Challenges in prostatic artery embolisation: patient radiation exposure and postembolisation syndrome

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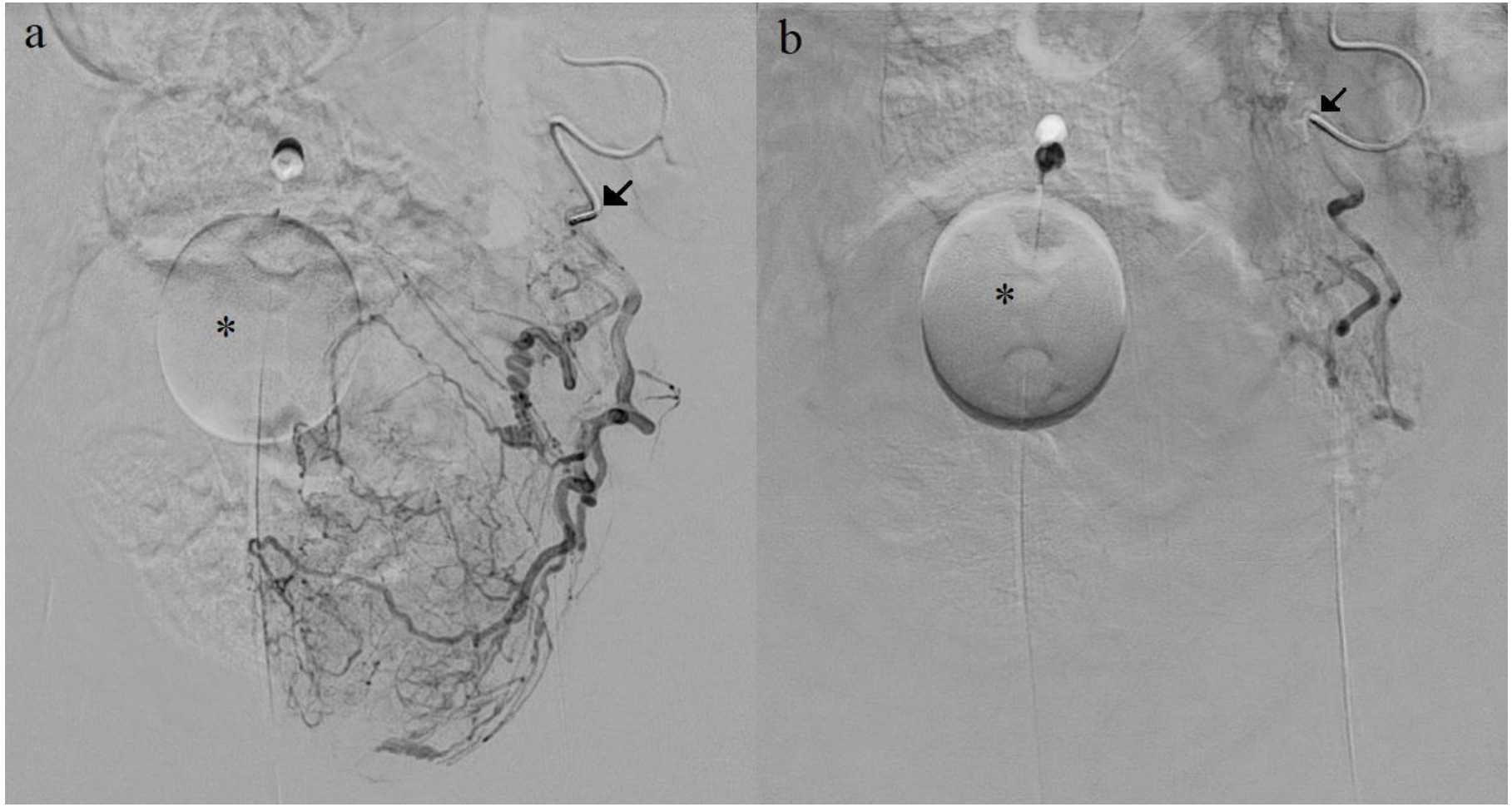
DFIR 2023

Why do a PhD on prostatic artery embolisation (PAE)?

50% men over 60 report some symptoms of benign prostatic hyperplasia (BPH)
70% men over 70 report some symptoms of BPH

What is PAE and what makes it special?



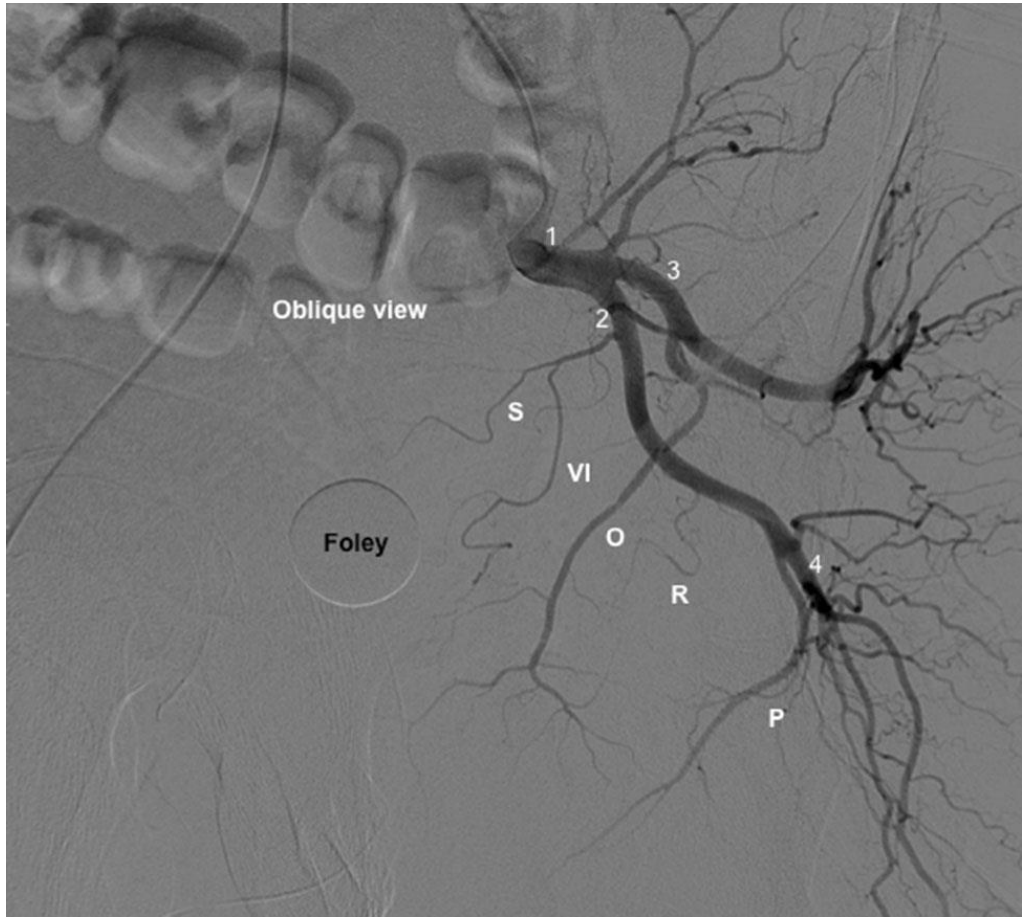
Frontal DSA with the microcatheter (arrow) in the prostate artery. a. Contrast medium attenuation in the left lobe of the prostate below the Foley catheter (*) before injection of embolic particles b. DSA demonstrating the angiographic endpoint with no visible flow in the prostate. DSA, digital subtraction angiography.

"Given the heterogeneity in the sparsely available literature in addition to safety concerns regarding radiation exposure, post-embolization syndrome, vascular access, technical feasibility, and adverse events, it is the opinion of the Panel that PAE should only be performed in the context of a clinical trial until sufficient evidence from rigorously performed studies is available to indicate benefit over other more well-established therapies."

American Urological Association, 2021

Why can patient radiation exposure in PAE be high?

1. Patient age
2. Variable anatomy
3. Size of target arteries
4. Bilateral embolisation



Paper I

European Radiology
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VASCULAR-INTERVENTIONAL

Center experience and other determinants of patient radiation exposure during prostatic artery embolization: a retrospective study in three Scandinavian centers

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3 centers 🇩🇰🇸🇪🇳🇴

352 PAE procedures

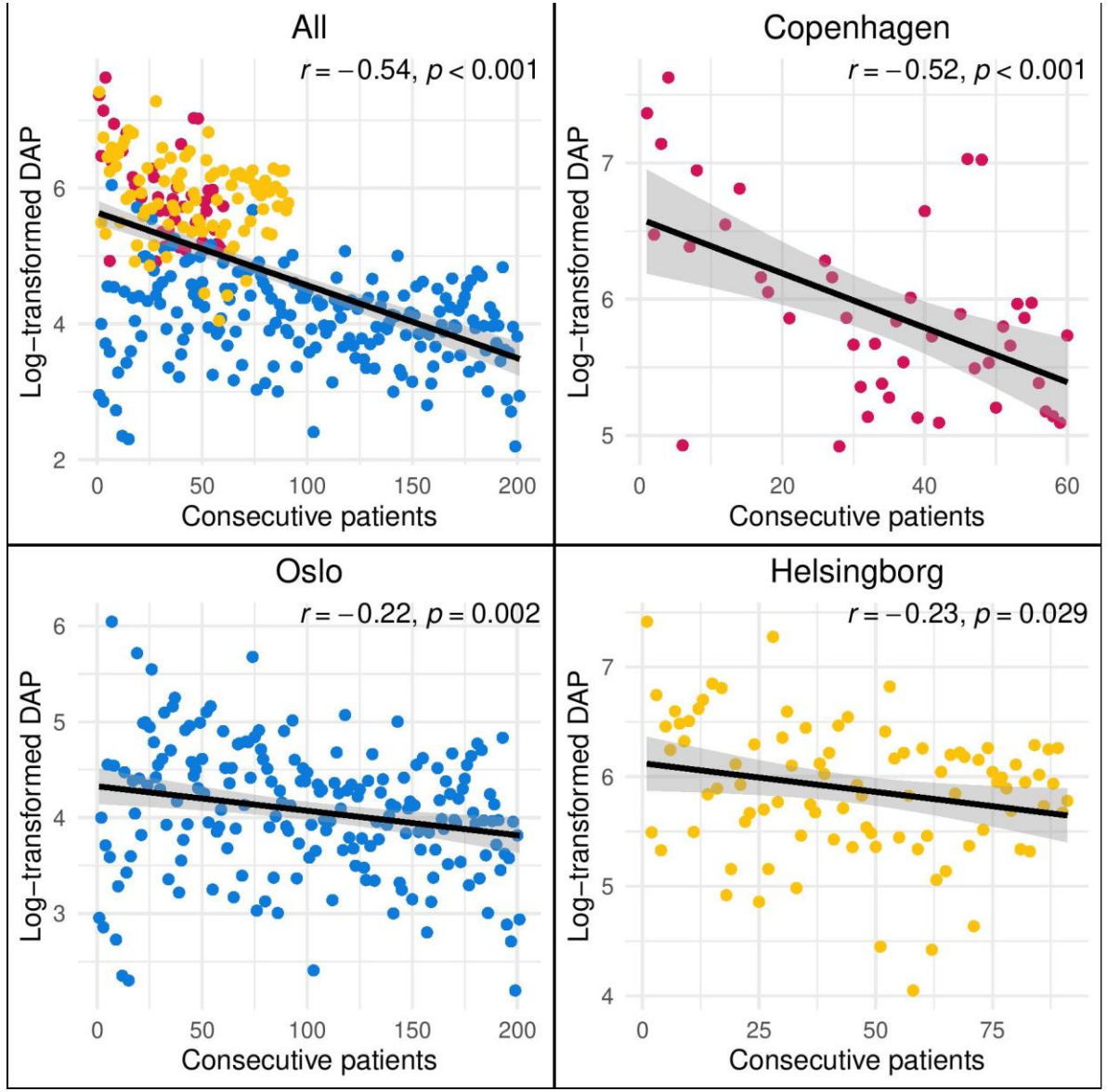
DAP ($Gy \cdot cm^2$)

Table 1 Baseline demographic data for the 319 patients that underwent PAE.

Variable	Copenhagen (n = 52)	Helsingborg (n = 90)	Oslo (n = 177)	All centers (n = 319)
Age (y), mean ± SD	72 ± 8.4	73 ± 8.2	71 ± 7.7	72 ± 8.1
BMI (kg/m^2), mean ± SD	24.9 ± 3.1	26.7 ± 3.3	26.3 ± 4.1	26.1 ± 3.7
PV (cm^3), median (IQR)	100 (65–135)	100 (75–178)	124 (80–150)	109 (75–150)
Indication for PAE, n (%)				
LUTS	35 (67)	80 (89)	157 (89)	272 (85)
Prostate cancer with LUTS	14 (27)	0 (0)	8 (4)	22 (7)
Bleeding	3 (6)	10 (11)	12 (7)	25 (8)
Missing	0 (0)	0 (0)	0 (0)	0 (0)

BMI body mass index; *IQR* interquartile range; *LUTS* lower urinary tract symptoms; *PV* prostate volume; *SD* standard deviation.

Variable	Copenhagen (n = 60)	Helsingborg (n = 91)	Oslo (n = 201)	All centers (n = 352)
DAP (Gy·cm^2), median (IQR)				
Intended bilateral PAE	343 (217–535)	379 (241–557)	88 (17–422)	237 (17–563)
Intended unilateral PAE	/	/	46 (10–135)	46 (10–135)
Overall	343(217–535)	379 (241–557)	60 (39–92)	105 (52–306)


All
r = −0.54, p < 0.001
Log−transformed DAP
Consecutive patients
Copenhagen
r = −0.52, p < 0.001
Log−transformed DAP
Consecutive patients
Oslo
r = −0.22, p = 0.002
Log−transformed DAP
Consecutive patients
Helsingborg
r = −0.23, p = 0.029
Log−transformed DAP
Consecutive patients

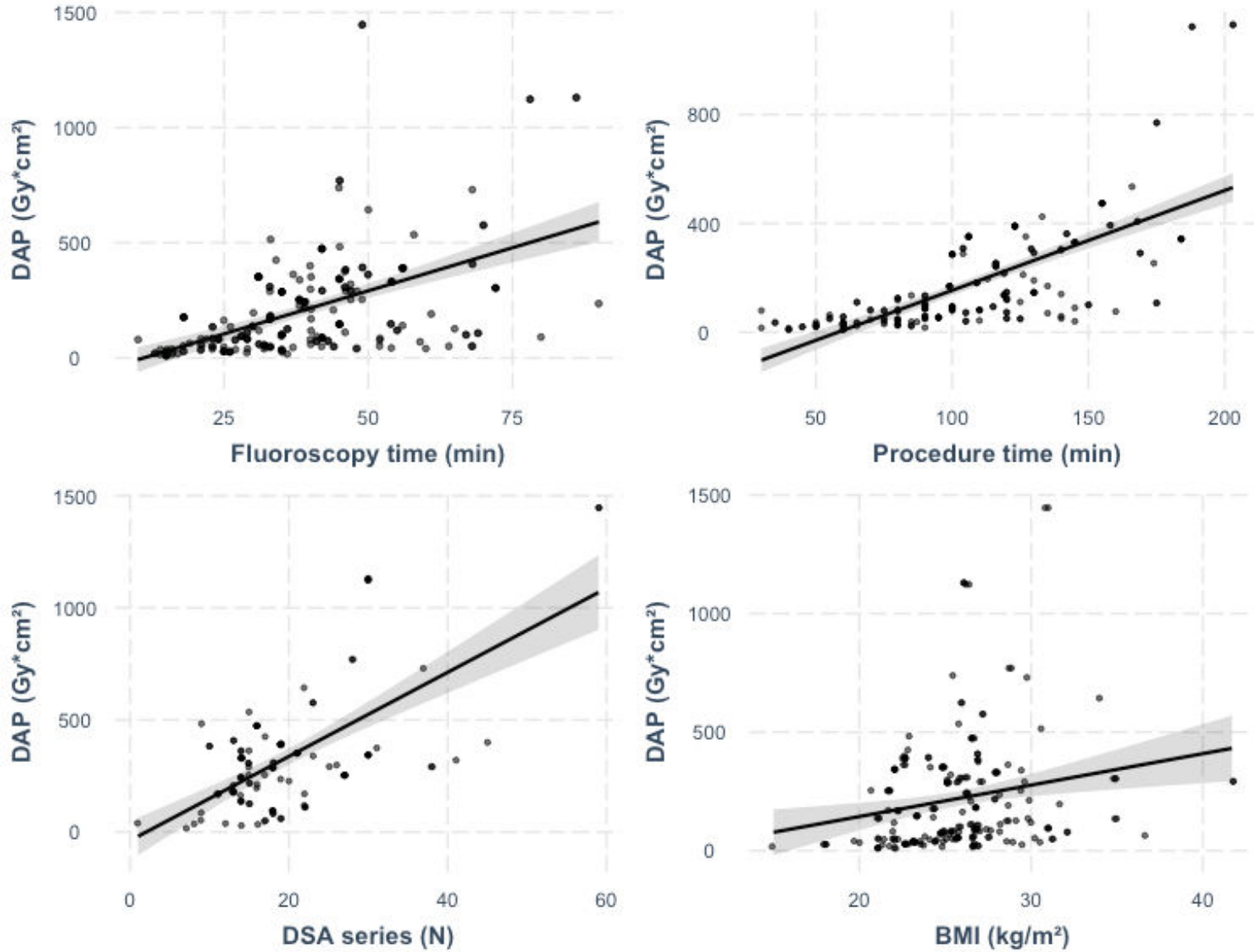

DAP (Gy*cm²)
1500
1000
500
0
25
50
75
Fluoroscopy time (min)
DAP (Gy*cm²)
800
400
0
50
100
150
200
Procedure time (min)
DAP (Gy*cm²)
1500
1000
500
0
0
20
40
60
DSA series (N)
DAP (Gy*cm²)
1500
1000
500
0
20
30
40
BMI (kg/m²)

Table 5. Multiple linear regression analysis of the relationship between log-transformed DAP in Gy·cm^2 and explanatory variables.

Variable (x)	Regression coefficient (β_x)	Effect of change in x on DAP (%)	95% CI of effect of change on DAP (%)	*P* value
BMI (per 1 kg/m^2)	0.062	6.4	4.1 to 8.3	*< 0.001*
Center experience (per 10 consecutive patients)	- 0.043	- 4.2	- 9.5 to - 2.0	*0.02*
Fluoroscopy time (per 1 min)	0.012	1.2	0.4 to 1.3	*< 0.001*
DSA acquisitions (per 1 acquisition)	0.030	3.0	2.2 to 3.9	*< 0.001*
Intended unilateral embolization	- 0.391	- 32.4	- 48.6 to -13.1	*0.03*

BMI body mass index; *CI* confidence interval; *DAP* dose area product; *DSA* digital subtraction angiography.

What is postembolisation syndrome (PES)?

Systemic response to tissue necrosis

Influenza-like symptoms, pelvic pain, worsening of lower urinary tract symptoms (LUTS), raised inflammatory parameters (CRP, leukocytes)

Self-limiting, lasts 2 - 5 days

Why is PES a clinical challenge?

Under-reported and under-recognized

Severe PES – unnecessary antibiotics treatment and hospitalization

Paper II

diagnostics

MDPI

Review

Postembolization Syndrome after Prostatic Artery Embolization: A Systematic Review

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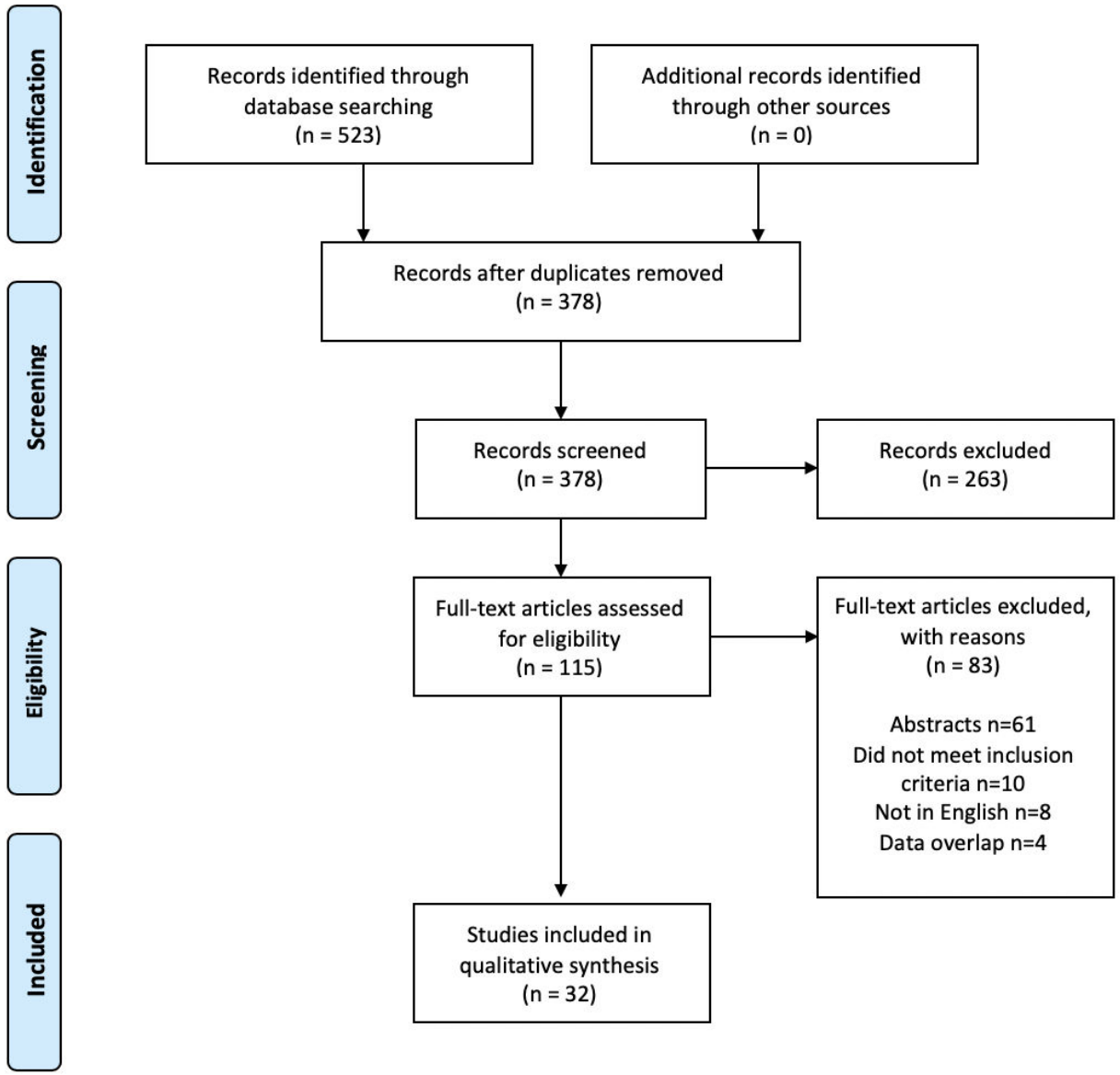
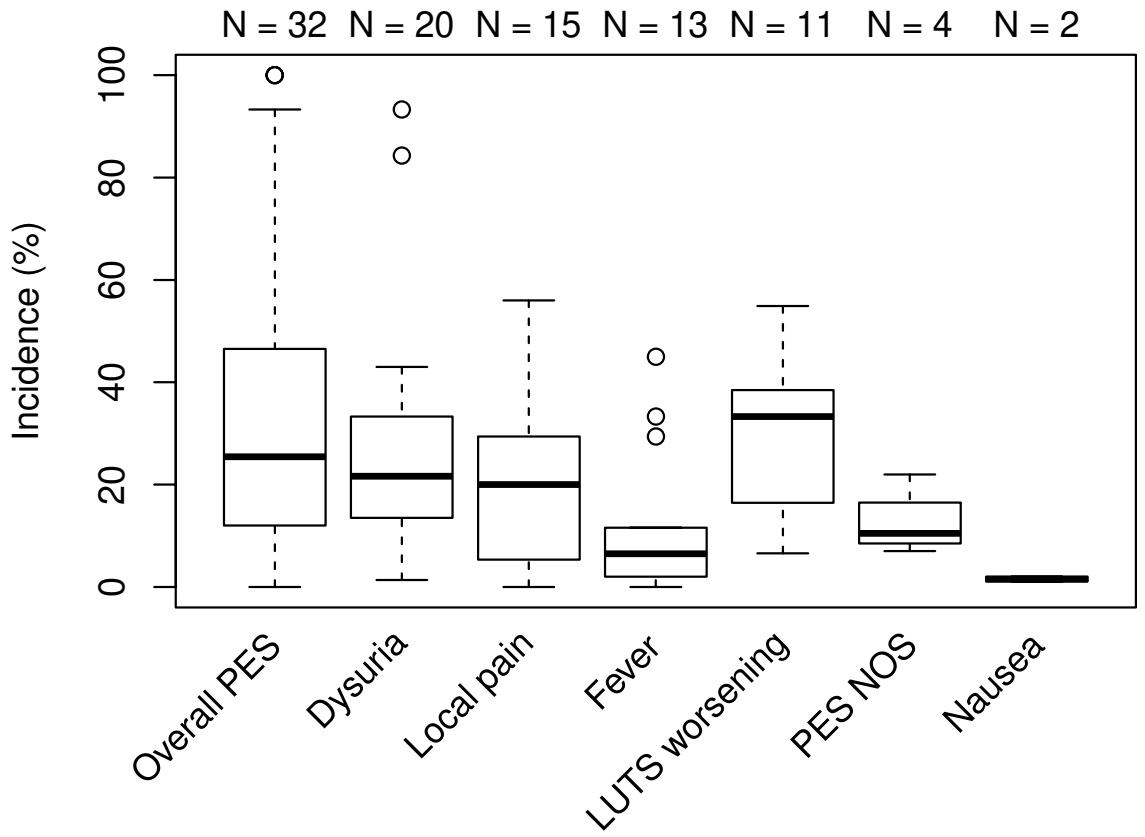

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 523)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 378)
Records screened (n = 378)
Records excluded (n = 263)
Full-text articles assessed for eligibility (n = 115)
Full-text articles excluded, with reasons (n = 83)
Abstracts n=61
Did not meet inclusion criteria n=10
Not in English n=8
Data overlap n=4
Studies included in qualitative synthesis (n = 32)



Box = 25th and 75th percentiles; bars = minimum and maximum values (1.5* IQR); bold line = median; N = number of studies included; outliers represented as circles. LUTS lower urinary tract symptoms, PES postembolization syndrome, NOS not otherwise specified.

Can we reduce PES following PAE?

Open access Protocol

BMJ Open

Efficacy of dexamethasone in reducing the postembolisation syndrome in men undergoing prostatic artery embolisation for benign prostatic hyperplasia: protocol for a single-centre, randomised, double-blind, placebo-controlled trial—the 'DEXAPAE' study

Petra Svarc ,[1,2] Hein Vincent Stroomberg ,[2,3] Ruben Juhl Jensen,[1] Susanne Frevert,[1] Mats Håkan Lindh,[1] Mikkel Taudorf,[1,2] Klaus Brasso,[2,3] Lars Lönn,[1,2] Martin Andreas Røder[2,3]

Paper III

EFFICACY OF HIGH DOSE DEXAMETHASONE IN REDUCING THE SYMPTOMS OF POSTEMBOLISATION SYNDROME FOLLOWING PROSTATIC ARTERY EMBOLISATION: RESULTS OF A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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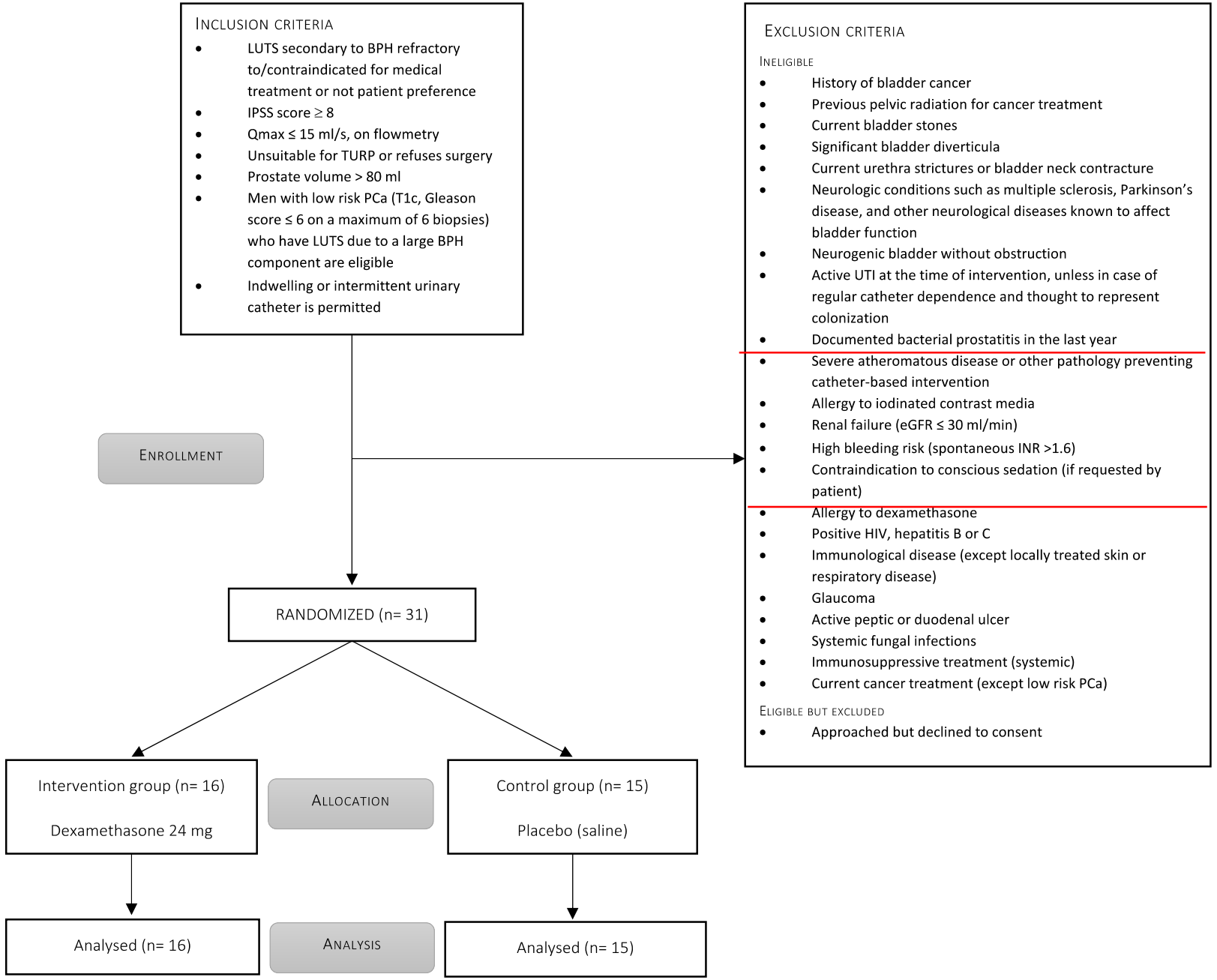
4. *Section of Biostatistics, Department of Public Health, University of Copenhagen, Denmark*

March 2021 to May 2022

Men with BPH who were PAE candidates

Randomized to receive 24 mg dexamethasone (DEXA) or placebo (1:1)

Follow-up: 6 months


Inclusion criteria
LUTS secondary to BPH refractory to/contraindicated for medical treatment or not patient preference
IPSS score ≥ 8
Qmax ≤ 15 ml/s, on flowmetry
Unsuitable for TURP or refuses surgery
Prostate volume > 80 ml
Men with low risk PCa (T1c, Gleason score ≤ 6 on a maximum of 6 biopsies) who have LUTS due to a large BPH component are eligible
Indwelling or intermittent urinary catheter is permitted
Exclusion criteria
Ineligible
History of bladder cancer
Previous pelvic radiation for cancer treatment
Current bladder stones
Significant bladder diverticula
Current urethra strictures or bladder neck contracture
Neurologic conditions such as multiple sclerosis, Parkinson's disease, and other neurological diseases known to affect bladder function
Neurogenic bladder without obstruction
Active UTI at the time of intervention, unless in case of regular catheter dependence and thought to represent colonization
Documented bacterial prostatitis in the last year
Severe atheromatous disease or other pathology preventing catheter-based intervention
Allergy to iodinated contrast media
Renal failure (eGFR ≤ 30 ml/min)
High bleeding risk (spontaneous INR >1.6)
Contraindication to conscious sedation (if requested by patient)
Allergy to dexamethasone
Positive HIV, hepatitis B or C
Immunological disease (except locally treated skin or respiratory disease)
Glaucoma
Active peptic or duodenal ulcer
Systemic fungal infections
Immunosuppressive treatment (systemic)
Current cancer treatment (except low risk PCa)
Eligible but excluded
Approached but declined to consent
Enrollment
RANDOMIZED (n= 31)
Intervention group (n= 16)
Dexamethasone 24 mg
Allocation
Control group (n= 15)
Placebo (saline)
Analysed (n= 16)
Analysis
Analysed (n= 15)

What were the primary outcomes?

1. Morning rectal temperature at 2 days post-PAE
2. Pain Severity and Pain Interference scores on Brief Pain Inventory – Short Form for the first 5 days post-PAE

What were the secondary outcomes?

Table 1. Outcome measures at each time point

	Screening	Day 0 (PAE)	Day 1	Day 2	Day 3	Day 4	Day 5	1 month	3 months	6 months
BT		x	x	x	x	x	x			
BPI-SF		x	x	x	x	x	x			
Medication usage		x	x	x	x	x	x			
Nausea and vomiting		x	x	x	x	x	x			
Dysuria		x	x	x	x	x	x			
Blood glucose [a]		x	x	x	x	x	x			
IPSS	x			x			x	x	x	x
IIEF-5	x							x	x	x
PSA	x			x				x	x	x
CRP	x			x						
Uroflowmetry	x								x	x
TRUS	x								x	x
Hospital admission		x	x	x	x	x	x			
UTI		x	x	x	x	x	x			
Acute urinary retention		x	x	x	x	x	x			

BT body temperature; *BP-SF* Brief Pain Inventory – Short Form; *IPSS* International Prostate Symptom Score; *IIEF-5* International Index of Erectile Function-5; *PSA* prostate specific antigen; *CRP* C-reactive protein; *TRUS* transrectal ultrasound; *UTI* urinary tract infection.

[a] Blood glucose is only collected for participants with diabetes.

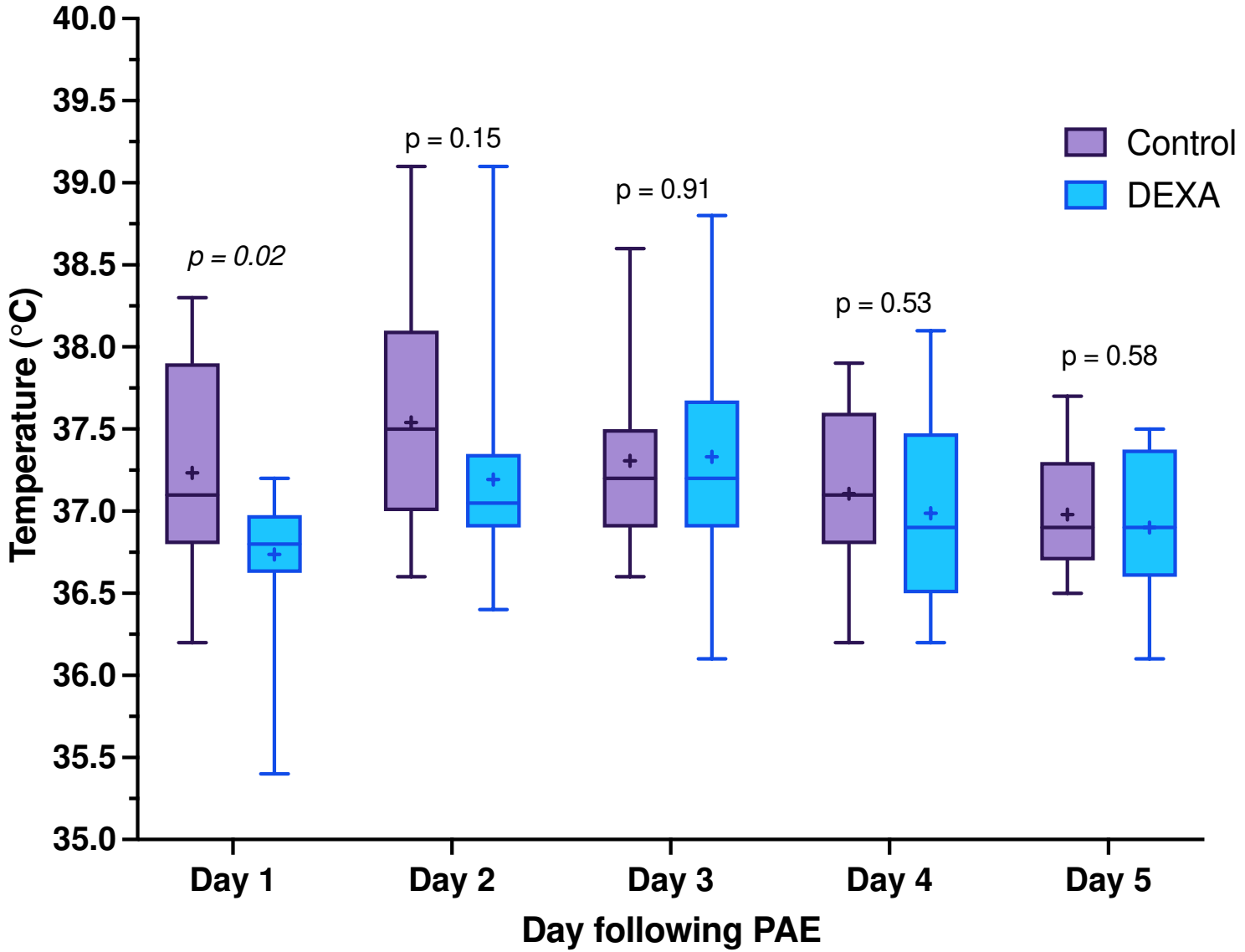
- Interim analysis after 30 patients showed no significant difference between groups
- Trial terminated after 31 patients (60 planned)

Table 2 – Patient demographics at baseline

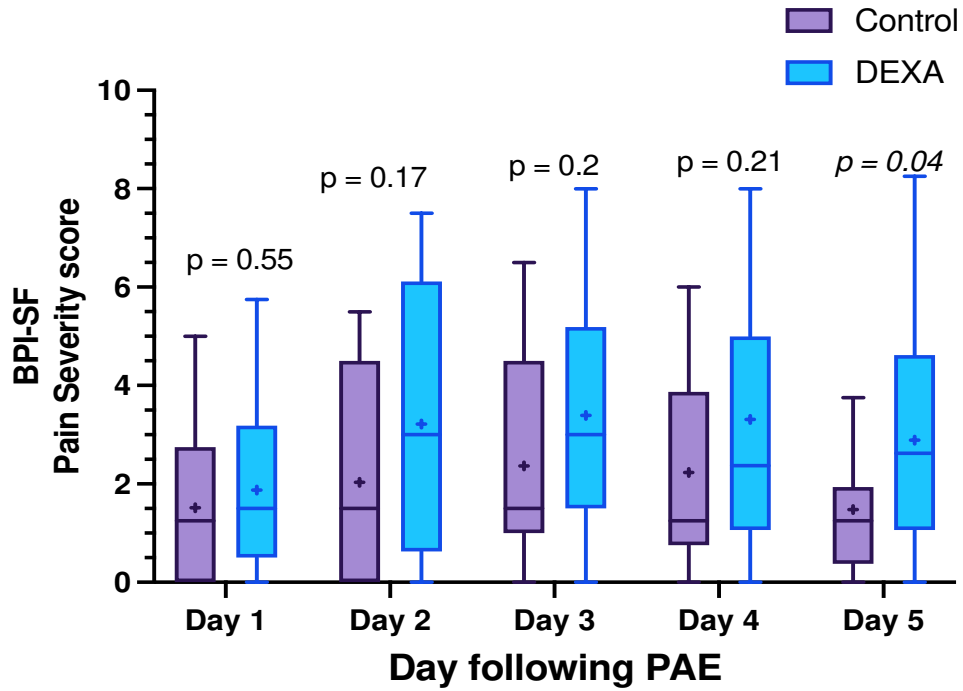
Variable [a]	Control (n = 15)	DEXA (n = 16)	*p* value
Age (y)	70 ± 5	69 ± 6.3	0.43
BMI (kg/m^2)	27.4 ± 5.7	27.4 ± 4.9	0.99
PV (ml)	135.8 ± 64.7	126.1 ± 54.1	0.65
IPSS	21 ± 7.5	25 ± 7.2	0.11
Temperature (°C)	36.5 ± 0.3	36.4 ± 0.4	0.83

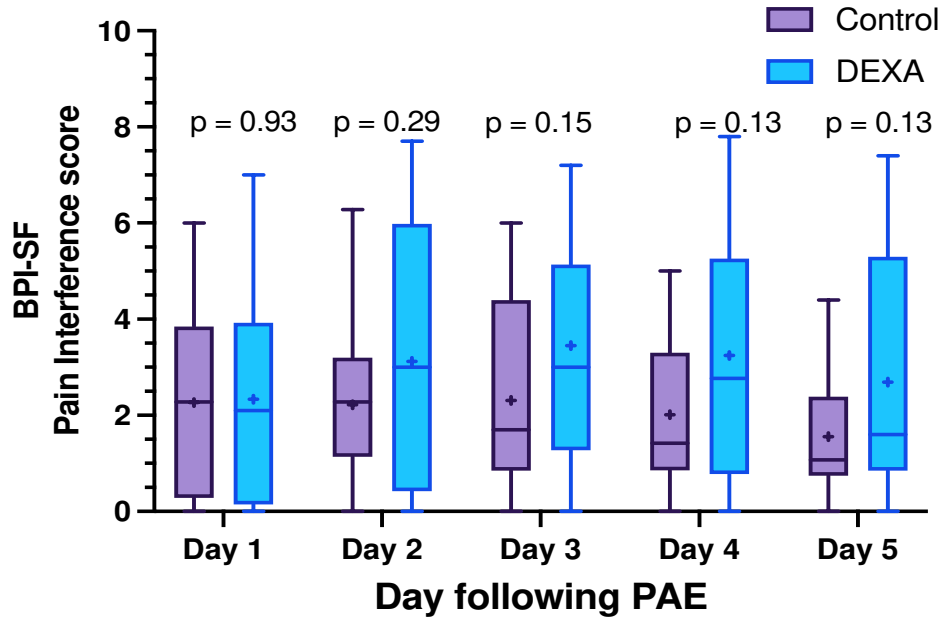
BMI = body mass index; IPSS = International Prostate Symptom Score; PV = prostate volume

[a] Results are presented as mean ± standard deviation.



Box = 25th and 75th percentiles; bars = minimum and maximum values (1.5* IQR); bold line = median; "+" = mean. Mann-Whitney test was used to compare the means of the two groups on Day 2, while independent t-test was used for the remaining days.





Box = 25th and 75th percentiles; bars = minimum and maximum values (1.5* IQR); bold line = median: "+" = mean. Mann-Whitney test was used to compare the scores.

Conclusion

Though safe, there seems to be no adjuvant benefit to DEXA in reducing PES following PAE

Patient education is paramount

Limitations:

Underpowered

Primary endpoints were self-reported

Further research

- Compare PAE to other minimally invasive techniques
- Technical aspects: preprocedural imaging, CBCT use, particle type and size
- Who is an ideal PAE candidate?