	1.07	48	14.5%	0.10 [-0.36, 0.56]
Mohanty. 2009	4	0.961	35	4.6	1.173	35	13.8%	-0.60 [-1.10, -0.10]
Wu. 2009	3.4	4.554	28	4.2	4.904	25	1.6%	-0.80 [-3.36, 1.76]
Yang. 2007	0.8	1.663	33	0.7	3.382	36	5.5%	0.10 [-1.14, 1.34]
Subtotal (95% CI)			**453**			**462**	**54.7%**	**-0.15 [-0.52, 0.21]**
Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 7.80$, df = 5 (P = 0.17); $I^2 = 36\%$								
Test for overall effect: Z = 0.82 (P = 0.41)								
1.3.2 solifenacin								
GAO Zhong-wei. 2014_mild	-0.4	1.9	48	0.9	1.7	40	10.1%	-1.30 [-2.05, -0.55]
GAO Zhong-wei. 2014_moderater	4.9	2.5	36	5.3	2.1	42	7.0%	-0.40 [-1.43. 0.63]
Seo. 2011	-0.15	3.827	27	1.1	5.378	29	1.8%	-1.25 [-3.68, 1.18]
Yamaguchi. 2011	2	3.004	21	0.9	3.448	19	2.5%	1.10 [-0.91, 3.11]
Subtotal (95% CI)			**132**			**130**	**21.5%**	**-0.63 [-1.56, 0.29]**
Heterogeneity: $Tau^2 = 0.40$; $Chi^2 = 5.80$, df = 3 (P = 0.12); $I^2 = 48\%$								
Test for overall effect: Z = 1.34 (P = 0.18)								
1.3.3 propiverine								
Lee. 2005	1	2.975	142	1.7	5.343	69	4.8%	-0.70 [-2.05, 0.65]
Subtotal (95% CI)			**142**			**69**	**4.8%**	**-0.70 [-2.05, 0.65]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.01 (P = 0.31)								
1.3.4 festoterodine								
Konstantinidis. 2012	0.6	0.874	24	0.2	1.169	23	12.4%	0.40 [-0.19, 0.99]
Subtotal (95% CI)			**24**			**23**	**12.4%**	**0.40 [-0.19, 0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.32 (P = 0.19)								
1.3.5 oxybutynin								
MacDiarmdi. 2008	-0.2	4.901	203	0.1	6.252	206	6.6%	-0.30 [-1.39, 0.79]
Subtotal (95% CI)			**203**			**206**	**6.6%**	**-0.30 [-1.39, 0.79]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.54 (P = 0.59)								
Total (95% CI)			**954**			**890**	**100.0%**	**-0.26 [-0.60, 0.09]**
Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 23.31$, df = 12 (P = 0.03); $I^2 = 49\%$								
Test for overall effect: Z = 1.47 (P = 0.14)								
Test for subgroup differences: $Chi^2 = 4.98$; df = 4 (P = 0.29); $I^2 = 19.6\%$								



근거표

KQ 8-2					
Reference	**Study type**	**Treatment (daily dose)**	**Patients (n)**	**Change in symptoms (% IPSS)**	**Change in Qmax (mL/s)**
Athanasopoulos et al. (2003)	randomized controlled trial	Tamsulosin Tamsulosin + tolterodine	25 25	8.2 -4.2-	1.16 1.32
Lee et al. (2005)	randomized controlled trial	Doxazosin Doxazosin + propiverine	69 142	-7.3 -7.4	1.7 1
Yang et al. (2007)	randomized controlled trial	Terazosin Terazosin + tolterodine	36 33	-5 -1.2	0.7 0.8
Chapple et al. (2008)	randomized controlled trial	Tamsulosin Tamsulosin + tolterodine	329 323	-6.3 -6.1	0.8 -0.2
MacDiarmid et al. (2008)	randomized controlled trial	Tamsulosin Tamsulosin + oxybutynin	206 203	-5.2 -6.9	0.1 -0.2
Mohanty et al. (2009)	randomized controlled trial	Tamsulosin Tamsulosin + tolterodine	35 35	-7 -10	4.6 4
Wu et al. (2009)	randomized controlled trial	Tamsulosin Tamsulosin + tolterodine	25 28	-6.7 -6	4.2 3.4
Yamaguchi et al. (2011)	randomized controlled trial	Tamsulosin Tamsulosin + solifenacin	215 213	-3.1 -3.1	-0.13 -0.66
Seo. et al. (2011)	randomized controlled trial	Tamsulosin Tamsulosin + solifenacin	29 27	-4.15 -5.72	1.1 -0.15
Gan et al. (2011)	randomized controlled trial	Doxazosin Doxazosin + tolterodine	62 51	-2.2 -4.4	2.9 3
Konstantinidis et al. (2012)	randomized controlled trial	Tamsulosin Tamsulosin + fesoterodine	23 24	-1.4 -0.6	0.2 0.6
Kerrebroeck. (2013)	randomized controlled trial	Tamsulosin Tamsulosin + solifenacin	179 180	-7.7 -7.7	1.2 1.3
GAO Zhong- wei et al. (2014)	randomized controlled trial	Tamsulosin Tamsulosin + solifenacin	40 48	-10.1 -8.9	5.3 4.9

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8-3. PDE5 억제제 병용요법

발기과정에 가장 핵심적인 역할을 하는 nictric oxide synthase (NOS) 혹은 nitric oxide (NO)는 음경에 존재하는 평활근의 수용성 guanylate cyclase을 활성화시킴으로써 세포 내의 cGMP

를 증가시키고, 증가된 세포 내 cGMP가 평활근을 이완시켜 음경발기를 유발하게 된다. 또한 NO는 척수 내 반사경로를 억제함으로써 배뇨주기에 관여하고, 요도, 전립선 또는 방광 내 신경전달에도 관여한다. Phosphodiesterase (PDE) 억제제는 세포 내 cGMP의 농도를 증가시키고 이의 활동을 연장시킴으로써 배뇨근, 전립선 및 요도의 평활근 긴장도를 줄여 주는 효과가 있다. 골반강 내 NO 체계의 변화로 발기부전이 발생하고 전립선비대증의 이행대는 평활근이 감소한 상태이므로 조직 내 NO가 감소하여 하부요로증상이 생긴다고 보았을 때 임상적으로 PDE5 inhibitor (PDE5I)를 사용하는 경우 배뇨증상이 개선될 수 있다.

지금까지 11개의 PDE가 알려져 있으며, PDE 4와 5가 인체 전립선의 이행대, 방광 및 요도에서 주된 형태이다. 또한 PDE4형과 5형이 다른 기관에서보다 전립선에 상대적으로 많이 발현되므로, 전립선에 NO가 특징적으로 작용한다고 볼 수 있는데 최근 저용량의 PDE5I의 매일 복용에 대한 연구가 진행되면서 PDE5I와 알파차단제의 병용 투여 시 배뇨증상과 성기능에 긍정적인 효과를 나타낼 수 있다는 연구들이 발표되었다[1].

PDE5 억제제는 위장관에서 흡수되고, 혈장에서 높은 단백 결합력을 보이며 간에서 일차적으로 대사되어 대변으로 배설된다. 그러나 그들의 반감기는 현저하게 차이가 있다. 현재 사용 가능한 선택적 경구 PDE5 억제제는 sildenafil, tadalafil, vardenafil, udenafil 및 mirodenafil의 다섯 가지로, PDE5 억제제는 발기부전 환자에서 필요에 따라 투여되지만, tadalafil은 필요에 따른 투여보다 낮은 용량 (5 mg)의 매일 투여 용법으로 허가되어 있다.

최초 개발되었던 sildenafil의 경우 발기부전 환자에서 PDE5 억제제가 IPSS 설문지에 의해 측정된 하부요로증상을 유의하게 감소시키고 방광증상 관련 삶의 질을 향상시킴을 보여 주었다[2,3].

이후 다양한 PDE5 억제제의 효능에 대한 무작위, 위약 대조 임상 시험 결과들이 발표되었고 증상의 변화(IPSS), 최대요속(Qmax) 및 배뇨 후 잔뇨량을 조사해 보았을 때 거의 모든 PDE5 억제제는 IPSS를 유의하게 감소시켰다. 방광 저장 및 배뇨 증상 모두 PDE5 억제제로 치료하는 동안 동일하게 감소하였으나 배뇨 후 잔뇨량은 대부분의 임상시험에서 변화가 없었다[4–6].

PDE5 억제제는 질산염을 복용하는 환자에서는 금기시되는데, 추가 혈관 확장으로 인해 저혈압, 관상동맥 질환자에서 심근 허혈, 뇌졸중을 유발할 수 있기 때문이다[7].

혈관 확장제 효과를 가지는 알파 아드레날린 차단제, PDE5 억제제의 병용 투여는 일부 환자에서 증상을 동반하는 저혈압을 유발할 수 있기 때문에 조심해야 하는데, doxazocin(매일 4, 8 mg)과 tadalafil(매일 5 mg 또는 간헐적 20 mg)의 병용 투여는 혈압을 더욱 많이 낮추며, 이들의 병

용 투여는 일부 환자에서 위험할 수도 있기 때문에 피하는 것이 좋다. Vardenafil은 tamsulosin과는 언제든지 병용 투여해도 되지만 vardenafil과 terazosin을 동시에 투여 받는 남성은 저혈압이 더 자주 발생함을 보고하고 있다[8]. 이런 저혈압 효과는 vardenafil과 terazosin을 6시간 이상의 간격으로 분할 투여함으로써 최소화된다.

PDE5 억제제는 일반적으로 두통, 홍조, 현기증, 소화 불량, 비충혈, 근육통, 저혈압, 실신, 이명, 결막염 또는 시각 이상 등을 초래할 수 있다. 그러나 부작용의 빈도는 개개의 PDE5 억제제에 따라 다르며 지속 발기증 또는 급성 요폐의 발생 가능성은 아주 적은 것으로 알려져 있다[7]. 모든 PDE5 억제제는 불안정 협심증, 최근 심근경색(이전 3 개월) 또는 뇌졸중(이전 6개월), 심부전, 저혈압, 조절되지 않는 혈압, 의미 있는 간 또는 신부전 환자, 또는 갑작스런 시각 소실을 동반한 비동맥염성 전방 허혈성 시신경 병증이 있거나 이전에 PDE5 억제제 사용 후 부작용을 경험했던 환자에서는 투여하지 않는 것이 좋다.

알파차단제와 병용한 PDE5 억제제의 효능을 비교한 임상시험들은 소수의 환자를 대상으로 6–12주의 제한된 기간 동안 진행된 것들이 대부분이다.

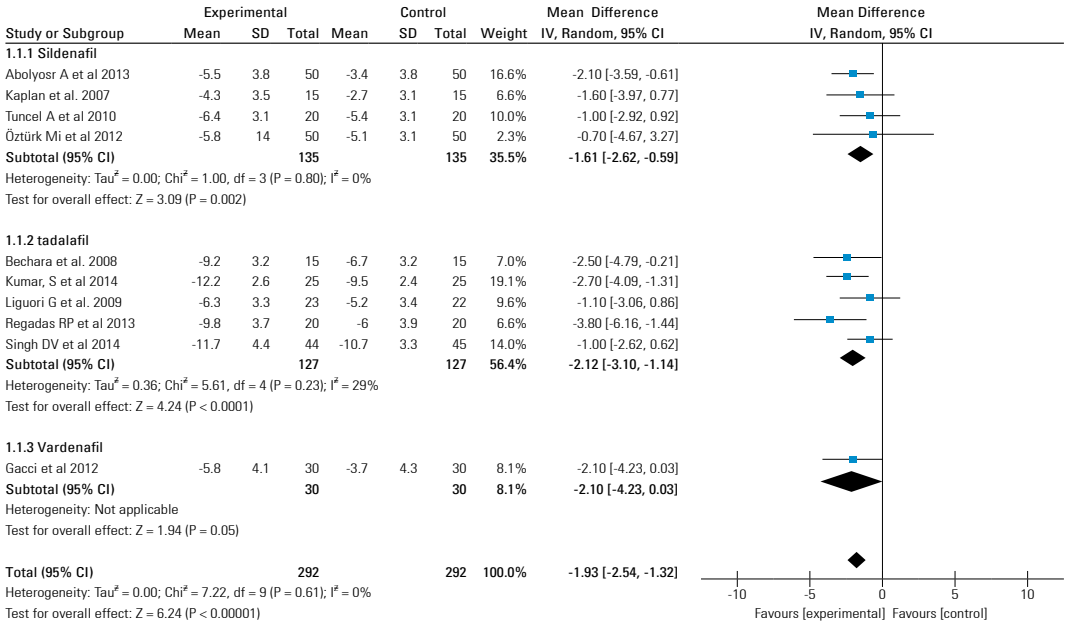
Medline, EMbase, Cochrane, KoreaMed에서 위 검색식을 적용하여 검색하였을 때, 총 935개의 문헌이 검색되고, 이를 기간을 1990년 1월 1일부터 2014년 7월 1일로 제한하였을 때, 629개의 문헌이 추출되었고, 이 중 관련 논문만을 총 10개의 문헌을 근거로 사용하였다. 메타분석상의 알파차단제와 PDE5 억제제의 병용요법과의 비교결과를 보면 단독요법에 대한 병용요법의 mean difference가 IPSS는 −1.93 (95% 신뢰구간 −2.54−−1.32) 정도로 증상 개선에 좀 더 효과적이었으며 Q–max의 mean difference는 0.71 (95% 신뢰구간 0.08 − 1.33)로 최고요속의 개선폭이 병용요법에서 더 컸으며 두 인자 모두 통계적으로 유의하였다. 또한 발기능의 지표인 IIEF 점수에 있어서 병용요법이 mean difference 3.99 (95% 신뢰구간 2.42 − 5.56)로 발기능의 개선이 의미있게 컸다. 통계적으로 유의하지는 않았지만 잔뇨량의 감소폭도 병용요법에서 더 높았다.

문헌고찰과 메타분석 결과를 토대로 보았을 때, 알파차단제와 PDE5 억제제의 병용요법은 임상적으로 알파차단제 요법에 비하여 성기능 개선 효과는 명확하나 증상 개선이나 요역동학적 인자들에 관련된 여러 임상지표에서 결정적 우위를 보이지는 못했다.

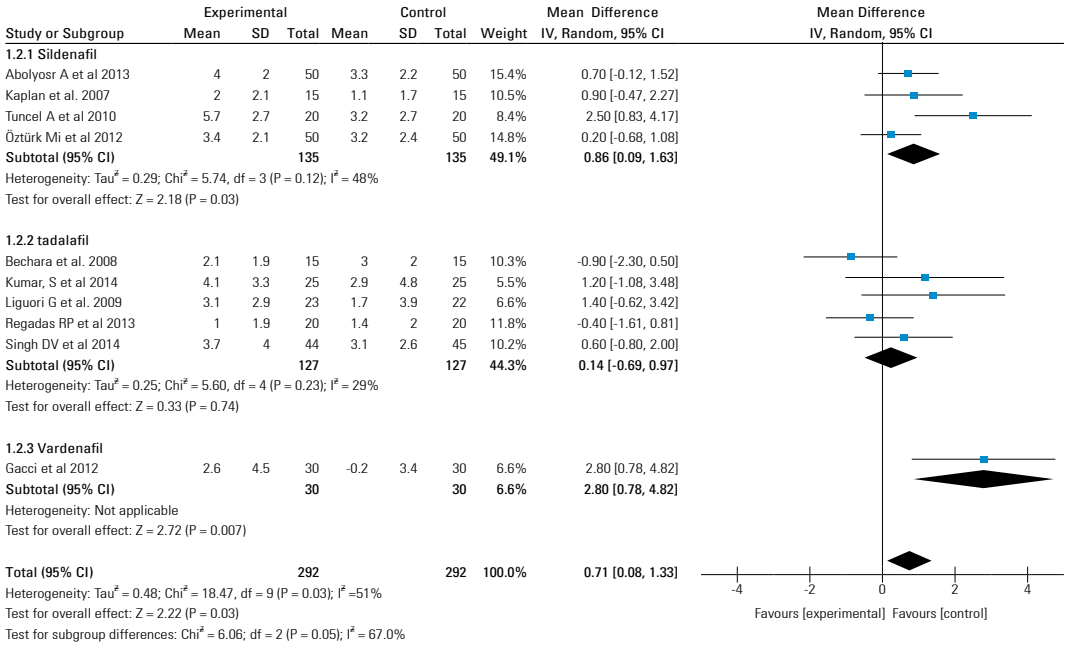
하지만 여러 연구에서 PDE5 억제제는 알파차단제와의 복합요법에서 발기부전 여부와 관계없이 하부요로증상의 호전을 보여, 성기능 개선뿐 아니라 배뇨장애 증상 호전에 유의한 효과를 보여주고 있다.

그림 8-3. 알파차단제 단독요법군과 알파차단제와 PED5 억제제의 병용요법군에서 효과에 대한 숲 그림(forest plot)

(A) IPSS



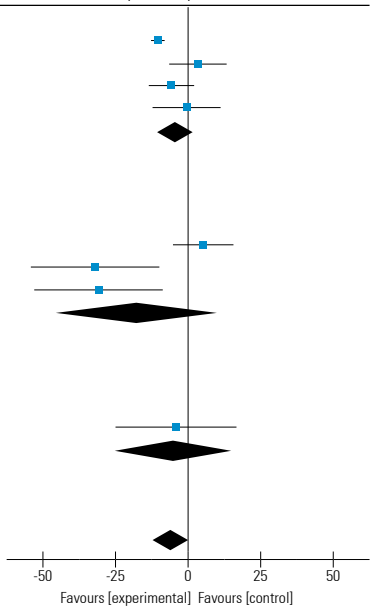
(B) Q-max



Abolyosr A et al 2013[16], Kaplan et al. 2007[9], Tuncel A et al 2010[12], Öztürk Mi et al 2012[14], Bechara et al. 2008[10], Kumar, S et al 2014[17], Liguori G et al. 2009[11], Regadas RP et al 2013[15], Singh DV et al 2014[16], Gacci et al 2012[13]

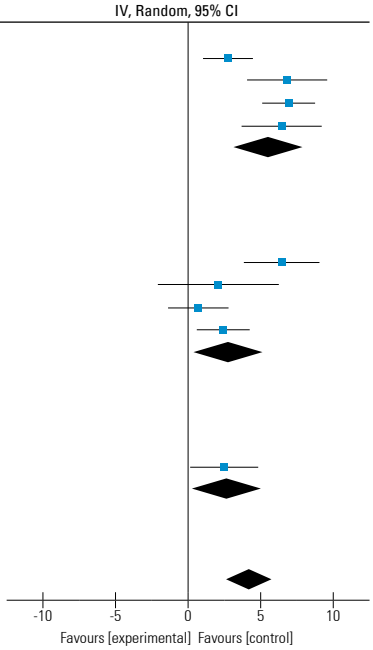
(C) PVR

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Sildenafil								
Abolyosr A et al 2013	-41.8	2.7	50	-31.5	3.3	50	22.9%	-10.30 [-11.48, -9.12]
Kaplan et al. 2007	-21	14.3	15	-23	12.7	15	14.5%	2.00 [-7.68, 11.68]
Tuncel A et al 2010	-3.8	12.8	20	3.3	9.4	20	17.7%	-7.10 [-14.06, -0.14]
Öztürk Mi et al 2012	-14.1	35.3	50	-12.8	20.1	50	12.8%	-1.30 [-12.56, 9.96]
Subtotal (95% CI)			**135**			**135**	**67.9%**	**-5.75 [-11.48, -0.02]**
Heterogeneity: Tau² = 21.02; Chi² = 9.10, df = 3 (P = 0.03); I² = 67%								
Test for overall effect: Z = 1.97 (P = 0.05)								
1.5.2 tadalafil								
Bechara et al. 2008	-35.2	14.4	15	-38.7	14.4	15	13.8%	3.50 [-6.81, 13.81]
Kumar, S et al 2014	-56.2	48.3	25	-23.4	27.3	25	5.8%	-32.80 [-54.55, -11.05]
Singh DV et al 2014	-79.5	59.1	44	-48.2	43.4	45	5.9%	-31.30 [-52.88, -9.72]
Subtotal (95% CI)			**84**			**85**	**25.5%**	**-18.83 [-45.97, 8.30]**
Heterogeneity: Tau² = 488.14; Chi² = 14.25, df = 2 (P = 0.0008); I² = 86%								
Test for overall effect: Z = 1.36 (P = 0.17)								
1.5.3 Vardenafil								
Gacci et al 2012	-10.2	30.1	30	-4.9	46.6	30	6.6%	-5.30 [-25.15, 14.55]
Subtotal (95% CI)			**30**			**30**	**6.6%**	**-5.30 [-25.15, 14.55]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.52 (P = 0.60)								
Total (95% CI)			**249**			**250**	**100.0%**	**-7.09 [-13.15, -1.04]**
Heterogeneity: Tau² = 41.39; Chi² = 23.85, df = 7 (P = 0.001); I² = 71%								
Test for overall effect: Z = 2.30 (P = 0.02)								
Test for subgroup differences: Chi² = 0.86; df = 2 (P = 0.65). I² = 0%								



(D) IIEF

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 Sildenafil								
Abolyosr A et al 2013	4.6	4.1	50	2	4.1	50	12.9%	2.60 [0.99, 4.21]
Kaplan et al. 2007	9.5	3.7	15	2.9	3.9	15	10.3%	6.60 [3.88, 9.32]
Tuncel A et al 2010	8.1	3	20	1.4	3.2	20	12.2%	6.70 [4.78, 8.62]
Öztürk Mi et al 2012	8	6.9	50	1.7	7	50	10.3%	6.30 [3.58, 9.02]
Subtotal (95% CI)			**135**			**135**	**45.7%**	**5.43 [3.10, 7.76]**
Heterogeneity: Tau² = 4.32; Chi² = 13.75, df = 3 (P = 0.003); I² = 78%								
Test for overall effect: Z = 4.57 (P < 0.00001)								
1.3.2 tadalafil								
Bechara et al. 2008	8.2	3.5	15	1.9	3.4	15	10.9%	6.30 [3.83, 8.77]
Kumar, S et al 2014	4.3	7.1	25	2.3	7.2	25	7.7%	2.00 [-1.96, 5.96]
Liguori G et al. 2009	5.3	3.5	23	4.6	3.6	22	11.8%	0.70 [-1.38, 2.78]
Singh DV et al 2014	6.4	4.4	44	4	4	45	12.6%	2.40 [0.65, 4.15]
Subtotal (95% CI)			**107**			**107**	**43.0%**	**2.85 [0.46, 5.24]**
Heterogeneity: Tau² = 4.30; Chi² = 11.96, df = 3 (P = 0.008); I² = 75%								
Test for overall effect: Z = 2.33 (P = 0.02)								
1.3.3 Vardenafil								
Gacci et al 2012	2.6	4	30	0.1	5.1	30	11.3%	2.50 [0.18, 4.82]
Subtotal (95% CI)			**30**			**30**	**11.3%**	**2.50 [0.18, 4.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.11 (P = 0.03)								
Total (95% CI)			**272**			**272**	**100.0%**	**3.99 [2.42, 5.56]**
Heterogeneity: Tau² = 4.30; Chi² = 35.14, df = 8 (P < 0.0001); I² = 77%								
Test for overall effect: Z = 4.98 (P < 0.00001)								
Test for subgroup differences: Chi² = 3.62; df = 2 (P = 0.16); I² = 44.7%								



● 근거표

KQ 8-3								
Trials	**Duration (wks)**	**Study type**	**Treatment**	**Patients**	**IPSS**	**Qmax (mL/s)**	**PVR (mL)**	**LE**
Kaplan et al. (2007)	12	randomized controlled trial	Alfuzosin 1 x 10 mg/day Alfuzosin 1 x 10 mg/day + Sildenafil 1 x 25 mg/day	20 21	-2.7 (-15.5%)† -4.3 (-24.1%)	+1.1† +4.3	-23† -21	2
Bechara et al. (2008)	6	randomized controlled trial	Tamsulosin 1 x 0.4 mg/day Tamsulosin 1 x 0.4 mg/day + tadalafil 1 x 20 mg/day	15 15	-6.7† (-34.5%) -9.2 (-47.4%)	+2.1 +3.0	-35.2 -38.7	2
Liguori G et al. (2009)	12	randomized controlled trial	Alfuzosin 1 x 10 mg/day Alfuzosin 1 x 10 mg/day + tadalafil 20 mg on alternative day	22 23	-27.6% -41.6%			2
Tuncel A et al. (2010)	8	randomized controlled trial	Tamsulosin 0.4 mg Tamsulosin 0.4 mg + sildenafil 25 mg. Four times/ week	20 20	-36.2% -40.1%			2
Gacci et al. (2012)	12	randomized controlled trial	Tamsulosin 0.4 mg + Placebo Tamsulosin 0.4 mg +Vardenafil 10 mg	30 30	-3.7 (18.1%) -5.8 (31.0%)	+0.1 +2.6	-4.9 -10.2	2
Öztürk Mİ et al. (2012)	12	randomized controlled trial	Alfuzosin 1 x 10 mg/day Alfuzosin 1 x 10 mg/day + Sildenafil 1 x 25 mg/day	50 50	-4.9 (26.8%) -5.8 (28.2%)	3.2 3.4	0.7 -1.6	2
Regadas RP et al. (2013)	4	randomized controlled trial	Tamsulosin 0.4 mg + tadalafil 5 mg/day Tamsulosin 0.4 mg	20 20	-9.75 (47.3%) -6.0 (29.4%)	+1.0 +1.4		2
Abolyosr A et al. (2013)	16	randomized controlled trial	Doxazosin 1 x 2 mg Doxazosin 1 x 2 mg + Sildenafil 1 x 50 mg/day	50 50	-3.36 (19.35%) -5.46 (32.1%)	3.3 4.02		2
Kumar, S et al. (2014)	12	randomized controlled trial	Alfuzosin 1 x 10 mg/day Alfuzosin 1 x 10 mg/day + + tadalafil 1 x 10 mg/day	25 25	-9.5 (55.5%) -12.1 (64.0%)	1.6 4.1	-22.8 -56.2	2
Singh DV et al. (2014)	12	randomized controlled trial	Tamsulosin 1 x 0.4 mg/day Tamsulosin 1 x 0.4 mg/day + tadalafil 1 x 10 mg/day	45 44	-50.90% -53.90%	3.11 3.66	-48.18 -79.53	2

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KQ 9. 전립선비대증 환자에서 급성요폐 발생 시 TWOC (Trial without catheter)는 수술적 치료 전에 우선적으로 고려되어야 하는가?

권고사항	권고수준	근거수준
9-1. 급성요폐 발생 시 TWOC는 수술적 치료 전에 고려할 수 있다.	Strong	A
9-2. 급성요폐를 치료하는 데 있어 요도 도관 유치 전후 알파차단제 사용이 도움이 된다.	Strong	B
9-3. 요도 도관은 급성요폐 후 2-7일간 유치하는 것이 도움이 된다.	Strong	B

전립선비대증으로 인한 합병증 중 급성요폐는 가장 흔한 비뇨기과적 응급 상황으로서 즉시 치료를 요하는 상태이다[1]. 최근 이러한 급성요폐를 치료하는 데 있어 요도 도관 유치 전후 알파차단제를 사용하고 일정 시간이 지나면 요도 도관을 제거(급성요폐 후 2-7일)한 후 자가 배뇨를 시키는 방법이 제안되고 있다[2,3]. 과거에는 전립선비대증에 의한 급성요폐의 일차적 치료로 조기에 경요도전립선절제술이 많이 시행되었으며 이것이 하부요로증상의 가장 뚜렷한 호전을 가져 오는 것으로 알려져 있었다[4]. 하지만 경요도전립선절제술 자체가 갖고 있는 합병증 및 위험성이 문제가 되었다[5]. Murray 등[6]이 급성요폐 환자를 대상으로 요역동학검사를 시행한 결과 23%에서 전립선절제술이 필요하지 않았다고 기술하였으며, Pickard 등[7]은 경요도전립선절제술을 시행 받은 환자의 약 9.2%에서 술 후 자가 배뇨를 하지 못해 요도 도관 유치 및 청결간헐적자가도뇨를 시행하여야 하고 이 중 0.9%가 영구적인 요도 도관 유치를 해야 하는 것으로 보고하면서 급성요폐가 있었던 환자에서의 전립선절제술은 술 후 합병증의 위험이 크다고 보고하였다.

전립선비대증으로 인한 급성요폐의 초기 치료로 일시적 요도 도관 유치와 알파차단제 사용 후 자가 배뇨를 시키는 방법이 많이 쓰이는 것은 술기의 간단함과 경제적 이득 및 조기에 경요도전립선절제술을 시행함으로써 발생할 수 있는 합병증 및 위험성을 피하고자 함이다. Manikandan 등[8]은 영국의 비뇨기과 의사 264명을 대상으로 전립선비대증으로 인한 급성요폐의 초기 치료에 대한 설문조사를 한 결과 98%가 일시적 요도 도관 유치법을 사용하는 것으로 나타났으며 70.5%가

요도 도관 유치와 동시에 알파차단제를 사용하였다고 보고하였다. 또한 Taube와 Gajraj[9]의 연구 그리고 Kumer 등[10]의 연구에서는 급성요폐의 초기 치료로서 요도 도관을 유치하고 자가 배뇨가 성공한 경우 적은 수의 환자들에서만 급성요폐가 재발하는 것으로 보고하고 있다. 따라서 급성요폐 환자에서 요도 도관 유치 후 자가 배뇨가 성공했다면 전립선비대증의 수술적 치료를 지연시키거나 피할 수 있을 것이라 보고하였다.

급성요폐 시 요도 도관 제거 시도의 성패에 영향을 미치는 인자로서 환자의 정체 소변량이 적은 경우[11], 전립선 크기가 작은 경우 및 급성요폐 전 알파차단제를 복용한 적이 없는 경우에 TWOC의 더 높은 성공률을 기대할 수 있다고 보고하였다[12,13]. 또한 Kim 등은 58세 이하의 젊은 환자에서 급성요폐가 발생했을 때 일차적으로 TWOC를 고려해 볼 수 있을 것이라 보고하였다[14]. TWOC의 실패 인자로 고령의 연령, 이전의 척추 수술을 보고한 국내 연구도 있다[15].

● 근거표

KQ 9	
Reference	1. Kurita Y, Masuda H, Terada H, Suzuki K, Fujita K. Transition zone index as a risk factor for acute urinary retention in benign prostatic hyperplasia. Urology 1998;51:595-600.
Study type	Retrospective
Patients	331
Purpose of Study	To examine the efficacy of various parameters obtained by transrectal ultrasonography (TRUS) as predictors of the onset of acute urinary retention in patients with benign prostatic hyperplasia (BPH).
Study Results	There were significant differences in the American Urological Association (AUA) symptom score, total prostate volume, TZ volume, TZ index, and PCAR between patients with and without acute urinary retention, but no significant differences in age and quality of life score. In patients with acute urinary retention, the area under the ROC curve was 0.924 for the TZ index, 0.834 for the TZ volume, 0.753 for the PCAR, 0.684 for the total prostate volume, and 0.628 for the AUA symptom score.
Level of Study	4
Reference	2. Lucas MG, Stephenson TP, Nargund V. Tamsulosin in the management of patients in acute urinary retention from benign prostatic hyperplasia. BJU Int 2005;95:354-7.
Study type	RCT
Patients	149

Purpose of Study	To evaluate the efficacy of tamsulosin compared to placebo for treating catheterized patients with acute urinary retention (AUR) caused by benign prostatic hyperplasia (BPH), by comparing the numbers of patients who voided successfully after removing their catheter.
Study Results	In all, 149 men (mean age 69.4 years) were randomly assigned to receive tamsulosin (75) or placebo (74); eight were not evaluable, so the intent-to-treat population was 141 men. Thirty-four men taking tamsulosin and 18 taking placebo did not require re-catheterization on the day of the trial without catheter (48% and 26% respectively, P = 0.011; odds ratio 2.47, 95% confidence interval, CI, 1.23-4.97). Success using free-flow variables was also higher in the men who received tamsulosin, at 37 (52%) vs 24 (34%) on placebo (P = 0.019; odds ratio 2.34, 95% CI 1.15-4.75). Withdrawals were high (120 men, 81%), mostly because of a need for re-catheterization (89 men, 60%). Dizziness and somnolence occurred in seven (10%) and four (6%) men who received tamsulosin, and two (3%) who received placebo, but overall the incidence of adverse events was similar in the two groups. One patient died from carcinomatosis.
Level of Study	2
Reference	3. McNeill SA, Hargreave TB, Roehrborn CG. Alfaur study group. Alfuzosin 10 mg once daily in the management of acute urinary retention: Results of a double-blind placebo-controlled study. Urology 2005;65:83-9.
Study type	RCT
Patients	360
Purpose of Study	To study the impact of alfuzosin 10 mg once daily (OD) on the outcome of a trial without catheter (TWOC) after a first episode of acute urinary retention (AUR) related to benign prostatic hyperplasia (BPH) and the subsequent management of BPH in these patients.
Study Results	Alfuzosin significantly increased the successful TWOC rate (146 of 236, 61.9%) compared with placebo (58 of 121, 47.9%; P = 0.012). In the second phase, 14 (17.1%) of the 82 alfuzosin-treated patients versus 20 (24.1%) of the 83 placebo-treated patients required BPH surgery, 5 (36%) of 14 versus 13 (65%) of 20 within 1 month, and 8 (57%) of 14 versus 17 (85%) of 20 within 3 months of treatment. Emergency surgery because of AUR relapse was the main cause of failure in both groups (11 [78.6%] of 14 in the alfuzosin group and 16 [80.0%] of 20 in the placebo group). Compared with placebo, alfuzosin improved the Kaplan-Meier survival rates by 9.6% (P = 0.04), 11.4% (P = 0.04), and 8.3% (P = 0.20), with surgical risk reductions of 61%, 52%, and 29% at 1, 3, and 6 months of treatment, respectively. High prostate-specific antigen values and the post-TWOC residual urine volume significantly increased the risk of AUR relapse and BPH surgery. Alfuzosin 10 mg OD was well tolerated.
Level of Study	2
Reference	4. The pathophysiology of lower urinary tract symptoms in the ageing male population. Br J Urol 1998;81(Suppl 1):29-33.
Study type	retrospective
Patients	3,885
Purpose of Study	To evaluate the immediate and postoperative complication of transurethral resection of prostate

Study Results	The mortality rate for transurethral prostatectomy was 0.2 per cent in 3,885 patients reviewed retrospectively. The immediate postoperative morbidity rate was 18 per cent. Increased morbidity was found in patients with a resection time of more than 90 minutes, gland size of more than 45 gm., acute urinary retention and patient age greater than 80 years, and in the black population. Of the patients 77 per cent had significant pre-existing medical problems. Operative mortality, significant morbidity and hospital stay were reduced in comparison to studies done 15 and 30 years ago.
Level of Study	4
Reference	6. Murray K, Massey A, Feneley RC. Acute urinary retention-a urodynamic assessment. Br J Urol 1984;56:468-73.
Study type	Prospective
Patients	30
Purpose of Study	Thirty male patients with acute urinary retention were studied by standard urodynamic techniques on admission to hospital. Ten individuals also underwent cystography and sequential urodynamic testing over 96 h.
Study Results	Twenty-three per cent of patients did not require subsequent prostatectomy. Inability to initiate a voiding contraction during cystometry at the time of admission was associated with a prolonged duration of retention and a greater retained volume. The internal urethral meatus is closed in retention, and release of the retention results in an increase in profile length and maximum urethral closure pressure and a decrease in maximum urethral pressure. Free catheter drainage was associated with a reduction in bladder capacity and the appearance of detrusor instability.
Level of Study	3
Reference	7. Pickard R, Emberton M, Neal DE. The management of men with acute urinary retention. National Prostatectomy Audit Group. Br J Urol 1998;81:712-20.
Study type	Prospective study
Patients	3,966
Purpose of Study	To determine the outcome of men with acute urinary retention undergoing prostatectomy and to assess whether discharge with a catheter before subsequent planned re-admission for prostatectomy had an adverse effect on outcome.
Study Results	Compared with those who underwent elective prostatectomy for symptoms alone, men presenting with acute retention had an excess risk of death at 30 days (relative risk [RR], 26.6, 95% confidence interval [CI], 3.5-204.5) and at 90 days after operation (RR 4.4, 95% CI 2.5-7.6), and an increased risk of perioperative complications. Although men with retention were older, had larger glands and had more comorbidity, these factors did not totally explain the excess risk. The final symptomatic outcome of men with acute retention was no different from that of men presenting for elective treatment. Men with retention who were managed by initial catheterization, sent home and subsequently re-admitted for planned operation had similar pretreatment characteristics, post-operative complications and outcomes to those who were kept in hospital throughout, although the men kept in hospital had a total increased length of stay.

Level of Study	3
Reference	8. Manikandan R, Srirangam SJ, O'Reilly PH, Collins GN. Management of acute urinary retention secondary to benign prostatic hyperplasia in the UK: a national survey. BJU Int 2004;93:84-8.
Study type	Retrospective
Patients	270
Purpose of Study	To analyse current practice in the management of acute urinary retention (AUR) secondary to benign prostatic hyperplasia (BPH) in the UK, and to assess how much of this is evidence-based
Study Results	We received 270 (66%) replies, of which six were excluded because they were from subspeciality interests (e.g. paediatric urology) or had ambiguous answers; 264 (64%) were therefore available for analysis. Urethral catheterization was the initial management of choice (98%), failing which a suprapubic catheter was inserted. Two-thirds (65.5%) admitted the patient after catheterization. Most consultants initiated alpha-blockers (70.5%), with 64% (118) of these using a TWOC 2 days after starting them. One failed TWOC was an indication for transurethral resection of the prostate for 192 (72.8%), with 136 (49.8%) re-admitting the patient for surgery later. Routine follow-up after a successful TWOC was advocated by 77.3%. Just over half the respondents (52.6%) felt that there was no need for uniform guidelines in the management of AUR secondary to BPH.
Level of Study	5
Reference	9. Taube M, Gajraj H. Trial without catheter following acute retention of urine. Br J Urol 1989;63:180-2.
Study type	prospective
Patients	60
Purpose of Study	A total of 60 patients with acute urinary retention were studied to establish whether a trial without a catheter was justified and to identify subgroups of patients most likely to benefit from this practice
Study Results	17 patients urinated satisfactorily after removal of the catheter. Re-establishment of micturition was not associated with the length of history or severity of symptoms of prostatism, with age or the presence of urinary tract infection. The mean retained volume of urine in patients with a satisfactory result was 786 ml and 1,069 ml in the failures. Of the 34 patients with retained volumes of less than 900 ml, 15 were successful in re-establishing micturition compared with 2 of 26 of those with retained volumes greater than 900 ml. The time of catheter removal was not important. The 17 successful patients were reviewed 6 months later. None reported further urinary retention; 6 had required prostatectomy for severe symptoms, 6 had minor symptoms and 5 were symptomless. It was concluded that a trial without a catheter is worthwhile, since 11 of 60 patients had not required surgery, but it should be avoided in patients with a residual volume exceeding 900 ml.
Level of Study	3
Reference	10. Kumar V, Marr C, Bhuvangiri A, Irwin P. A prospective study of conservatively managed acute urinary retention: prostate size matters. BJU Int 2000;86:816-9.

Study type	Prospective
Patients	40
Purpose of Study	To evaluate in a prospective study the medium- to long-term outcome of a policy of conservatively managing acute urinary retention (AUR), arising solely by bladder outlet obstruction caused by benign prostatic enlargement (BPE), and to identify the factors favouring a positive outcome of a trial without catheter (TWOC).
Study Results	Of the 40 men with AUR, 22 (55%) voided spontaneously after removing the catheter and continued to do so with mean peak flow rates of 12.2 mL/s and mean PVRs of 69.6 mL over a follow-up of 8-24 months. These patients remained asymptomatic, with a mean IPSS of 5.2 and quality-of-life score of 0.9. These men had a mean prostatic size of 15.9 g and a mean catheterized residual volume of 814 mL, while in those who had an unsuccessful TWOC the mean prostate size was 27.5 g (P = 0.006) and a mean catheterized residual volume of 1062 mL (P = 0.09). Prostate size as assessed by the DRE was the most significant factor in predicting the outcome of a TWOC.
Level of Study	3
Reference	11. Ko YH, Kim JW, Kang SG, Jang HA, Kang SH, Park HS, et al. The efficacy of in-and-out catheterization as a way of trial without catheterization strategy for treatment of acute urinary retention induced by benign prostate hyperplasia: variables predicting success outcome. Neurourol Urodyn 2012;31:460-4.
Study type	retrospective
Patients	515
Purpose of Study	To evaluate the efficacy and proper use of in-and-out catheterization as a strategy for trial without catheterization (TWOC) for treatment of acute urinary retention (AUR)
Study Results	TWOC success rate was 25.1% for Group 1 and 30.3% for Group 2. In successful cases, age, retention volume, and prostate sizes were significantly lower than those of failure counterparts in both Groups 1 and 2. Among these, age and retention volume were finally selected for LDA. When comparing successful cases, these two were significantly lower in Group 1 than Group 2. LDA showed an 81.6% hit ratio for cases with successful TWOC. In a prospective trial of 28 patients, using an equation from LDA, five of seven patients in Group 1 (71.4%) and 16 of 21 patients (76.2%) in Group 2 succeeded in their initial TWOC.
Level of Study	4
Reference	12. Park SH, Kwon TG, Kim DY, Park CH, Seo JH, Lee JH, et al. The factors that influence the clinical outcomes after trial without catheter for acute urinary retention due to benign prostatic hyperplasia: a multicenter trial. Kor J Uro 2006;47:1074-8.
Study type	Retrospective
Patients	455
Purpose of Study	Benign prostatic hyperplasia (BPH) is a common problem that's experienced by aging men, and it can lead to serious outcomes, including acute urinary retention (AUR). We studied the factors that influence the clinical outcomes after trial without catheter (TWOC) for AUR due to BPH.

Study Results	From the 292 cases of group I and the 163 cases of group II, the multivariate analysis revealed statistically significant differences in the retention volume (p-0.01), the prostate volume (p-0.01) and the previous use of α-blockers before AUR (p-0.01). The prostate volume, retention volume and previous use of α-blockers before AUR were thought to influence the clinical outcomes of TWOC for the BPH patients with AUR, and these factors should be considered in future treatment planning
Level of Study	4
Reference	13. Park KS, Kim SH, Ahn SG, Lee SJ, Ha US, Koh JS, et al. Analysis of the treatment of two types of acute urinary retention. Korean J Urol 2012;53:843-7.
Study type	299
Patients	retrospective
Purpose of Study	This study analyzed the type of acute urinary retention (AUR) and evaluated the treatments used, including trial without catheter (TWOC)
Study Results	Of 299 men with AUR, 160 (54%) had spontaneous AUR and 139 (46%) had precipitated AUR. Compared with group P, patients in group S were more likely to be treated by surgery, either immediately (16.9% vs. 3.6%, p<0.05) or after prolonged catheterization (42.2% vs. 29.1%, p<0.05). The success rate of TWOC was lower in men of older ages (≥70 years) and in those with enlarged prostates (≥50 ml), higher PSA levels (≥3 ng/ml), and a large drained volume at catheterization (≥1,000 ml).
Level of Study	4
Reference	14. Kim MJ, Lee JG, Cheon J. The factors that influence the success rate of treatment without using a catheter for the management of acute urinary retention: comparison of in-and-out catheterization and foley indwelling catheterization. Korean J Urol 2008;49:337-42.
Study type	127
Patients	retrospective
Purpose of Study	Acute urinary retention (AUR) is a serious outcome of benign prostatic hyperplasia (BPH). Although Foley indwelling catheterization is a standard treatment for the conservative management of AUR, we studied the success rate of in-and-out catheterization and the factors that favor a positive outcome of a trial treatment without using a catheter (TWOC)
Study Results	Of the 62 patients who underwent in-and-out catheterization, 30 had no further episodes of AUR during 1-year follow up (group I) and the other patients had repeated episodes (group II). For the clinical parameters, only the retained urine volume was significantly difference between the two groups. The multivariate analysis revealed that the statistically significant influencing factor was urinary retention volume (p<0.01).
Level of Study	4
Reference	15. Lee KS, Lim KH, Kim SJ, Choi HJ, Noh DH, Lee HW, et al. Predictors of successful trial without catheter for postoperative urinary retention following non-urological surgery. Int Neurourol J 2011;15:158-65.

Study type	104
Patients	retrospective
Purpose of Study	To investigate the success rate of trial without catheter (TWOC) for postoperative urinary retention (POUR) after non-urological surgery and to determine predictors of successful TWOC.
Study Results	The mean age of the patients was 65.2 (range, 23 to 92) years. There were 45 male and 59 female patients. Intraoperative indwelling catheterization was performed in 69 (66.3%) patients. Mean duration of indwelling catheterization for POUR was 5.0 (range, 3.0 to 7.0) days and 83 (79.8%) patients received medication with an alpha-blocker. A successful TWOC was observed in 70 (67.4%) patients. The mean age of the patients with failure of TWOC was significantly higher than that of the patients with successful TWOC. The percentages of female patients, spinal surgery, and prone position during surgery in patients with unsuccessful TWOC were higher than in those with successful TWOC. In the multivariate logistic regression analysis, age and location of surgery (spine vs. non-spine) were the independent predictors of successful TWOC for POUR.
Level of Study	4

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4. Lepor H. The pathophysiology of lower urinary tract symptoms in the ageing male population. Br J Urol 1998;81(Suppl 1):29-33.
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7. Pickard R, Emberton M, Neal DE. The management of men with acute urinary retention. National Prostatectomy Audit Group. Br J Urol 1998;81:712-20.
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catheter for acute urinary retention due to benign prostatic hyperplasia: a multicenter trial. Kor J Uro 2006;47:1074-8.

13. Park KS, Kim SH, Ahn SG, Lee SJ, Ha US, Koh JS, et al. Analysis of the treatment of two types of acute urinary retention. Korean J Urol 2012;53:843-7.
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15. Lee KS, Lim KH, Kim SJ, Choi HJ, Noh DH, Lee HW, et al. Predictors of successful trial without catheter for postoperative urinary retention following non-urological surgery. Int Neurourol J 2011;15:158-65.

KQ 10. 전립선비대증 환자에서 경요도전립선절제술은 개복전립선절제술에 비해서 우선적으로 고려되어야 하는가?

권고사항	권고수준	근거수준
10-1. 경요도전립선절제술은 전립선비대증 수술에 우선적으로 고려하여야 한다.	Strong	C
10-2. 70 g 이상의 큰 전립선비대증 환자에서 경요도를 통한 내시경 수술은 개복전립선수술과 함께 1차 수술법으로 고려할 수 있다.	Strong	A

경요도전립선절제술은 전립선 막힘으로 인한 하부요로증상에 대한 가장 대표적인 수술적 치료방법이다. 1920년대에 개발된 이후 장비와 술기의 발전을 거듭하여 왔으며, 그동안 많은 약물치료법과 여러 수술적 치료법이 개발되었지만 아직도 양성전립선비대증의 수술 치료 중 가장 기본이 되는 방법(gold standard)으로 여겨지고 있다[1-3]. 중등도 이상의 하부요로증상이 있는 경우 수술을 고려할 수 있으며 경요도전립선절제술 후 환자의 78-96%에서 증상이 호전되었고, 85%에서 증상점수가 감소하였다. 경요도절제기구와 술기의 발달로 경요도전립선절제술 후의 출혈 등 합병증이 현저히 감소하였다.

개복전립선절제술은 TURP에 비해서 재치료율이 낮고 전립선 선종을 좀 더 완전하게 제거할 수 있으며, TURP 환자의 약 2%에서 발생하는 희석성 저나트륨혈증의 발생도 피할 수 있다는 장점이 있다[4-6]. 단점이라면 절개를 해야 하므로 경요도전립선절제술보다 입원 및 회복기간이 길고 수술 전후 출혈의 가능성도 높다는 점이다. 개복전립선절제술은 폐색조직의 크기가 클 경우(75 g 이상)뿐 아니라, 큰 방광게실이 동반된 경우, 큰 방광결석이 있어서 요도를 통해서 제거가 곤란한 경우, 정형외과적인 문제로 경요도전립선절제술의 자세를 취할 수 없는 경우 등에서 고려할 수 있다. 최근 Giulianelli 등[7]은 100 g이 넘는 큰 전립선 크기에서도 양극성 경요도전립선절제술이 개복전립선절제술과 비슷한 정도의 치료 효과가 있음을 보고하였다[8-10]. 또한 최근 홀뮴 레이저를 이용한 enucleation이 70 g 이상의 큰 전립선비대증에 효과가 있음이 보고되었다[11]. 비록 큰 전립선비대증 환자에서 경요도전립선절제술과 개복전립선절제술 중 어느 것이 우월한지에 대한 자료는 부족한 실정이나 전립선비대증의 일차적 수술 치료로 우선적으로 경요도를 통한 내시경 수술을 고

려해야 할 것이다[12].

● 근거표

KQ 10	
Reference	2. Baazeem A, Elhilali MM. Surgical management of benign prostatic hyperplasia: current evidence. Nat Clin Pract Urol 2008;5:540-9.
Study type	Review
Patients	
Purpose of Study	Benign prostatic hyperplasia (BPH) is one of the most common male urological disorders. The surgical management of BPH is evolving at a rapid rate, with several new procedures available that challenge transurethral resection of the prostate as the standard treatment in the surgical management of small to medium sized glands.
Study Results	The new procedures aim to achieve results comparable to transurethral resection of the prostate while minimizing morbidity and cost. In this Review, we discuss some of the current surgical options for the treatment of BPH that seem popular in the literature.
Level of Study	5
Reference	3. Borboroglu PG, Kane CJ, Ward JF, et al. Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999;162:1307-10.
Study type	Retrospective study
Patients	520
Purpose of Study	We compare the morbidity, mortality, hospitalization and urethral catheter time of contemporary transurethral prostatectomy to historical series, and evaluate recent trends in hospitalization and urethral catheter time during the last 8 years
Study Results	A total of 520 patients were identified with an average age of 67 years (range 44 to 89). Significant co-morbidity (2 or more co-morbid disease processes) was identified preoperatively in 30.3% of the patients. The most common indications for transurethral prostatectomy were lower urinary tract symptoms (80.9%) and urinary retention (15.2%). Average preoperative International Prostate Symptom Score was 23.8. Average weight of resected tissue was 18.8 gm. There was no perioperative patient mortality. Blood transfusion rate was 0.4%. The rate of intraoperative and immediate postoperative complications was 2.5% and 10.8%, respectively. Average hospital stay was 2.4 days, and 1.1 from 1997 through 1998. The rate of late postoperative complication was 8.5% and the average postoperative symptom score was 6.4 with an average followup of 42 months (range 6 to 84).
Level of Study	4
Reference	4. Tubaro A, Carter S, Hind A, et al. A prospective study of the safety and efficacy of suprapubic transvesical prostatectomy in patients with benign prostatic hyperplasia. J Urol 2001;166:172-6.

Study type	prospective
Patients	32
Purpose of Study	We investigate the safety and efficacy of suprapubic transvesical prostatectomy, and the change in bladder wall thickness after surgery.
Study Results	An average of 63 gm. prostate adenoma were enucleated at surgery. An indwelling catheter was required for an average plus or minus standard deviation of 5.4 +/- 2.6 days after treatment. The International Prostate Symptom Score decreased from 19.9 +/- 4.4 to 1.5 +/- 2.7 and the quality of life score decreased from 4.9 +/- 1.0 to 0.2 +/- 0.4 at year 1, respectively. Maximum flow rate improved from 9.1 +/- 5.3 to 29.0 +/- 8.9 ml. per second. Residual urine decreased from 128 +/- 113 to 8 +/- 18 ml. Before surgery 30 patients had obstruction and 2 were in the equivocal zone of the International Continence Society nomogram. At 6 months after prostatectomy 30 patients did not have obstruction, and 2 who were subsequently operated on for bladder neck sclerosis were equivocal and had obstruction, respectively. No patient had significant postoperative bleeding and no heterologous blood transfusions were required. There were 4 men who had urinary tract infection and 1 who had wound infection. A slight decrease in erectile function was observed 6 weeks postoperatively, and no change in patient libido and quality of sex life was reported. The total complication rate was 31.3%. The bladder was unstable in 7 men before and 3 after surgery. A significant decrease in bladder wall thickness was observed from 5.2 +/- 0.7 at baseline to 2.9 +/- 0.9 mm. at year 1 postoperatively.
Level of Study	3
Reference	5. Mearini E, Marzi M, Mearini L, et al. Open prostatectomy in benign prostatic hyperplasia: 10-year experience in Italy. Eur Urol 1998;34:480-5.
Study type	review
Patients	
Purpose of Study	This study reports the experience of 47 Italian urology units together with the urology unit at the University of Perugia concerning open surgery in the management of benign prostatic hyperplasia (BPH).
Study Results	Until 20-25 years ago, open surgery was the most common approach. In the late 1970s the development of endoscopes and their methodology has led to a gradual reduction in open surgery operations, which decreased rapidly with the introduction of mini-invasive endoscopic techniques. Therefore, open surgery for BPH is declining, though still performed. Skill in traditional surgery is mandatory because, until an alternative is devised, indications for open surgery still exist and cannot be ignored. The survey shows the indications and contraindications, complications and results of a 10-year nationwide experience. Guidelines for open surgery in patients with BPH have been drawn up.
Level of Study	5
Reference	6. Serretta V, Morgia G, Fondacaro L, et al. Open prostatectomy for benign prostatic enlargement in southern Europe in the late 1990s: a contemporary series of 1800 interventions. Urology 2002;60:623-7.
Study type	retrospective

Patients	5,636
Purpose of Study	Contemporary series of open prostatectomies from Western countries are rare. Frequently, the analysis of the outcome of open prostatectomy refers to old experiences or to series from developing countries. Any comparison with transurethral resection of the prostate can be invalidated by complications of open surgery because of the lack of an adequate healthcare system and technology.
Study Results	Twenty-six units (72.3%) replied. Of 31,558 patients treated for symptomatic benign prostatic hyperplasia, 5636 underwent surgery. Open prostatectomy (n = 1804) accounted for 32% of all surgical treatment. The median prostate volume was 75 cm(3) and the median serum prostate-specific antigen level was 3.7 ng/mL. The postoperative median hospitalization time was 7 days. Concomitant low urinary tract disease was present in 25% of the patients. Severe bleeding occurred in 11.6% of open prostatectomies. Blood transfusions were given in 8.2% of cases. Sepsis was reported in 8.6% of the patients. Reinterventions, within 2 years, mainly due to bladder neck stenosis, were reported in 3.6% of cases.
Level of Study	5
Reference	7. Giulianelli R, Brunori S, Gentile BC, Vincenti G, Nardoni S, Pisanti F, et al. Comparative randomized study on the efficaciousness of treatment of BOO due to BPH in patients with prostate up to 100 gr by endoscopic gyrus prostate resection versus open prostatectomy. Preliminary data. Arch Ital Urol Androl 2011;83:88-94.
Study type	RCT
Patients	140
Purpose of Study	Aim of this study was to evaluate efficacy and safety of Bipolar TURP (Gyrus electro surgical system) versus standard open prostatectomy in patients with lower urinary tract symptoms (LUTS) due to bladder outlet obstruction (BOO) with markedly enlarged glands refractory to medical therapy.
Study Results	Comparative data on IPSS symptom score, IIEF-5 and QoI, PSA, peak urinary flow rates and post-void residual urine volume in the 2 groups were similar but showed a significative improvement with respect to baseline value. Postoperative haemoglobin levels, postoperative catheterization, hospital stay and 3-yr overall surgical re-treatment-free rate were significantly better in the Bipolar group.
Level of Study	2
Reference	8. Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomised clinical trial. European Urology 2008;53:160-6.
Study type	RCT
Patients	46
Purpose of Study	To report 5-year follow-up results of a randomised clinical trial comparing holmium laser enucleation of the prostate (HoLEP) with open prostatectomy (OP).

Study Results	Five years postoperatively, a total of 46 patients (38.3%) were lost to follow-up or had to be excluded from the study. All the remaining 74 patients (42 HoLEP vs. 32 OP patients, p=0.11) had undergone the 5-yr follow-up assessments. Mean AUA-SS was 3.0 in both groups (p=0.98), mean Qmax was 24.4 ml/s in both groups (p=0.97) and PVRU volume was 11 ml in the HoLEP and 5 ml in the OP group (p=0.25). Late complications consisted of urethral strictures and bladder-neck contractures; reoperation rates were 5% in the HoLEP and 6.7% in the OP group (p=1.0). No patient developed benign prostatic hyperplasia recurrence.
Level of Study	2
Reference	9. Naspro R, Suardi N, Salonia A, Scattoni V, Guazzoni G, Colombo R, et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates >70 g: 24-month follow-up. European Urology 2006;50:563-8.
Study type	RCT
Patients	80
Purpose of Study	Prospectively evaluate perioperative outcomes and 2-yr follow-up after holmium laser enucleation (HoLEP) and standard open prostatectomy (OP) for treating benign prostatic hyperplasia-related obstructed voiding symptoms, with prostates >70 g.
Study Results	Operating room time was significantly shorter for the OP group (72.09+/-21.22 min vs. 58.31+/-11.95 min, p<0.0001); catheter removal (1.5+/-1.07 d and 4.1+/-0.5 d, p<0.001) and hospital stay (2.7+/-1.1 d vs. 5.4+/-1.05 d, p<0.001) were shorter in the HoLEP group. Blood loss was less and blood transfusions fewer in the HoLEP group (p<0.001). In both groups urodynamic and uroflowmetry findings improved from baseline, were still evident at the 24-mo follow-up, and were comparable between the two groups. Late complications were also comparable.
Level of Study	2
Reference	10. Skolarikos A, Papachristou C, Athanasiadis G, Chalikopoulos D, Deliveliotis C, Alivizatos G. Eighteen-month results of a randomized prospective study comparing transurethral photoselective vaporization with transvesical open enucleation for prostatic adenomas greater than 80 cc. Journal of Endourology 2008;22:2333-40.
Study type	RCT
Patients	125
Purpose of Study	This is a prospective randomized study showing that for large prostatic adenomas, photoselective vaporization of the prostate requires less blood transfusions, shorter catheterization time and shorter hospital stay compared to open prostatectomy, while achieving similar functional results at the same time
Study Results	Longer length of operation time, shorter length of catheterization and hospital stay were experienced by patients who underwent PVP. Although patients who underwent OP showed a higher transfusion rate, adverse events in general were minor and of similar profile in both groups. All functional parameters improved significantly compared to baseline values in both groups. There was no difference in IPSS between the two groups at 3, 6, 12, and 18 months postoperatively. Patients who underwent OP scored better in the IPSS-Quality of life score at 18 months postoperatively.

Study Results	At 18 months there were no significant differences between the two groups in the Qmax, post void residual urine volume and in the International Index for Erectile function-5 questionnaire. At three months prostate volume was significantly lower in the OP group and remained as such throughout follow-up.
Level of Study	2
Reference	11. Chen H, Tang P, Ou R, Deng X, Xie K. Holmium laser enucleation versus open prostatectomy for large volume benign prostatic hyperplasia: a meta-analysis of the therapeutic effect and safety. Nan Fang Yi Ke Da Xue Xue Bao 2012;32:882-5.
Study type	Metanalysis
Patients	
Purpose of Study	To compare holmium laser enucleation (HoLEP) versus open prostatectomy (OP) for large volume benign prostatic hyperplasia.
Study Results	Three RCTs were included in the analysis. No significant differences were found in IPSS or Qmax between HoLEP and OP (P>0.05). Compared with OP, HoLEP was associated with significantly less blood loss, a shorter catheterization time and a shorter hospital stay, but a longer operating time. HoLEP and OP were similar in terms of urethral stricture, stress incontinence, transfusion requirement and the rate of reintervention.
Level of Study	1
Reference	12. Lee SW, Choi JB, Lee KS, Kim TH, Son H, Jung TY, et al. Transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement: a quality and meta-analysis. Int Neurourol J. 2013;17:59-66.
Study type	meta-analysis
Patients	
Purpose of Study	Thanks to advancements in surgical techniques and instruments, many surgical modalities have been developed to replace transurethral resection of the prostate (TURP). However, TURP remains the gold standard for the surgical treatment of benign prostatic hyperplasia (BPH). We conducted a meta-analysis on the efficacy and safety of minimally invasive surgical therapies for BPH compared with TURP.
Study Results	Only 2 articles (5.56%) were assessed as having a low risk of bias by use of the Cochrane collaboration risk of bias tool. On the other hand, by use of the Jadad scale, there were 26 high-quality articles (72.22%). Furthermore, 28 articles (77.78%) were assessed as high-quality articles by use of the van Tulder scale. Holmium laser enucleation of the prostate (HoLEP) showed the highest reduction of the International Prostate Symptom Score compared with TURP (P<0.0001). Bipolar TURP, bipolar transurethral vaporization of the prostate, HoLEP, and open prostatectomy showed superior outcome in postvoid residual urine volume and maximum flow rate. The intraoperative complications of the minimally invasive surgeries had no statistically significant inferior outcomes compared with TURP. Also, there were no statistically significant differences in any of the modalities compared with TURP.
Level of Study	1

참고문헌

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2. Baazeem A, Elhilali MM. Surgical management of benign prostatic hyperplasia: current evidence. Nat Clin Pract Urol 2008;5:540-9.
3. Borboroglu PG, Kane CJ, Ward JF, et al. Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999;162:1307-10.
4. Tubaro A, Carter S, Hind A, et al. A prospective study of the safety and efficacy of suprapubic transvesical prostatectomy in patients with benign prostatic hyperplasia. J Urol 2001;166:172-6.
5. Mearini E, Marzi M, Mearini L, et al. Open prostatectomy in benign prostatic hyperplasia: 10-year experience in Italy. Eur Urol 1998;34:480-5.
6. Serretta V, Morgia G, Fondacaro L, et al. Open prostatectomy for benign prostatic enlargement in southern Europe in the late 1990s: a contemporary series of 1800 interventions. Urology 2002;60:623-7.
7. Giulianelli R, Brunori S, Gentile BC, Vincenti G, Nardoni S, Pisanti F, et al. Comparative randomized study on the efficaciousness of treatment of BOO due to BPH in patients with prostate up to 100 gr by endoscopic gyrus prostate resection versus open prostatectomy. Preliminary data. Arch Ital Urol Androl 2011;83:88-94.
8. Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomised clinical trial. European Urology 2008;53:160-6.
9. Naspro R, Suardi N, Salonia A, Scattoni V, Guazzoni G, Colombo R, et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates >70 g: 24-month follow-up. European Urology 2006;50:563-8.
10. Skolarikos A, Papachristou C, Athanasiadis G, Chalikopoulos D, Deliveliotis C, Alivizatos G. Eighteen-month results of a randomized prospective study comparing transurethral photoselective vaporization with transvesical open enucleation for prostatic adenomas greater than 80 cc. Journal of Endourology 2008;22:2333-40.
11. Chen H, Tang P, Ou R, Deng X, Xie K. Holmium laser enucleation versus open prostatectomy for large volume benign prostatic hyperplasia: a meta-analysis of the therapeutic effect and safety. Nan Fang Yi Ke Da Xue Xue Bao 2012;32:882-5.
12. Lee SW, Choi JB, Lee KS, Kim TH, Son H, Jung TY, et al. Transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement: a quality and meta-analysis. Int Neurourol J. 2013;17:59-66.

KQ 11. 전립선비대증 환자에서 심각한 기저질환 등으로 수술이 적당하지 않은 경우에는 어떠한 치료가 권장되는가?

권고사항	권고수준	근거수준
11-1. 전립선비대증 환자에서 심각한 기저질환 등으로 수술이 적당하지 않은 경우 간헐적 자가도뇨 또는 도뇨관 유치를 권장한다.	Strong	B
11-2. 전립선비대증 환자에서 심각한 기저질환 등으로 수술이 적당하지 않은 경우 TUMT 또는 TUNA를 고려할 수 있다. 그러나 장기적인 치료효과(재치료 및 증상 개선 정도)는 TURP에 비해 좋지 않다.	Strong	A
11-3. 전립선비대증 환자에서 심각한 기저질환 등으로 수술이 적당하지 않은 경우 전립선 내 약물 주입이 시도되고 있으나 임상 적용은 권고하지 않는다.	Strong	A

전립선비대증의 수술적 치료는 약물치료에도 불구하고 하부요로증상이 호전되지 않는 환자, 약물치료를 원하지 않고 적극적인 치료를 원하는 중등도 이상의 하부요로증상을 호소하는 환자, 불응성 혹은 재발성 요폐 환자, 일상생활에 지장을 줄 정도의 심한 하부요로증상 환자, 전립선비대증으로 인한 신기능의 저하, 5α환원효소억제제를 이용한 약물치료에도 불구하고 지속되는 혈뇨 환자, 그리고 방광결석 환자가 그 적응이 되고 있다. 그러나, 심각한 기저질환이 있거나 이로 인한 약물치료를 중단하기 어려운 경우(예, 항혈소판제제, 항응고제), 수술적 치료로 인한 부작용을 원치 않은 경우, 극히 고령의 환자인 경우에는 수술적 치료를 시행하기 어렵거나 선뜻 수술적 치료를 결정하기 어렵다. 이러한 환자들을 대상으로 몇 가지 방법이 소개되거나 현재 시도되고 있으며, 대표적인 방법으로 도뇨관을 이용한 배뇨[1-5], 경요도극초단파온열요법(TUMT)이나 경요도침소작술(TUNA) 등의 최소침습적 치료, stent의 삽입 그리고 ethanol이나 botulinum toxin 등의 전립선 내 약물 주입 등이 있다.

우선 도뇨관을 이용하는 경우 환자 및 보호자의 삶의 질이나 만족도, 그리고 감염 등의 부작용 측면에서 간헐적 도뇨를 우선 선택하는 것이 유리하다[2-4]. 그러나 환자 스스로 이를 시행하기 어렵거나 소변으로 인한 위생 악화 그리고 피부 질환 등이 문제가 되는 경우에는 요도 및 치골 상부

를 통한 도뇨관 유치를 고려할 수 있다.

최소 침습적 치료(예, TUMT, TUNA)를 고려하는 경우 기존 경요도전립선절제술(TURP)에 비해 합병증이 적고, 국소마취하에서도 시술이 가능하며, 치료 효과 또한 TURP와 비교하여 별다른 차이가 없다고 보고되었으나 재치료율 등 장기적인 치료효과 측면에서 다소 미흡한 점이 있음을 고려해야 한다[6-11].

최근 다른 최소 침습적 치료로 전립선 내 enthanol[12], botulinum toxin[13-15], NX-1203[16], PRX-302[17] 등의 약물 주입이나 전립선 동맥 색전술[18] 등이 시행된 연구 결과가 보고되고 있으나, 임상적 적용에는 좀 더 많은 연구가 필요한 실정이다.

Stent의 삽입을 고려하는 경우 임시적 혹은 영구적인 삽입이 가능하며, 특히 기저질환이 급성 악화를 보이며 도뇨관의 유치를 원하지 않을 경우 임시적인 stent 삽입을 고려할 수 있다. 추가로 요도를 통해 장기간 도뇨관을 유치하는 경우 이를 대신해 시행할 수 있다. 그러나 유치된 stent의 이동, 요도 상피의 증식에 의한 폐색, 회음부의 불편감 및 저장 증상의 악화 등 부작용이 발생할 수 있음을 고려해야 한다[19-20].

● 근거표

KQ 11	
Reference	1. Ghalayini IF, Al-Ghazo MA, Pickard RS. A prospective randomized trial comparing transurethral prostatic resection and clean intermittent self-catheterization in men with chronic urinary retention. BJU Int 2005;96:93-7.
Study type	RCT
Patients	41 patients
Purpose of Study	To determine whether a preliminary period of clean intermittent self catheterization (CISC) before transurethral resection of the prostate (TURP) improves bladder contractility and surgical outcome in men with chronic urinary retention (CUR), and whether pressure-flow studies (PFS) before TURP predict the outcome.
Study Results	Of the 41 patients, 17 (mean age 67 years, range 52–84) were randomized to immediate TURP and 24 (mean age 69 years, range 55–85) to CISC. There was a significant improvement in IPSS and quality of life at 6 months in both groups (P<0.001). In the CISC group there was a significant improvement in voiding and end-filling pressures, indicating recovery of bladder function (P<0.001 for each). Of the 41 men, nine (22%) with voiding pressures of ≤45 cmH2O had no significant improvement in symptoms or urodynamic variables. Detrusor overactivity was found in 17 (41%) patients, of whom six had upper tract dilatation which

Level of Study	2
Reference	2. Logan K, Shaw C, Webber I, Samuel S, Broome L. Patients' experiences of learning clean intermittent self-catheterization: A qualitative study. J Adv Nurs 2008;62:32-40.
Study type	Qualitative study
Patients	15 patients
Purpose of Study	To explore the experiences of learning to carry out clean intermittent self-catheterization and user views of service provision.
Study Results	Themes identified were psychological issues, physical problems and service interaction. The communication skills of nurses helped facilitate the learning experience. In conjunction with nurses' skills, a friendly relaxed approach alleviated embarrassment and anxiety, thus facilitating information exchange and retention of information.
Level of Study	3
Reference	3. Saint S, Lipsky BA, Baker PD, McDonald LL, Ossenkop K. Urinary catheters: What type do men and their nurses prefer? J Am Geriatr Soc1999;47:1453-7.
Study type	Qualitative study-interviews
Patients	104 patients, 99 nursing staff members
Purpose of Study	Urinary catheters are used frequently, but the relative risks and benefits of different types of devices are not clear. We sought to determine the beliefs of both older male patients and nursing staff about the relative merits and problems of condom and indwelling catheters.
Study Results	Patients were mostly older and predominantly hospitalized on the medical service. Compared with those using an indwelling catheter, patients using a condom catheter were more likely to believe that their catheter was comfortable (86 vs 58%, P = .04) and less likely to believe it was painful (14 vs 48%, P = .008) or to restrict their activity (24 vs 61%, P = .002). The nursing staff had a mean of 13 years nursing experience, and the majority worked in the nursing home unit. Most of the nursing staff respondents believed that condom catheters were less painful and restrictive for patients and were easier to apply, but they also believed that they fell off and leaked more often and required more nursing time.
Level of Study	3
Reference	4. Shaw C, Logan K, Webber I, Broome L, Samuel S. Effect of clean intermittent self-catheterization on quality of life: A qualitative study. J Adv Nurs 2008;61:641-50.
Study type	Quallitative study
Patients	15 patients
Purpose of Study	to describe the experience of people carrying out clean intermittent self-catheterization and the impact on their quality of life

Study Results	The core category consisted of two subcategories of positive and negative impacts. Positive impacts were related to improvement in lower urinary tract symptoms, whereas the negative impacts resulted from the practical difficulties encountered, and the psychological and cultural context of worry and stigma. The factors influencing variations in quality of life impacts were sex, lifestyle, frequency and duration of carrying out self-catheterization, technical difficulties, type of catheter, comorbidities and individual predispositions.
Level of Study	3
Reference	5. Jakobsson L. Indwelling catheter treatment and health-related quality of life in men with prostate cancer in comparison with men with benign prostatic hyperplasia. Scand J Caring Sci 2002;16:264-71.
Study type	Cohort study
Patients	108 patients
Purpose of Study	The aim of this study was to investigate what was felt of uneasiness when having an indwelling urinary catheter installed and while wearing it, and the problems related to catheter handling in men with prostate cancer in comparison with men with BPH. The aim was also to investigate the association between health-related quality of life (HRQOL) and SOC in the two groups
Study Results	Men with catheter experience (prostate cancer n = 71, BPH n = 37) were selected from a larger questionnaire study. Assessment was made with study-specific questions together with the QLQ C-30 assessing HRQOL and the SOC questionnaire measuring sense of coherence. Data reduction method was applied to study specific variables to determine problem patterns. Correlation between HRQOL and SOC was determined. Results showed similar problem patterns in men with prostate cancer and BPH: discomfort in wearing catheter (e.g. uneasiness 48.2%), practical and psychosocial difficulties in handling and wearing catheter (e.g. attaching catheter 32.4%) and discomfort at installation (e.g. pain 29.7%). There was lack of knowledge about wearing and practical handling of the catheter. Having a cancer diagnosis did not add to uneasiness or practical problems. Life quality was correlated to SOC (p <or= 0.001).
Level of Study	3
Reference	6. D'Ancona FC, van der Bij AK, Francisca EA, Kho H, Debruyne FM, Kiemeney LA, et al. Results of high-energy transurethral microwave thermotherapy in patients categorized according to the ameerican society of anesthesiologists operative risk classification. Urology 1999;53:322-9.
Study type	Cohort study
Patients	246 patients
Purpose of Study	To evaluate the relation between the American Society of Anesthesiologists (ASA) classification and response to transurethral microwave thermotherapy (TUMT) in patients with lower urinary tract symptoms and benign prostatic hyperplasia (BPH).
Study Results	There was a significant improvement in objective and subjective parameters at 12, 26, and 52 weeks of follow-up in both ASA 1 and 2 patients and ASA 3 and 4 patients. There was no difference in objective and subjective improvement between both groups at each point of follow-up. Objective and subjective improvement in ASA 3 and 4 patients with cardiovascular disease and ASA 3 and 4 patients with noncardiovascular disease was the same, although patients with cardiovascular disease received less energy during TUMT. Using logistic regression analysis, ASA classification was not predictive of response after high-energy TUMT.

Level of Study	3
Reference	7. de la Rosette JJ, Laguna MP, Gravas S, de Wildt MJ. Transurethral microwave thermotherapy: The gold standard for minimally invasive therapies for patients with benign prostatic hyperplasia? J Endourol 2003;17:245-51.
Study type	Meta-analysis
Patients	4 studies
Purpose of Study	Describes the status of TUMT in the treatment of lower urinary tract symptoms related to BPH, focusing on variations in the outcomes with different devices, the durability of treatment outcomes, morbidity, selection criteria, and cost. The relation of TUMT to medical management and TURP also is addressed.
Study Results	The literature supports TUMT as the only viable treatment among the minimally invasive options for BPH that have appeared during the past decade. The clinical trials report durable and significant symptomatic and objective improvement with minimum morbidity. In sum, TUMT is anesthesia free, safe and effective. Also, economic considerations favor this truly outpatient-based procedure.
Level of Study	1
Reference	8. Hill B, Belville W, Bruskewitz R, Issa M, Perez-Marrero R, Roehrborn C, et al. Transuethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. J Urol 2004;171:2336-40.
Study type	RCT
Patients	121 patients
Purpose of Study	the 5-year efficacy and safety of transurethral needle ablation of the prostate (TUNA) compared to transurethral resection of the prostate (TURP) for the treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).
Study Results	Improvement from baseline for TUNA and TURP retained statistical significance at each interval for International Prostate Symptom Score, quality of life and peak flow rate. Post-void residual volume was statistically significant at all time points for TURP and at year 5 for TUNA. The TURP group reported 41% retrograde ejaculation, while the TUNA group reported none. The incident of erectile dysfunction, incontinence and stricture formation was also greater in TURP than in TUNA cases with significantly fewer adverse events for TUNA than for TURP.
Level of Study	2
Reference	9. Mattiasson A, Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, et al. Five- year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: A prospective randomized multicenter study. Urology 2007;69:91-6.
Study type	RCT
Patients	154 patients

Purpose of Study	To compare the efficacy and safety of transurethral microwave thermotherapy (TUMT) with ProstaLund Feedback Treatment, using the CoreTherm device, with transurethral resection of the prostate (TURP) 5 years after treatment.
Study Results	Of the 154 patients, 66% completed the 60 months of follow-up. Statistically significant improvements in the TUMT and TURP groups were observed for IPSS, QOL, and Qmax at 60 months. The average values for the TUMT group were an IPSS of 7.4, QOL score of 1.1, and Qmax of 11.4 mL/s. The values for the TURP group were IPSS of 6.0, QOL score of 1.1, and Qmax of 13.6 mL/s. No statistically significant differences were found in any of these variables between the two treatment groups. In the TUMT group, 10% needed additional treatment versus 4.3% in the TURP group.
Level of Study	2
Reference	10. Bouza C, Lopez T, Magro A, Navalpotro L, Amate JM. Systemic review and meta-analysis of transurethral needle ablation in symptomatic benign prostatic hyperplasia. BMC Urol 2006;6:14.
Study type	Systemic review and meta-analysis
Patients	35 studies
Purpose of Study	To ascertain the efficacy and safety of TUNA in the treatment of BPH.
Study Results	35 studies (9 comparative, 26 non-comparative) were included. Although evidence was limited by methodological issues, the analysis of relevant outcomes indicates that while TUNA significantly improves BPH parameters with respect to baseline, it does not reach the same level of efficacy as TURP in respect to all subjective and objective variables. Further, its efficacy declines in the long-term with a rate of secondary-treatment significantly higher than of TURP [OR: 7.44 (2.47, 22.43)]. Conversely, TUNA seems to be a relatively safe technique and shows a lower rate of complications than TURP [OR:0.14 (0.05, 0.14)] with differences being particularly noteworthy in terms of postoperative bleeding and sexual disorders. Likewise, TUNA has fewer anesthetic requirements and generates a shorter hospital stay than TURP [WMD: -1.9 days (-2.75, -1.05)]. Scarce data and lack of replication of comparisons hinder the assessment of TUNA vs. other local therapies. No comparisons with medical treatment were found.
Level of Study	1
Reference	11. Hoffman RM, Monga M, Elliott SP, Macdonald R, Langsjoen J, Tacklind J, et al. Microwave thermotherapy for benign prostatic hyperplasia. Cochrane Database Syst Rev 2012:CD004135.
Study type	Systemic review
Patients	15 studies, 1,585 patients
Purpose of Study	To assess the therapeutic efficacy and safety of microwave thermotherapy techniques for treating men with symptomatic benign prostatic obstruction.
Study Results	In this update, we identified no new randomized comparisons of TUMT that provided evaluable effectiveness data. Fifteen studies involving 1,585 patients met the inclusion criteria, including six comparisons of microwave thermotherapy with TURP, eight comparisons with sham thermotherapy procedures, and one comparison with an alpha-blocker. Study durations ranged from 3 to 60 months. The mean age of participants was 66.8 years and the baseline symptom scores and urinary flow rates, which did not differ across treatment groups, demonstrated moderately severe lower urinary tract symptoms. The pooled mean urinary symptom scores decreased by 65% with TUMT and by 77% with TURP. The weighted mean difference (WMD) with 95% confidence interval (CI) for the International Prostate Symptom Score (IPSS) was -1.00 (95% CI -2.03 to -0.03), favoring TURP. The pooled mean peak urinary flow increased by

	70% with TUMT and by 119% with TURP. The WMD for peak urinary flow was 5.08 mL/s (95% CI 3.88 to 6.28 mL/s), favoring TURP. Compared to TURP, TUMT was associated with decreased risks for retrograde ejaculation, treatment for strictures, hematuria, blood transfusions, and the transurethral resection syndrome, but increased risks for dysuria, urinary retention, and retreatment for BPH symptoms. Microwave thermotherapy improved IPSS symptom scores (WMD -5.15, 95% aCI -4.26 to -6.04) and peak urinary flow (WMD 2.01 mL/s, 95% CI 0.85 to 3.16) compared with sham procedures. Microwave thermotherapy also improved IPSS symptom scores (WMD -4.20, 95% CI -3.15 to -5.25) and peak urinary flow (WMD 2.30 mL/s, 95% CI 1.47 to 3.13) in the one comparison with alpha-blockers. No studies evaluated the effects of symptom duration, patient characteristics, prostate-specific antigen levels, or prostate volume on treatment response.
Level of Study	1
Reference	12. Li Y, Zhao Q, Dong L. Efficacy and safety of ultrasound-guided transrectal ethanol injection for the treatment of benign prostatic hyperplasia in patients with high-risk comorbidities: A long-term study at a single tertiary care institution. Urology 2014;83:586-91.
Study type	Prospective cohort study
Patients	70 patients
Purpose of Study	To evaluate the efficacy and safety of ultrasound-guided transrectal ethanol injection for the treatment of benign prostatic hyperplasia (BPH) in patients with high-risk comorbidities.
Study Results	After 24 months of treatment, prostate volume, international prostate symptom score, quality of life score, and postvoid residual of patients were significantly reduced when compared with the pretreatment values (55.9 ± 16.7 vs 46.8 ± 8.1 mL, 29.3 ± 6.7 vs 9.8 ± 2.4 points, 5.3 ± 1.7 vs 1.9 ± 0.7 points, and 130.8 ± 71.5 vs 25.9 ± 12.0 mL, respectively, P <.05). Qmax significantly increased to 15.3 ± 3.2 mL/s than the pretreatment Qmax of 4.7 ± 3.1 mL/s (P = .001). Four of 36 patients who received a high dose of ethanol developed liquefaction necrosis and urinary tract injury (2 patients each). However, the subsequent 34 patients received a reduced dose of ethanol and had no complications.
Level of Study	2
Reference	13. Kuo H-C. Prostate botulinum A toxin injection-an alternative treatment for benign prostatic obstruction in poor surgical candidates. Urology 2005;65:670-4.
Study type	Prospective cohort study
Patients	10 patients
Purpose of Study	To evaluate, in a prospective study, the effectiveness of prostate injection of botulinum A toxin in patients who were poor surgical candidates. Patients with benign prostatic hyperplasia (BPH) are usually successfully treated with medical treatment or transurethral resection. However, some patients with chronic urinary retention or a large postvoid residual urine volume due to BPH are poor surgical candidates or are patients in whom medical treatment has failed.
Study Results	All patients had an improvement in spontaneous voiding after treatment. Of them, 8 had an excellent result (80%) and 2 had an improved result. Both voiding pressure and postvoid residual volume were significantly decreased after treatment. The total prostate volume was significantly reduced, and the maximal flow rate was significantly increased after treatment. The maximal effects of botulinum A toxin appeared at about 1 week and were maintained at 3 and 6 months after treatment. At 6 to 12 months (mean 9) of follow-up, no patient had had recurrence of urinary retention and the voiding condition in all patients remained at the post-treatment status. No adverse effect was noted.
Level of Study	3

Reference	14. Silva J, Silva C, Saraiva L, Silva A, Pinto R, Dinis P, et al. Intraprostatic botulinum toxin type a injection in patients unfit for surgery presenting with refractory urinary retention and benign prostatic enlargement. Effect on prostate volume and micturition resumption. Eur Urol 2008;53:153-9.
Study type	Prospective cohort study
Patients	21 patients
Purpose of Study	To evaluate the effect of intraprostatic injection of botulinum toxin A (BoNTA) on prostate volume and refractory urinary retention in patients with benign prostatic enlargement.
Study Results	Patients had a mean age of 80 _ 2 yr. Injections were done without anaesthetic support as an outpatient procedure. No significant local effects occurred. Baseline prostate volume of 70 _ 10 ml decreased to 57 _ 10 ml ($p < 0.0006$) at 1mo and to 47 _7ml ($p = 0.03$ against 1 mo) at 3 mo. At 1 mo, 16 patients (76%) could resume voiding with a mean Qmax of 9.0 _ 1.2 ml/s. At 3 mo, 17 patients (81%) voided with a meanQmax of 10.3 _ 1.4 ml/s. Residual urine was 80 _ 19 ml and 92 _ 24 ml at the two time points, respectively. Mean serum total PSA decreased from 6.0 _ 1.1 ng/ml at baseline to 5.0 _ 0.9 ng/ml at 3 mo ($p = 0.04$).
Level of Study	3
Reference	15. Marchal C, Perez JE, Herrera B, Machuca FJ, Redondo M. The use of botulinum toxin in benign prostatic hyperplasia. Neurourol Urodyn 2012;31:86-92.
Study type	Meta-analysis
Patients	24 studies
Purpose of Study	To summarize the action mechanisms of BoNT/A on experimental animals and to analyze its effectiveness according to published clinical studies
Study Results	We located 24 papers on the treatment of HBP with BoNT/A. The doses applied ranged from 100 (OnabotA) to 600 U (OnabotA and AbobotA). The IPSS score presented a mean post-treatment reduction, for all series, of 10.8 þ 2.66 points. Other significant results included the overall mean reduction in QoL score of 2.1 _ 0.62 points, and the pre and post-treatment differences in prostate volume (22.43 _ 20.2 cm^3), post-voiding residue (76.77 þ 51.72 cm^3) and PSA (1.15 þ 0.93 ng/ml). However, only two clinical trials were on sufficient quality to be selected for meta-analysis, and it was observed that the difference of the means, pre- and post-treatment of maximum flow, prostate volume, IPSS and PSA were not statistically significant (P ¼ 0.18). Neither was there any statistically significant difference between pre- and post-treatment post-voiding residue(P ¼ 0.65). In conclusion, BoNT/A alleviates lower urinary tract symptoms due to HBP, but different studies present considerable variations regarding the dose administered, inclusion criteria and follow-up time, as well as poorly defined retreatment, losses to follow up and, above all, a high degree of variability in the communication of results (with large standard deviations).
Level of Study	1
Reference	16. Andersson KE. Intraprostatic injections for lower urinary tract symptoms treatment. Curr Opin Urol 2014;24:1-7.

Study type	Systemic review
Patients	2 RCT Patient : 85
Purpose of Study	The purpose of this study is to review and discuss recently published (2013-2014) experimental and clinical studies of intraprostatic injection therapy as an alternative treatment of lower urinary tract symptoms (LUTS).
Study Results	Recent focus has been on intraprostatic injection of botulinum toxin both with regard to mechanism of action and efficacy. In contrast to the promising findings in several previous studies, a recent large, randomized, placebo-controlled trial found no differences between onabotulinumtoxin A treatment and placebo. There is little new information on the use of anhydrous ethanol and agents such as NX-1207 and PRX302, which previously have been reported to have promising effects.
Level of Study	1
Reference	17. Denmeade SR, Egerdie B, Steinhoff G, Merchant R, Abi-Habib R, Pommerville P. Phase 1 and 2 studies demonstarate the safety and efficacy of intraprostatic injection of PRX302 for the targeted treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. Eur Urol 2011;59:747-54.
Study type	Studies without consistently applied reference standards
Patients	Phase 1: 15 patients, Phase 2: 18 patients
Purpose of Study	To evaluate the safety and efficacy of PRX302 in men with moderate to severe BPH.
Study Results	Sixty percent of men in the phase 1 study and 64% of men in the phase 2 study treated with PRX302 had ≥30% improvement compared to baseline in IPSS out to day 360. Patients also experienced improvement in QoL and reduction in prostate volume out to day 360. Patients receiving ≥1 ml of PRX302 per deposit had the best response overall. PRX302 had no deleterious effect on erectile function. Adverse events were mild to moderate and transient in nature. The major study limitation was the small sample size.
Level of Study	3
Reference	18. Pisco JM, Rio Tinto H, Campos Pinheiro L, Bilhim T, Duarte M, Fernandes L, et al. Embolisation of prostatic arteries as treatment of moderate to severe lower urinary symptoms (LUTS) secondary to benign hyperplasia: Results of short- and mid-term follow-up. Eur Radiol 2013;23:2573-4.
Study type	Cohort study
Patients	255 patients
Purpose of Study	To evaluate the short- and medium-term results of prostatic arterial embolisation (PAE) for benign prostatic hyperplasia (BPH).
Study Results	PAE was technically successful in 250 patients (97.9 %). Mean follow-up, in 238 patients, was 10 months (range 1-36). Cumulative rates of clinical success were 81.9 %, 80.7 %, 77.9 %, 75.2 %, 72.0 %, 72.0 %, 72.0 % and 72.0 % at 1, 3, 6, 12, 18, 24, 30 and 36 months, respectively. There was one major complication.
Level of Study	3

Reference	19. Masood S, Djaladat H, Kouriefs C, Keen M, Palmer JH. The 12-year outcome analysis of an endourethral wallstent for treating benign prostatic hyperplasia. BJU Int 2004;94:1271-4.
Study type	Cohort study
Patients	62 patients
Purpose of Study	To evaluate the long-term results of using the Urolume(TM) endourethral prosthesis (American Medical Systems, Minnetonka, MN, USA) for managing benign prostatic hyperplasia (BPH), an alternative minimally invasive option.
Study Results	Twenty-two and 11 patients completed the 5- and 12-year follow-up, respectively. Twenty-one (34%) patients died with the stent in situ from causes unrelated to BPH and Urolume insertion. Twenty-nine (47%) stents were removed; 18 in the first 2 years, seven at 3-5 years and four at 9-10 years. Early stent explantation was primarily a result of poor case selection, or stent malposition/migration. Four stents were removed because the patient was dissatisfied. Late stent explantation was for symptom progression. At 5 years, the symptom score and PFR were 6.82 an 11.7 mL/s, respectively, compared with 20.4 and 9 mL/s at basleine ($P < 0.05$); at 12 years, the symptom score, PFR and PVR were 10.82, 11.5 mL/s and 80 mL, respectively. The mean quality of life score was 2 and no patient opted for any further treatment.
Level of Study	3
Reference	20. Armitage JN, Cathcart PJ, Rashidian A, De Nigris E, Emberton M, van der Meulen JH. Epithelializing stent for benign prostatic hyperplasia: A systematic review of the literature. J Urol 2007;177:1619-24.
Study type	Systemic review
Patients	20 studies, 990 patients
Purpose of Study	To review the literature on the effectiveness, durability and safety of the UroLume stent for men with benign prostatic hyperplasia.
Study Results	A total of 20 case series evaluated the UroLume stent in a total of 990 patients with benign prostatic hyperplasia. Of the patients 84% who were catheter dependent voided spontaneously after stent insertion. Ten studies assessed symptoms before stent insertion and at some point within 1 year after stent insertion. All reported decreases in symptom scores, including Madsen-Iversen by 7.9 to 14.3 points and International Prostate Symptom Score by 10 to 12.4 points. Peak urine flow rates increased by 4.2 to 13.1 ml per second. A total of 104 stents (16%) failed in 606 patients who were evaluable at 1 year and migration was the commonest cause of failure (38 stents or 37%). Most patients initially experienced perineal pain or irritative voiding symptoms following stent placement.
Level of Study	1

● 참고문헌

1. Ghalayini IF, Al-Ghazo MA, Pickard RS. A prospective randomized trial comparing transurethral prostatic resection and clean intermittent self-catheterization in men with chronic urinary retention. BJU Int 2005;96:93-7.
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qualitative study. J Adv Nurs 2008;62:32-40.

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17. Denmeade SR, Egerdie B, Steinhoff G, Merchant R, Abi-Habib R, Pommerville P. Phase 1 and 2 studies demonstarate the safety and efficacy of intraprostatic injection of PRX302 for the targeted treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. Eur Urol 2011;59:747-54.
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KQ 12. 전립선비대증으로 진단 받은 환자의 추적관찰에 필요한 진단적 검사는 무엇이며, 추적관찰의 기간은 어떻게 설정하여야 하는가?

권고사항	권고수준	근거수준
12-1. 전립선비대증 치료 후 추적관찰 간격과 검사의 종류는 개별 환자의 중증도와 임상지표를 고려하여 임상의사의 경험이나 판단에 따른다.	Strong	C
12-2. 전립선비대증의 진행을 확인하기 위해서는 국제전립선증상점수, 직장수지검사, 혈청 전립선특이항원검사, 요속검사, 잔뇨량 측정 그리고 전립선초음파 등을 시행한다.	Strong	C

추적관찰

전립선비대증을 진단 받은 모든 환자는 증상의 진행이 있는지, 치료 방침의 변화가 필요한지, 또는 추가적인 검사가 필요한지 확인하기 위해 추적관찰이 필요하다. 추적관찰 간격은 치료 종류에 따라 차이가 있으며, 적절한 간격에 대한 근거는 아직 부족한 실정이어서 임상의사의 경험이나 판단에 따른다.

1. 대기요법 또는 행동요법

대기요법 또는 행동요법을 시행하는 환자들은 첫 6개월째, 그 이후에는 1년마다 재평가를 통해 증상의 변화 여부 및 수술적 치료가 필요한지를 확인한다. 권장하는 검사는 국제전립선증상점수, 직장수지검사, 요속검사 그리고 잔뇨량 측정이다.

2. 알파차단제

알파차단제를 투여하는 경우, 투여 시작 후 2-6주에 추적관찰을 하여 증상 호전이 있거나 알파차단제로 인한 부작용이 없는 경우 치료를 지속할 수 있다. 이후에는 6-12개월 간격으로 추적관찰하도록 한다[1-4].

권장하는 검사는 국제전립선증상점수, 직장수지검사, 요속검사 그리고 잔뇨량 측정이다.

3. 5α환원효소억제제

5α환원효소억제제의 효과는 12–24주에 나타나므로 투여 시작 후 12–24주에 추적관찰하여 치료 반응을 확인하고 부작용 여부를 확인한다[3,5,6]. 그 이후에는 6–12개월 간격으로 추적하도록 한다.

5α환원효소억제제를 투여하는 환자의 여명이 10년 이상인 경우, 전립선암이 발견되어 치료방침이 바뀔 수 있는 경우에는 5α환원효소억제제 투여 6개월째 전립선특이항원 수치를 측정하고 이를 새로운 기준점으로 잡고 이후 연속적인 전립선특이항원 수치 측정을 통해 증가 여부를 확인하도록 한다.

권장하는 검사는 국제전립선증상점수, 직장수지검사, 요속검사, 잔뇨량 측정, 혈청전립선특이항원검사 그리고 전립선초음파 등이다.

4. 항콜린제, 데스모프레신

항콜린제를 투여하는 경우에는 증상이 안정화될 때까지는 4–6주 간격으로 추적하며 효과 및 부작용 여부를 확인한다. 증상이 안정화된 이후에는 6–12개월 간격으로 추적관찰을 권장한다.

데스모프레신을 투여하는 경우 투여 시작 후 3일, 7일, 그리고 1달째 혈중 나트륨 수치를 측정하고 이후 매 3개월마다 재확인하도록 한다. 또한 배뇨일지를 작성하여 치료 반응을 확인하도록 한다.

5. 수술치료

수술치료 이후, 도뇨관을 제거하고 4–6주 뒤 치료 결과와 조직검사 결과 확인을 위해 추적관찰하여야 한다[6–8]. 치료에 실패한 환자들은 압력요류검사를 포함한 요역동학검사를 시행하여야 한다.

권장하는 검사는 국제전립선증상점수, 직장수지검사, 요속검사 그리고 잔뇨량 측정이다.

6. 보완대체요법

아직 보완대체요법들의 효과와 지속성에 대한 확실한 증거가 미약하기 때문에 장기추적관찰이 필요하다. 추적관찰 간격은 치료방법에 따라 달라질 수 있으며 보통은 6주, 3개월, 6개월 간격으로 추적하도록 한다.

권장하는 검사는 국제전립선증상점수, 직장수지검사, 요속검사 그리고 잔뇨량 측정이다.

● 근거표

KQ 12	
Reference	1. Chung BH. Medical management for benign prostatic hyperplasia. Korean J Urol 2007;48:233-44.
Study type	Review
Patients	
Purpose of Study	To summarize our current management for benign prostatic hyperplasia
Study Results	
Level of Study	5
Reference	2. Joung JY, Park JK, Park CH, Lee JG, Chung BH, Hong SJ, et al. The role of alpha 1 (A) adrenoceptor antagonist tamsulosin for the treatment of patients with benign prostatic hyperplasia:the effect on lower urinary tract symptoms and nocturia. Korean J Urol 2006;47:1-6.
Study type	Case-control study
Patients	268 patients with BPH treated with tamsulosin at a dose of 0.2 mg/day.
Purpose of Study	effectiveness of administering alpha 1 (A)-adrenoceptor antagonist tamsulosin for the patients with benign prostatic hyperplasia
Study Results	The change of nocturnal frequency was 2.2 at baseline to 1.4 after 12 weeks of treatment.
Level of Study	4
Reference	3. Jeong DH, Park YI. Clinical experience of symptomatic management of BPH with terazosin, doxazosin or combination of terazosin and finasteride. Korean J Urol 1998;39:772-6.
Study type	Single blind case-control study
Patients	60 patients were divided 3 groups (terazosin group, doxazosin group, terazosin with finasteride group.
Purpose of Study	To compare the efficacy of terazosin, doxazosin and terazosin (alpha-1 adrenoreceptor antagonist) with finasteride (5-alpha reductase inhibitor) in the treatment of patient with benign prostatic hyperplasia
Study Results	At baseline, 1-PSS, QOL index and Qmax were 18.8+/-4.3, 3.7+/-1.0, 8.6+/-1.7 in terazosin group, 19.3+/-3.9, 3.6+/-1.0, 7.8+/-1.8 in doxazosin group, 20.1+/-4.4, 3.8+/-1.0, 72 +/-1.6 in combination group, respectively. After 12 weeks trial, 1-PSS, QOL index and Qmax were 12.0+/-2.8, 1.9+/-0.9, 11.4+/-2.8 respectively in terazosin group, 11.3+/-3.0, 1.7+/- 0.7, 10.6+/-2.6 in doxazosin group, 10.9+/-4.0, 1.8+/-0.9, 9.8+/-1.0 in combination group, respectively.
Level of Study	4

Reference	4. Chung BH, Chung HJ, Hong SJ. Long-term efficacy and safety of terazosin in the symptomatic treatment of benign prostatic hyperplasia. Korean J Androl 1999;17:45-50.
Study type	Case-control study
Patients	228 male patients aged 50 years or older who had clinical evidence of BPH
Purpose of Study	To evaluate the long-term efficacy and safety of terazosin, a selective alpha-1 blocker, in the treatment of benign prostatic hyperplasia
Study Results	The mean IPSS was reduced by 35% or greater. In the hypertensive patients, the mean systolic BP was reduced by 11.9% (-18 mmHg) and the mean diastolic BP by 16.8% (-17 mmHg), whereas in normotensive patients, the reductions were 4.0% (-5 mmHg) and 1.2% (-1 mmHg), respectively. There were no significant differences in the IPSS improvement in these two groups.
Level of Study	4
Reference	5. Cho SH, Lee SK. The experience with combination of finasteride and tamsulosin on benign prostatic hyperplasia. Korean J Urol 2003;44:1110-5.
Study type	Case-control study
Patients	210 men with symptomatic benign prostatic hyperplasia who were treated with a combination of finasteride and tamsulosin for 12 months.
Purpose of Study	To evaluate the sustained efficacy and the safety of finasteride and tamsulosin in combination in the treatment of benign prostatic hyperplasia
Study Results	Finasteride plus tamsulosin combination therapy produced statistically significant improvements in the urinary obstructive symptoms score and led to overall reduction from baseline of 9.8% in prostatic volume and 55% in serum PSA at the end of a 12-month trial. In men with prostatic volume greater than 30ml (n=28), a decrease in prostatic volume was higher than that less than 30ml (n=31) (13.1% vs. 6.9% from baseline respectively, p=0.0001, p=0.02).
Level of Study	4
Reference	6. Noh JH, Oh BR, Park YI. The efficacy of combination therapy of 5alpha-reductase inhibitor and of -adrenergic blocker in benign prostate hyperplasia. Korean J Urol 1998;39:1190-6.
Study type	Case-control study
Patients	85 patients with BPH divided into three groups: Group 1 (doxazosin 3 mg/day), Group 2 (finasteride 5 mg) and Group 3 (combination of both drugs). 6 months followup.
Purpose of Study	To evaluate the efficacy of the combination of 5 alpha -reductase inhibitor (finasteride) and alpha1-adrenergic blocker (doxazosin)
Study Results	In Group 1 and 3, IPSS were more decreased than In Group 2 immediately ($p < 0.001$). In Group 1 and 3, maximal flow rate was more increased than in group 2 immediately ($p < 0.001$)
Level of Study	4

Reference	7. Yu HS, Kim WT, Ham WS, Choi YD. Transurethral resection of prostate in benign prostatic hyperplasia patients with large prostate volume. Korean J Urol 2008;49:906-11.
Study type	Case-control study
Patients	211 patients treated with TURP in BPH with large prostate. Each group was divided by prostate volume (group 1; 60-69.9, group 2; 70-79.9, group 3; 80-89.9, group 4; 90-99.9, group 5; >100 cc of prostate volume)
Purpose of Study	To investigate the safety and efficacy of transurethral resection of the prostate in benign prostatic hyperplasia more than 60 cc
Study Results	Prostate volume, adenoma volume, resection time, Resection volume, irrigation volume of each groups were different significantly. But, resection volume/resection time and irrigation volume/ resection time were not different significantly
Level of Study	4
Reference	8. Kim HG, Lee BK, Paick SH, Lho YS. Efficacy of bipolar transurethral resection of the prostate: comparison with standard monopolar transurethral resection of the prostate. Korean J Urol 2006;47:377-80.
Study type	Case-control study
Patients	25 patients with symptomatic benign prostatic hyperplasia (BPH) who underwent TURP compared with standard monopolar TURP.
Purpose of Study	to assess the efficacy of bipolar transurethral resection of the prostate (TURP) compared with standard monopolar TURP
Study Results	The mean weight of resection was 29.7 g for the bipolar TURP and 22.5 g for the monopolar TURP. The operative time was shorter (82.5 vs 98.1 minutes, respectively), the estimated blood loss was less (252 vs 268 cc, respectively) and the mean post-operative hospital stay was shorter (5.3 vs 5.7 days, respectively) in the bipolar TURP group. However, these differences were not statistically significant. The acute complications were significant hyponatremia in one patient and clot retention in one patient after monopolar TURP, but no complications occurred after bipolar TURP. The maximal flow rate increased from 6.4 to 14.7 ml/sec in the bipolar TURP group, and it increased from 6.7 to 15.2 ml/sec in the monopolar TURP group
Level of Study	4

● 참고문헌

1. Chung BH. Medical management for benign prostatic hyperplasia. Korean J Urol 2007;48:233-44.
2. Joung JY, Park JK, Park CH, Lee JG, Chung BH, Hong SJ, et al. The role of alpha 1 (A) adrenoceptor antagonist tamsulosin for the treatment of patients with benign prostatic hyperplasia: the effect on lower urinary tract symptoms and nocturia. Korean J Urol 2006;47:1-6.

3. Jeong DH, Park YI. Clinical experience of symptomatic management of BPH with terazosin, doxazosin or combination of terazosin and finasteride. Korean J Urol 1998;39:772-6.

4. Chung BH, Chung HJ, Hong SJ. Long-term efficacy and safety of terazosin in the symptomatic treatment of benign prostatic hyperplasia. Korean J Androl 1999;17:45-50.

5. Cho SH, Lee SK. The experience with combination of finasteride and tamsulosin on benign prostatic hyperplasia. Korean J Urol 2003;44:1110-5.

6. Noh JH, Oh BR, Park YI. The efficacy of combination therapy of 5alpha-reductase inhibitor and of -adrenergic blocker in benign prostate hyperplasia. Korean J Urol 1998;39:1190-6.

7. Yu HS, Kim WT, Ham WS, Choi YD. Transurethral resection of prostate in benign prostatic hyperplasia patients with large prostate volume. Korean J Urol 2008;49:906-11.

8. Kim HG, Lee BK, Paick SH, Lho YS. Efficacy of bipolar transurethral resection of the prostate: comparison with standard monopolar transurethral resection of the prostate. Korean J Urol 2006;47:377-80.

KQ 13. 전립선비대증으로 진단 받은 환자들 중에 반드시 비뇨기과 전문의에게 의뢰해야 하는 경우는 무엇인가?

권고사항	권고수준	근거수준
13-1. 전립선비대증 환자에서 하부요로증상이 1차 약물치료로 호전되지 않는 경우에는 비뇨기과 의사에게 의뢰해야 한다.	Strong	B
13-2. 전립선비대증 환자에서 요로감염, 혈뇨, 반복적인 요폐색과 같은 하부요로증상의 객관적인 이상이나 악화 소견이 동반될 때 비뇨기과 의사에게 의뢰해야 한다.	Strong	A
13-3. 전립선비대증 환자에서 혈청 전립선특이항원검사가 정상범위를 벗어나거나 직장수지검사에서 이상소견이 관찰되는 경우 전립선암과의 감별을 위해 비뇨기과 의사에게 의뢰해야 한다.	Strong	A

전립선비대증과 이로 인한 하부요로증상의 경우 1차적인 약물치료로 많은 수의 환자들이 증상의 호전을 보일 수 있다. 특히 다뇨증이 없는 경우에 1차 약제로 추천되는 알파차단제를 기본으로 한 약물치료에 중장기적인 호전을 보이는 경우가 많은데, 만약 1차 약물치료로 호전이 되지 않고 약물 증량이나 수술적 치료가 필요하다고 판단되면 비뇨기과 의사에게 의뢰해야 한다[1].

전립선비대증의 증상이 심한 경우 약물치료의 호전이 없을 수 있으며 약물 용량의 조절, 약물의 추가, 그리고 비뇨기과적 검사(uroflowmetry, PVR, Urethrocystoscopy, TRUS 등)가 추가로 필요하므로 비뇨기과 의사에게 의뢰해야 한다. 또한 반복적인 요로감염이나 혈뇨, 높은 수치의 전립선특이항원검사 결과를 보이거나, 직장수지검사에서 이상소견을 보이는 경우에도 추가적인 비뇨기과 검사 및 조직 검사 등이 필요할 수 있으므로 우선적인 의뢰를 고려해야 한다[2-5].

이외에 약물 치료 중에도 반복적으로 요폐색이 오거나[6], 요실금이 발생하는 경우, 방광기능의 장애가 의심되는 경우에도 추가적인 비뇨기과적 검사 및 처치가 필요하다[7-10].

비록 전립선비대증이 전립선암으로 진행하는 전구단계는 아니지만 전립선비대증 환자 중에서 전립선암으로 진단 받는 경우가 많고 일부에서는 전립선암의 증상과 전립선비대증의 증상이 혼동

되기도 한다. 따라서 주기적인 혈액검사에서 전립선특이항원 수치가 높거나[11-12], 직장수지검사에서 이상소견이 있는 경우에는 비뇨기과 전문의에게 의뢰해야 한다.

또한 환자의 기저질환 혹은 기저질환과 관련된 약제들이 하부요로증상을 일으킬 만한 원인을 갖고 있을 때, 하부요로증상과 함께 비뇨기과적 증상이 동반되어 있어 비뇨기과적 신체검사가 필요한 경우, 하부요로증상으로 인해 삶의 질이 현저히 악화되는 경우에도 비뇨기과 전문의의 진찰이 권장된다. 특히 전립선특이항원 수치의 비정상적인 상승이나 직장수지검사에서 이상소견이 관찰되는 경우에는 전립선암과의 감별진단이 필요하므로 비뇨기과 전문의에게 의뢰하는 것이 필요하다[14].

● 근거표

KQ 13	
Reference	1. Abrams P, Chapple C, Khoury S, et al. Evaluation and treatment of lower urinary tract symptoms in older men. J Urol 2009;181:1779–87.
Study type	Expert opinion
Patients	
Purpose of Study	The 6th International Consultation on New Developments in Prostate Cancer and Prostate Diseases met from June 24-28, 2005 in Paris, France to review new developments in benign prostatic disease.
Study Results	The Consultation endorsed the appropriate use of the current terminology lower urinary tract symptoms/benign prostatic hyperplasia/benign prostate enlargement and benign prostatic obstruction, and recommended that terms such as "clinical benign prostatic hyperplasia" or "the benign prostatic hyperplasia patient" be abandoned, and asked the authorities to endorse the new nomenclature. The diagnostic evaluation describes recommended and optional tests, and in general places the focus on the impact (bother) of lower urinary tract symptoms on the individual patient when determining investigation and treatment. The importance of symptom assessment, impact on quality of life, physical examination and urinalysis is emphasized. The frequency volume chart is recommended when nocturia is a bothersome symptom to exclude nocturnal polyuria. The recommendations are summarized in 2 algorithms, 1 for basic management and 1 for specialized management of persistent bothersome lower urinary tract symptoms.
Level of Study	5
Reference	2. Kaplan SA. Update on the American Urological Association guidelines for the treatment of benign prostatic hyperplasia. Rev Urol 2006;8(Suppl.4):S10–17.
Study type	Expert opinion
Patients	

Purpose of Study	The updated 2003 American Urological Association (AUA) Guidelines for the treatment of benign prostatic hyperplasia (BPH) are the culmination of an exhaustive effort predicated on scientifically accepted methods of reviewing the medical literature. In this second publication of the guidelines, a multidisciplinary panel reviewed a new meta-analysis of outcome data from the BPH literature from before and after 1994
Study Results	The major differences between the 2 guidelines are the changes in our understanding of the biology of the prostate and the introduction of new therapies. The vast majority of randomized controlled trials, particularly with respect to minimally invasive therapies and progression of BPH, were performed after the release of the 1994 guidelines. Also, the most recent AUA panel carefully reviewed unpublished data to make the guidelines as timely as possible. Studies that were subsequently published included those on the value of combination medical therapy for BPH. The panel agreed on updated recommendations for the treatment of moderate-to-severe lower urinary tract symptoms associated with BPH, and diagnostic algorithms were revised. The durability and utility of the present guidelines should exceed that of its predecessor.
Level of Study	5
Reference	3. Grosse H. Frequency, localization and associated disorders in urinary calculi: analysis of 1671 autopsies in urolithiasis. Z Urol Nephrol 1990; 83:469–74.
Study type	Cross sectional study
Patients	27,133
Purpose of Study	In the area of Rügen-Stralsund a maximum value of urolithiasis and cholelithiasis was found. In 27,133 autopsies the frequency of urolithiasis was 6%. Obesity, hypertension and diabetes mellitus may increase the tendency of cholelithiasis patients to develop additional urolithiasis
Study Results	Ureteral and urinary bladder calculi are more frequently among male patients. In cases with benign prostatic hyperplasia the incidence of urolithiasis was not higher than in female patients. In the autopsy material multiple calculi and bilateral cases occur more frequently. Hypertension and increased heart weight did occur more frequently in patients suffering from oxalate lithiasis. Some of the calculi may develop in the terminal age of life
Level of Study	3
Reference	4. Wasson JH, Reda DJ, et al. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. N Engl J Med 1995;332:75–9.
Study type	RCT
Patients	556
Purpose of Study	Transurethral resection of the prostate is the most common surgical treatment for benign prostatic hyperplasia. We conducted a multicenter randomized trial to compare this surgery with watchful waiting in men with moderate symptoms of benign prostatic hyperplasia.

Study Results	Of the men randomly assigned to the surgery group, 249 underwent surgery within two weeks after the assignment. Surgery was not associated with impotence or urinary incontinence. The average follow-up period was 2.8 years. In an intention-to-treat analysis, there were 23 treatment failures in the surgery group, as compared with 47 in the watchful-waiting group (relative risk, 0.48; 95 percent confidence interval, 0.30 to 0.77). Of the men assigned to the watchful-waiting group, 65 (24 percent) underwent surgery within three years after the assignment. Surgery was associated with improvement in symptoms and in scores for urinary difficulties and interference with activities of daily living ($P < 0.001$ for all comparisons). The outcomes of surgery were best for the men who were most bothered by urinary symptoms at base line.
Level of Study	2
Reference	5. Holtgrewe HL, Mebust WK, et al. Transurethral prostatectomy: practice aspects of the dominant operation in American urology. J Urol 1989;141:248–53.
Study type	Expert opinion
Patients	
Purpose of Study	In a national survey of all American urologists transurethral prostatectomy accounted for 38 per cent of the major surgical procedures performed by the respondents.
Study Results	They regarded the operation as complex and they believe achievement of proficiency requires that more be performed during residency training than any other urological operation. Furthermore, they assigned transurethral prostatectomy a significantly higher relative value than have medical economists doing research in the field of physician reimbursement. The effect of recent legislated congressional reductions in the allowable Medicare fees for transurethral prostatectomy is discussed along with the impact of these reductions on urological patient care and the American urologist. Practice patterns and geographic variations in the costs of transurethral prostatectomy also are considered.
Level of Study	5
Reference	6. McConnell JD, Roehrborn C, et al. The long-term effects of doxazosin, finasteride and the combination on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2385–96.
Study type	RCT
Patients	2,872
Purpose of Study	We examined the effects of doxazosin, finasteride and combination therapy among men with benign prostatic hyperplasia on quality of life assessed with MOS-SF-36 (Medical Outcomes Study Short-Form 36) and 2 disease specific instruments (BII, benign prostatic hyperplasia Impact Index and I-PSS-QoL, International Prostate Symptom Score-QoL) during 4 years.
Study Results	Compared with men assigned to placebo, men assigned to doxazosin and combination experienced a statistically significant improvement in the BII at year 4. Men assigned to each of the drug groups also experienced a significant improvement in the I-PSS-QoL compared with those assigned to placebo. Considering longitudinal changes during 4 years, a significant improvement in BII and I-PSS-QoL scores was observed in men assigned to the drug groups compared with those assigned to placebo. However, there were no significant differences for the MOS-SF-36 subscales and summary scores when drug groups were compared with the placebo group.

Level of Study	2
Reference	7. Levin RM, Longhurst PA, et al. Effect of bladder outlet obstruction on the morphology, physiology, and pharmacology of the bladder. Prostate [Suppl] 1990;3:9–26.
Study type	Observational study
Patients	
Purpose of Study	Bladder outlet obstruction secondary to benign prostatic hyperplasia induces numerous changes in bladder morphology, physiology, and pharmacology. These changes have been studied experimentally in various animal models, and while each species has advantages and disadvantages, it is unclear which is the most like man. It has been shown that tissue hypertrophy leading to an increase in tissue mass develops rapidly after bladder outlet obstruction.
Study Results	It has been shown that tissue hypertrophy leading to an increase in tissue mass develops rapidly after bladder outlet obstruction. Ischemia induced by the obstruction results in acute muscle dysfunction. The degree of functional impairment is directly related to the degree of tissue hypertrophy. However, the bladder contractile apparatus appears to have a surprising regenerative ability, such that recovery of bladder function becomes obvious 14 days after obstruction. Urodynamic changes include an increase in urinary frequency and voiding pressure and a decrease in voided volume. Clinically, involuntary bladder contractions are often present. Determination of which of these specific aspects of outlet obstruction the investigator is interested in studying will dictate the selection of the most appropriate animal model.
Level of Study	5
Reference	8. McConnell JD, Barry MJ, et al. Benign prostatic hyperplasia: diagnosis and treatment. Clinical practice guideline no. 8. Rockville, MD: U.S. Department of Health and Human Services, Agency for Health Care Policy and Research, Public Health Service; 1994; 1–17.
Study type	Expert opinion
Patients	
Purpose of Study	This Quick Reference Guide for Clinicians contains highlights from the Clinical Practice Guideline of Benign Prostatic Hyperplasia: Diagnosis and Treatment.
Study Results	The Benign Prostatic Hyperplasia Guideline Panel, a private-sector panel of health care providers, developed the guideline after comprehensively analyzing the research literature. As a result, this guideline comprises the most current scientific knowledge of the development, diagnosis, and treatment of benign prostatic hyperplasia (BPH). The guideline makes specific recommendations to identify both the most effective methods for diagnosing BPH and the most appropriate treatments for BPH based on patient preference and clinical need. BPH affects quality of life and is very rarely a life-threatening disease. Motivation to seek active treatment will, for most patients, depend on how much their symptoms bother them. Many patients choose a regimen of "watchful waiting." The guideline details the relative benefits and harms associated with all diagnostic and treatment approaches. Treatment options discussed include watchful waiting, alpha blocker and finasteride medications, balloon dilation, and the surgical options of transurethral incision, transurethral resection, and open prostatectomy.

Level of Study	5
Reference	10. DiPaola RS, Kumar P, et al. State-of-the-art prostate cancer treatment and research. A report from the Cancer Institute of New Jersey. N J Med 2001;98:23–33.
Study type	Expert opinion
Patients	
Purpose of Study	Prostate cancer is a devastating disease that will be diagnosed in approximately 200,000 men in 2001. New methods for screening, prevention, and treatment are being developed
Study Results	Novel agents for the treatment of resistant prostate cancer are being developed in clinical trials. This review summarizes the recent efforts in diet, screening, novel systemic therapies, and alternative medicine for prostate cancer.
Level of Study	5
Reference	11. Madersbacher S, Alivizatos G, Nordling J, et al. EAU 2004 guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH guidelines). Eur Urol 2004;46:547–54.
Study type	Expert opinion
Patients	
Purpose of Study	To provide the first update of the EAU guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction (BPO).
Study Results	During initial assessment the following tests are recommended: medical history, physical examination including digital-rectal examination, International Prostate Symptom Score, urinalysis, serum creatinine and prostate specific antigen measurement, uroflowmetry and post-void residual volume. All other tests are optional or not recommended. Aim of treatment is to improve LUTS and quality of life and to prevent severe BPE-related complications. Development of a 5alpha-reductase type I and II inhibitor and the data of the MTOPS trial providing scientific evidence for a combination therapy were the most significant innovations since the first version. Finally a more detailed knowledge on the natural history with identification of several risk factors for progression is the basis for a risk-profile orientated (preventive) therapy.
Level of Study	5
Reference	12. Roehrborn CG, Malice M, Cook TJ, Girman CJ. Clinical predictors of spontaneous acute urinary retention in men with LUTS and clinical BPH: a comprehensive analysis of the pooled placebo groups of several large clinical trials. Urology 2001;58:210–16.
Study type	Meta analysis
Patients	5,355
Purpose of Study	To comprehensively evaluate clinical predictors of spontaneous acute urinary retention (AUR) across pooled data of placebo-treated patients from clinical trials conducted in men with lower urinary tract symptoms and clinically diagnosed benign prostatic hyperplasia.

Study Results	The different methods of analysis identified consistent potential predictors of episodes of AUR. When prostate volume was included in the analyses, it was selected as the initial variable discriminating men with and without subsequent AUR. Omitting prostate volume because of its availability in only a subset of men, a logistic model including serum prostate-specific antigen (PSA), urinating more than every 2 hours, symptom problem index, maximum urinary flow rate, and hesitancy of urination had good predictive properties (area under the receiver-operating characteristic curve [AUC] = 0.742 +/- 0.047), as did a model with PSA (AUC = 0.716 +/- 0.045). A classification and regression decision tree with the same variables predicted AUR (AUC = 0.74, sensitivity = 72%, specificity = 67%) as well as did a tree with PSA alone (AUC = 0.70, sensitivity = 75%, specificity = 64%).
Level of Study	1
Reference	13. M. Oelke (chairman), A. Bachmann, A. Descazeaud, M. Emberton, S. Gravas, M.C. Michel, et al. Guidelines on the Management of Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). EAU2012.
Study type	Expert opinion
Patients	
Purpose of Study	To present a summary of the 2013 version of the European Association of Urology guidelines on the treatment and follow-up of male lower urinary tract symptoms (LUTS).
Study Results	Men with mild symptoms are suitable for watchful waiting. All men with bothersome LUTS should be offered lifestyle advice prior to or concurrent with any treatment. Men with bothersome moderate-to-severe LUTS quickly benefit from α1-blockers. Men with enlarged prostates, especially those >40 ml, profit from 5α-reductase inhibitors (5-ARIs) that slowly reduce LUTS and the probability of urinary retention or the need for surgery. Antimuscarinics might be considered for patients who have predominant bladder storage symptoms. The phosphodiesterase type 5 inhibitor tadalafil can quickly reduce LUTS to a similar extent as α1-blockers, and it also improves erectile dysfunction. Desmopressin can be used in men with nocturia due to nocturnal polyuria. Treatment with an α1-blocker and 5-ARI (in men with enlarged prostates) or antimuscarinics (with persistent storage symptoms) combines the positive effects of either drug class to achieve greater efficacy. Prostate surgery is indicated in men with absolute indications or drug treatment-resistant LUTS due to benign prostatic obstruction. Transurethral resection of the prostate (TURP) is the current standard operation for men with prostates 30-80 ml, whereas open surgery or transurethral holmium laser enucleation is appropriate for men with prostates >80 ml. Alternatives for monopolar TURP include bipolar TURP and transurethral incision of the prostate (for glands <30 ml) and laser treatments. Transurethral microwave therapy and transurethral needle ablation are effective minimally invasive treatments with higher retreatment rates compared with TURP. Prostate stents are an alternative to catheterisation for men unfit for surgery. Ethanol or botulinum toxin injections into the prostate are still experimental.
Level of Study	5
Reference	14. Aziz DC, Barathur RB. Prostate-specific antigen and prostate volume: a meta-analysis of prostate cancer screening criteria. J Clin Lab Anal 1993;7:283-92.
Study type	

Patients	Meta analysis
Purpose of Study	To establish the value of serum prostate-specific antigen (PSA) and prostate-specific antigen per unit volume of prostate gland (PSAD) in detecting prostate carcinoma (CaP) in a hypothetical screening algorithm, a meta-analysis of the sensitivities, specificities, predictive values and likelihood ratios were combined from the published data.
Study Results	Hypothetical cohorts of 1,000 men between the ages of 60 and 70 years were screened using three different screening decision algorithms. Using a serum PSA cutoff of 3.0 ng/ml for referral for transrectal biopsy, 59 of 80 (74%) CaP would be detected and 21 (26%) would be missed. 209 transrectal biopsies would be performed, and 150 (72%) of them would be negative for CaP. Using a serum PSA cutoff of 4.0 ng/ml, 52 of 80 (65%) CaP would be detected and 28 (35%) would be missed. 146 transrectal biopsies would be performed, and 94 (64%) of them would be unnecessary. Using a cutoff of 2.0 ng/ml for serum PSA and 0.1 ng/ml/cc for PSAD, 55 of 80 (69%) of the cancers would be detected and 25 (31%) would be missed. Only 84 transrectal biopsies would be performed, and 29 (35%) of them would be negative for cancer.
Level of Study	1

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