

Interwencje prenatalne

**- nadzieje i fakty z punktu widzenia
nefrologa**

Prenatal interventions:

***- expectations and reality
from nephrologist's view***

Ryszard Grenda i Maria Roszkowska-Blaim

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Systematic review of the effectiveness of antenatal intervention for the treatment of congenital lower urinary tract obstruction

RK Morris,^a GL Malin,^b KS Khan,^a MD Kilby^{a,b}

BJOG 2010;117:382–390.

Background

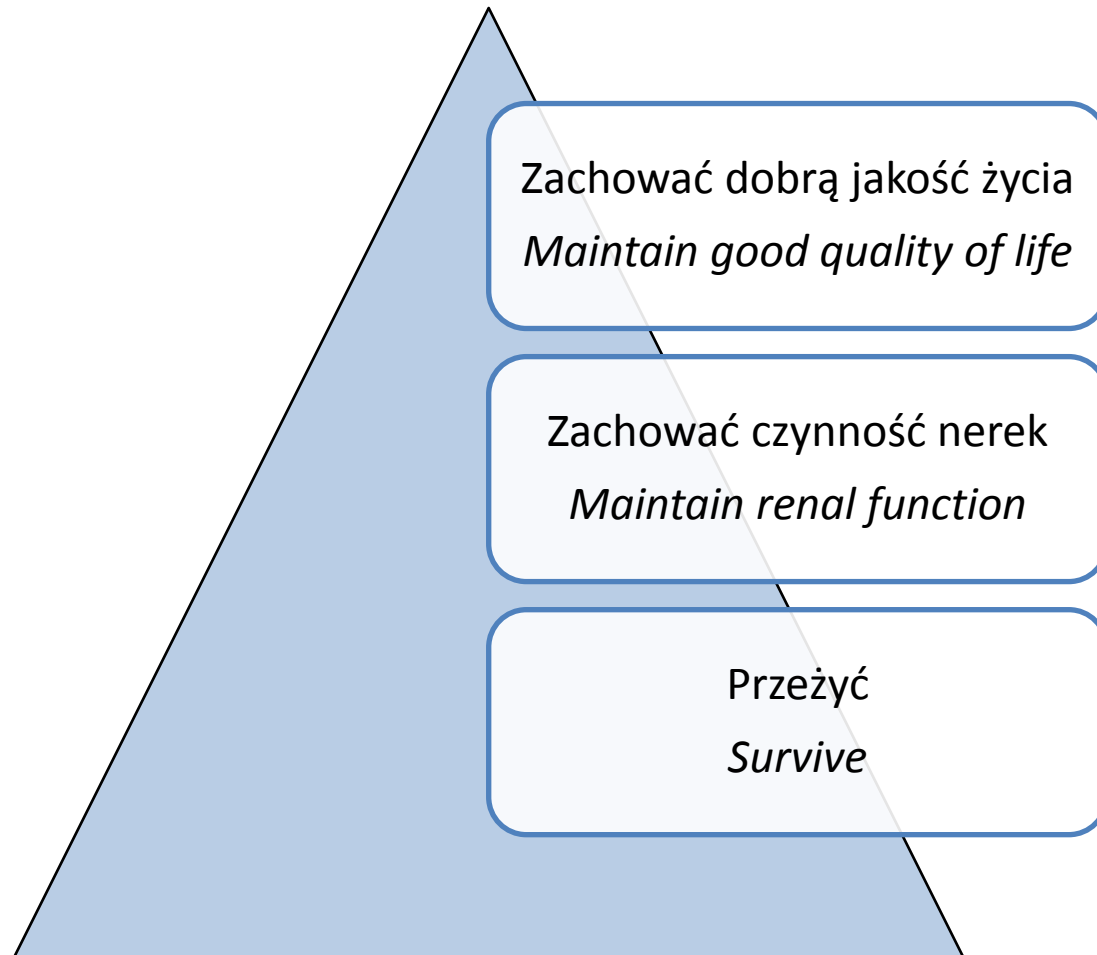
Congenital lower urinary tract (bladder neck) obstruction (LUTO) comprises a heterogeneous group of conditions: commonly, congenital posterior urethral valves and urethral atresia. The incidence is approximately 2.2 in 10 000 births.¹ The natural history of the condition has a high mortality, up to 45%, largely as a result of pulmonary hypoplasia or severe early onset renal failure.² Those that survive the neonatal period also have a poor long-term prognosis, with obstructive uropathy accounting for large numbers of childhood renal failure.

Wrodzone wady zaporowe:

- częstość 2,2/10 000
- przy naturalnym przebiegu wysoka śmiertelność (do 45%)głównie wskutek hipoplazji płuc i/lub schyłkowej niewydolności nerek
- u noworodków i niemowląt, które przeżywają okres okołoporodowy często rozwija się przewlekła choroba nerek

Czego oczekujemy po interwencji prenatalnej?

What do we expect from prenatal intervention?



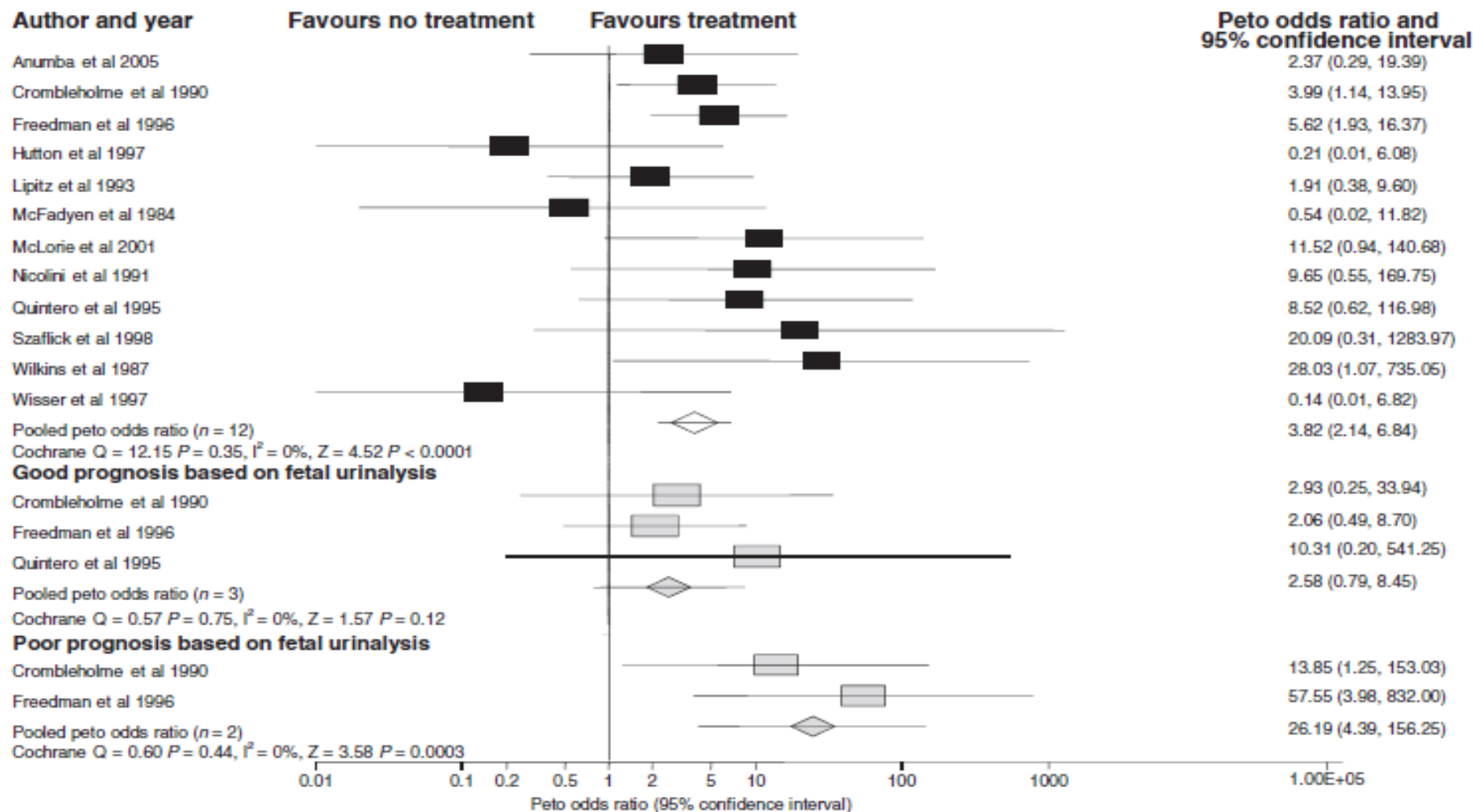


Figure 2. Effect of antenatal intervention on perinatal survival compared with no treatment (including voluntary termination of pregnancies) stratified by predicted prognosis.

Wpływ podjęcia/zaniechania interwencji prenatalnej na przeżycie dziecka w okresie okołoporodowym

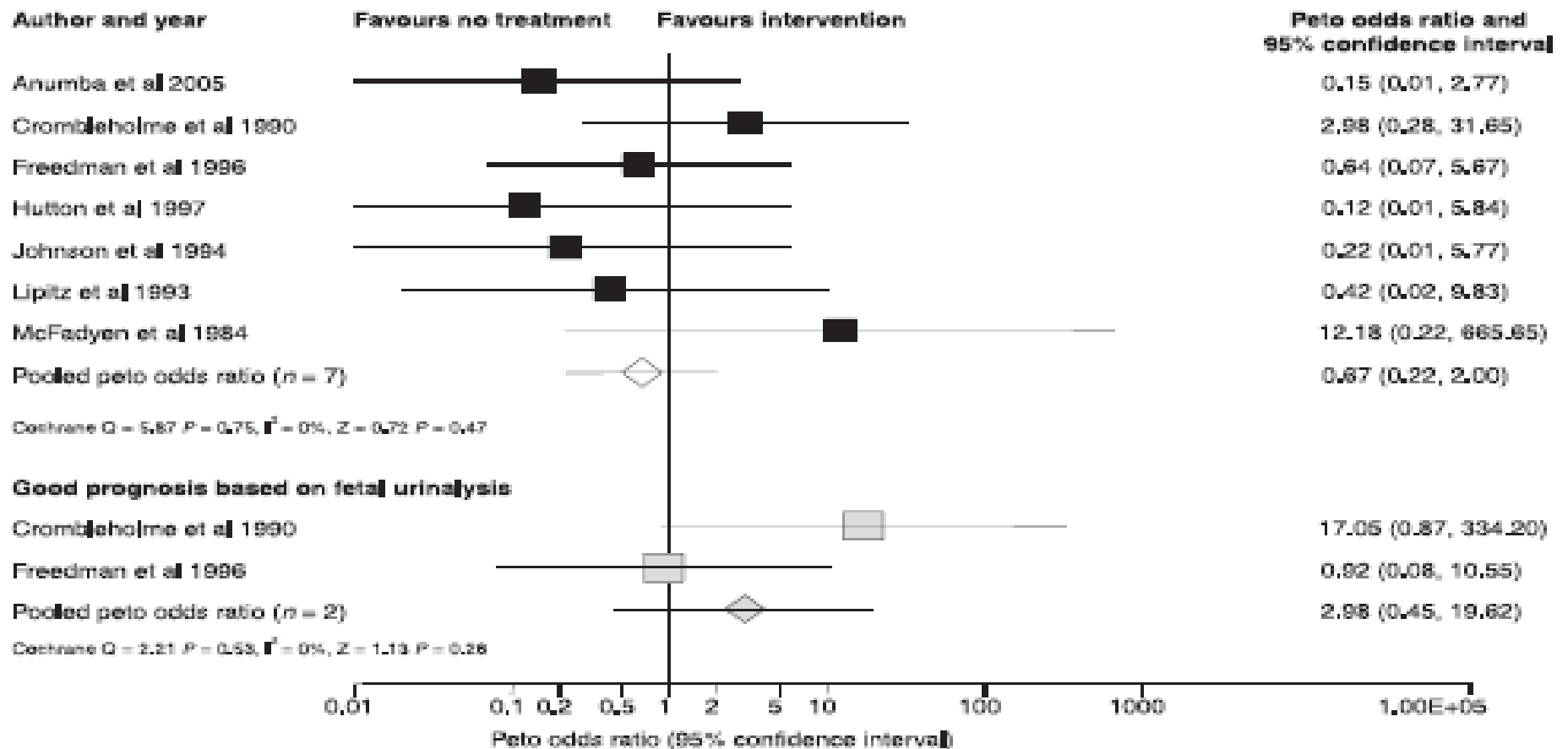


Figure 3. Effect of antenatal intervention compared with no treatment on postnatal survival with normal renal function (excluding intrauterine deaths and voluntary termination of pregnancy) stratified according to predicted prognosis.

Wpływ podjęcia/zaniechania interwencji prenatalnej na przeżycie dziecka w okresie okołoporodowym z zachowaniem prawidłowej czynności nerek

BJOG 2010;117:382–390.

Randomised research with long-term follow up is necessary to determine the role of antenatal treatment in clinical practice.

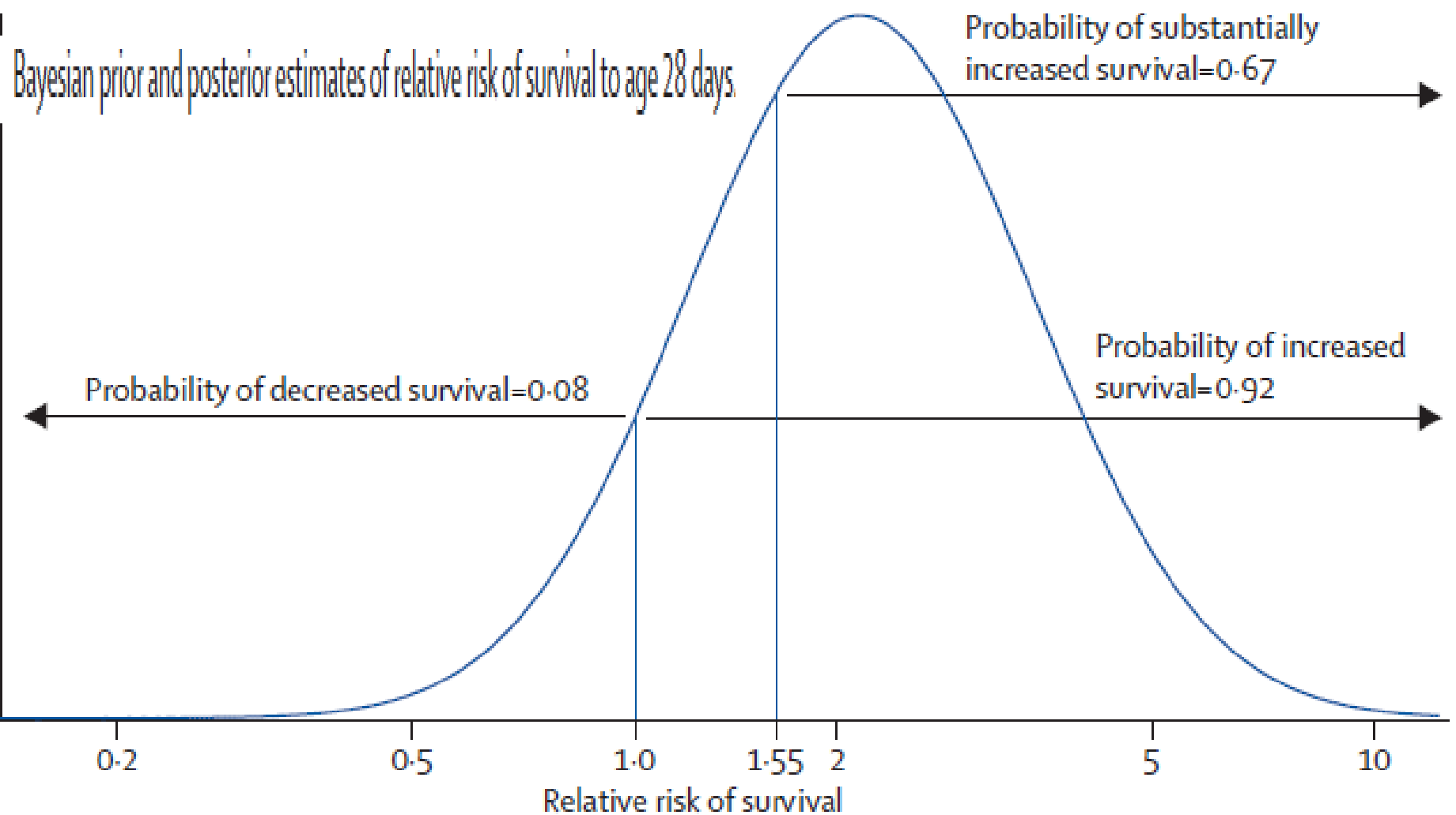
Wniosek z metaanaliz:
konieczne przeprowadzenie badania
randomizowanego

Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial

Lancet 2013; 382: 1496–506

Rachel K Morris, Gemma L Malin, Elisabeth Quinlan-Jones, Lee J Middleton, Karla Hemming, Danielle Burke, Jane P Daniels, Khalid S Khan, Jon Deeks, Mark D Kilby, for the Percutaneous vesicoamniotic shunting in Lower Urinary Tract Obstruction (PLUTO) Collaborative Group

	Vesicoamniotic shunt (n=16)	Conservative management (n=15)
Maternal age (years)	27 (23–33)	28 (26–33)
Gestational age (weeks)	20 (16–22)	21 (19–22)
Anteroposterior renal pelvis dilatation diameter > 90th centile‡		
Bilateral	13	12
Unilateral	2	0
Neither	0	1
Not recorded	1	2
Bladder wall thickness > 3 mm		
Yes	6	9
No	8	5
Not recorded	2	1



Interwencja/brak interwencji – bez istotnego wpływu na przeżycie pierwszego miesiąca życia

	Vesicoamniotic shunt	Conservative management	1year		
Livebirths			n	7	3
n	12	12	Required surgery from perinatal period to 1year	6	0
Days from randomisation to delivery	93 (69-118)	104 (94-112)	Days in hospital	0, 1, 3, 20, 25, 84, 102	22, 39, NR
Gestational age at delivery (days)	249 (234-263)	255 (242-262)	Weight <10th centile	4†	2†
Preterm labour (<37 weeks)	7	8	Serum creatinine, µmol/L	34, 37, 58, 64, 81, 88, 226	60, 60, 501
Vaginal delivery	8	7*	Renal function§		
Mean birthweight, kg (SD)	2.8 (0.5)	2.8 (0.4)	Normal	2	0
Birthweight <10th centile	5	4	Mild impairment	1	0
Admitted to neonatal ICU or children's hospital	10	10	Moderate impairment	4	3
Required ventilation	6†	7‡	2 years		
Required treatment for renal impairment	4†	3‡	n	7	3
Perinatal (about 28 days)			Required surgery between 1 and 2 years	4	1
n	8	4	Days in hospital	0, 1, 5, 19, 30, 37, 116	23, 37, 40
Required surgery in perinatal period	5	3	Weight <10th centile	3‡	2
Still an inpatient	3†	2	Serum creatinine, µmol/L	65, 34, 87, 227, 60, 74, NR	502, 61, 72
Serum creatinine, µmol/L	29, 29, 88, 96, 105, 108, 119, 342	70, 126, 449, 620	Renal function§		
Renal function§			Normal	2	0
Normal	2	0	Mild	0	0
Mild impairment	2	1	Moderate	5	2
Moderate impairment	4	2	End-stage renal failure	0	1¶
End-stage renal failure	0	1			

Bez istotnych różnic aż do 2 roku życia w zakresie czynności nerek
Dzieci po interwencji częściej i dłużej przebywały w szpitalu

	Proportion affected*	Outcome
Spontaneous rupture of membranes after shunt insertion	3/15	Intrauterine death at 16 weeks' gestation (n=1); pregnancy affected by chorioamnionitis and parents chose to terminate at 17–22 weeks' gestation (n=2)
Dislodged	3/15	Spontaneous rupture of membranes with chorioamnionitis and parents chose to terminate at 17 weeks' gestation (n=1); subsequent pregnancy urinary ascites and neonatal death due to pulmonary hypoplasia (n=1); shunt reinserted, subsequent preterm labour at 26 weeks' gestation, alive at 28 days (n=1)
Blocked	1/15	Parents chose to terminate at 19 weeks' gestation (not related to treatment; persistent fetal bradycardia; n=1)

Four of 15 pregnancies were lost in the vesicoamniotic shunt group (three from spontaneous rupture of membranes and one after blockage). *Six were affected in total, with some having more than one complication.

Table 5: Complications of vesicoamniotic shunting

Seven complications occurred in six fetuses from the shunt group, including spontaneous ruptured membranes, shunt blockage, and dislodgement.

- U 6 dzieci spośród 15 poddanych interwencji wystąpiły działania niepożądane: - przerwanie worka owodniowego, - niedrożność przetoki; - przemieszczenie shuntu

Interpretation Survival seemed to be higher in the fetuses receiving vesicoamniotic shunting, but the size and direction of the effect remained uncertain, such that benefit could not be conclusively proven. Our results suggest that the chance of newborn babies surviving with normal renal function is very low irrespective of whether or not vesicoamniotic shunting is done.

Wskaźnik ogólnego przeżycia wydaje się być wyższy u dzieci poddanych interwencji, ale zakres i kierunek tego efektu nie jest jasny... Wyniki wskazują, że szansa na przeżycie z zachowaniem dobrej czynności nerek jest niewielka, niezależnie od tego czy wykonano połączenie pęcherzowo-owodniowe, czy nie.

Evaluation of the Cost Effectiveness of Vesico-Amniotic Shunting in the Management of Congenital Lower Urinary Tract Obstruction (Based on Data from the PLUTO Trial)

Lavanya Diwakar¹, Rachel K. Morris^{2,4}, Pelham Barton¹, Lee J. Middleton³, Mark D. Kilby^{2,4}, Tracy E. Roberts^{1*}

Main Outcome Measures: Survival at 28 days, 1 year and disease free survival at 1 year.

Results: VAS was more expensive but appeared to result in higher rates of survival compared with conservative management in patients with LUTO. Using ITT analysis the incremental cost effectiveness ratios based on outcomes of survival at 28 days, 1 year, or 1 morbidity-free year on the VAS arm were £15,506, £15,545, and £43,932, respectively.

Conclusions: VAS is a more expensive option compared to the conservative approach in the management of individuals with LUTO. Data from the RCT suggest that VAS improves neonatal survival but does not result in significant improvements in morbidity. Our analysis concludes that VAS is not likely to be cost effective in the management of these patients given the NICE (National Institute of Health and Clinical Excellence) cost threshold of £20,000 per QALY.

Ogólny koszt leczenia przy interwencji: 3 x wyższy niż przy postępowaniu zachowawczym

Fetal Surgery for Posterior Urethral Valves: Long-Term Postnatal Outcomes

PEDIATRICS Vol. 108 No. 1 July 2001

Nicholas Holmes, MD*; Michael R. Harrison, MD†; and Laurence S. Baskin, MD*

TABLE 3. Valve Patient Information

Patient Number	Fetal Intervention/ Gestational Age	Time of Death Postintervention	Serum Creatinine (mg/dL) at Age >12 Months	Bladder Status	Renal Transplantation
1	CU/20 wk	12 wk	—	—	—
2	BM/18 wk	—	0.5	Vesicostomy → intact	No
3	BM/24 wk	—	2.2	Intact	Yes
4	ABL/25 wk	—	1.4	Vesicostomy → intact	No
5	ABL/22 wk	3 wk	—	—	—
	VAS/24 wk				
6	VAS/18 wk	1 wk	—	—	—
7	VAS/19 wk	72 h (terminated)	—	—	—
8	VAS/19 wk	16 wk	—	—	—
9	VAS-3/19 wk	—	1.0	CU → intact	No
10	VAS/24 wk	—	3.1	Intact	Awaiting
11	VAS/24 wk	—	3.3	Vesicostomy → AC	Yes × 2
12	VAS/25 wk	—	2.0	CU → intact	No
13	VAS/28 wk	2 wk	—	—	—
14	VAS/30 wk	—	0.5	Intact	No

Bold indicates living patient; VAS, vesicoamniotic shunt; BM, bladder marsupialization; ABL, in utero ablation; CU, cutaneous ureterostomies; AC, augmentation cystoplasty.

Interwencje prenatalne: śmiertelność: 43%
Z tych, które przeżyły: 37,5 % wymaga transplantacji nerki

Long-term outcome in children after antenatal intervention for obstructive uropathies

Andrew L Freedman, Mark Paul Johnson, Craig A Smith, Ricardo Gonzalez, Mark I Evans

Lancet 1999; 354: 374–77

Between 1987 and 1996, 34 patients with antenatal obstructive uropathies underwent vesicoamniotic shunt placement at our institution. Intervention was done between 14.5 and 31 weeks' gestation (mean 22.4 weeks). Of the 34 cases, 13 (38%) died, and 21 (62%) survived. Causes of death were pulmonary hypoplasia (six), chorioamnionitis (two), postnatal sepsis (two), intrauterine fetal demise (one), voluntary termination (one), and previable preterm labour (one). Of the 21 survivors, 17 are older than 2 years and four are less than 2 years old. Three of the older children were lost to follow up, and 14 children were reviewed.

**34 dzieci; czas interwencji 14,4-31 tydzień;
13 (38%) dzieci zmarło**

Diagnosis (n=14)	Pulmonary function			Voiding function			Bladder augmentation	Renal function		
	Prolonged ventilatory support	Recurrent bronchitis	Mild asthma	Voids	Voids and caths	Caths		Normal	Insufficient	Failure
Prune belly syndrome (n=7)	2	2	0	5	1	1	0	2	1	4
Posterior urethral valves (n=4)	0	1	1	1	2	1	3	1	2	1
Other (n=3)*	0	0	0	2	1	0	0	3	0	0

*Megacystitis, urethral atresia, bilateral reflux. Caths=clean intermittent catheterisation.

Diagnosis-specific outcomes

The children underwent a total of 62 operative procedures (median 3, range 1–10) including 47 major procedures.

U 14 dzieci które przeżyły i były w obserwacji , wykonano łącznie 62 operacje i zabiegi (od 1 do 10/pacjenta; średnio – 3); w tym 47 rozległych operacji

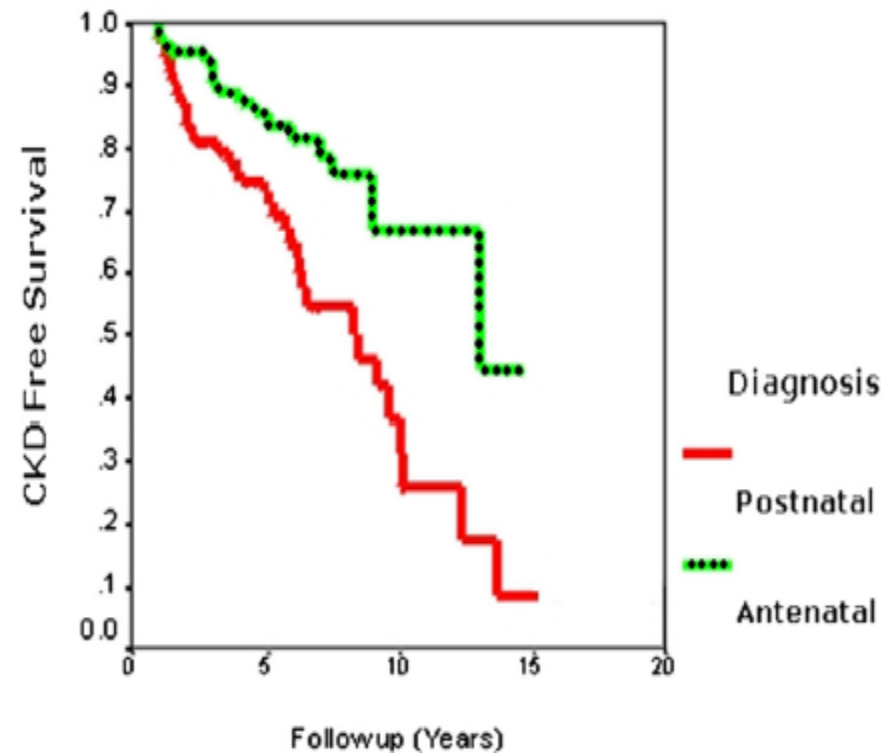
Pytania do wszystkich

Questions to all panelists:

- Czy takie wyniki skłaniają Was do rekomendowania rodzicom pacjentów interwencji prenatalnej w podobnych przypadkach?
- Do this results encourage you to recommend prenatal intervention to patient's parents?*
- Jeżeli tak: jakie będą argumenty za?
- Jeżeli nie: jakie będą argumenty przeciw?
- If positive, what will be your arguments for?*
- If negative, what will be your arguments against?*

Did Antenatal Diagnosis Protect Against Chronic Kidney Disease in Patients With Posterior Urethral Valves? A Multicenter Study

Osama M. Sarhan, Tamer E. Helmy, Abdulhakim A. Alotay, Mustafa S. Alghanbar, Ziad M. Nakshabandi, and Ashraf T. Hafez



Może należy ograniczyć się do diagnostyki prenatalnej i wczesnej interwencji ?

Maybe the activity should be limited to prenatal diagnostics and early postnatal intervention ?

Figure 2. Kaplan-Meier curve shows the incidence of chronic kidney disease stratified by age at presentation.

Czy należy ściśle ograniczyć wskazania do interwencji prenatalnej do wybranych przypadków? Jak tak, to do jakich?

Should the clinical indications to prenatal intervention be limited to pre-selected patients?

If so, to whom?

Kiedy najlepiej dokonać
instrumentacji?

Optimal timing for intervention ?

Fetal stage**Lung structure****Embryonic**
0-7 weeks**Trachea** 24 days**Extrapulmonary
Main Bronchus** 28 days**Bronchi** 4-12 weeks
8-13 generations**Bronchioli** 12-16 weeks
3-10 generations**Terminal Bronchiolus** 16-17 weeks
1 generation**Respiratory bronchioli** 18-25 weeks
1 generation**Alveolar ducts** 25 wk-1yr
2-3 generations**Alveoli** 30 wk-2-3yr
1 generation
ie 1000/acinus**Acinus**

pleura



Table 1 congenital malformations or diseases associated with abnormal lung development and the stage of their development.

Embryonic

- Pulmonary agenesis
- Tracheal or laryngeal agenesis or stenosis
- Tracheo- or broncho-malacia
- Bronchial malformations
- Ectopic lobes
- A-V malformations
- Congenital lobar cysts

Pseudoglandular

- Cystic adenomatoid malformation
- Pulmonary sequestration
- Lung hypoplasia ←
- Lung cysts
- Congenital pulmonary lymphangiectasia
- Congenital diaphragmatic hernia

Canalicular

- Lung hypoplasia ←
- Respiratory distress syndrome
- Acinar dysplasia

Saccular/Alveolar

- Pulmonary hypoplasia ←
- Respiratory distress syndrome/Chronic Lung disease of prematurity
- Acinar dysplasia
- Alveolar capillary dysplasia

[Fetal Diagn Ther.](#) 1995 Sep-Oct;10(5):343-8.

Severe urethral obstruction diagnosed at 14 weeks' gestation: variability of outcome with and without drainage.

[MacMahon RA](#)¹, [Renou PM](#), [Shekleton PA](#), [Paterson PJ](#).

We present 3 case reports to illustrate the variability of outcome of severe fetal posterior urethral obstruction. Two of the described cases support the view that early in-utero decompression of an obstructed fetal urinary system into the amniotic cavity, in the selected patient, will allow adequate lung development and will prevent the development of severe renal dysplasia. It will not prevent the abdominal wall deformity of the prune belly syndrome.

The evidence suggests that to allow maximum time for lung development and to prevent increasing renal dysplasia, drainage should be performed before 18 weeks of gestation. To obtain maximum effect, this drainage should continue until at least 32-33 weeks' gestation, so that the possible respiratory problems of prematurity would not be severe enough to compound the degree of lung hypoplasia which might be present.

Optymalny czas :

- dla wykonania odbarczenia zastoju to < 18 tygodnia życia płodowego
- utrzymywania drenażu: do 32-33 tygodnia życia płodowego

[Fetal Diagn Ther.](#) 1998;13(3):133-5.

Fetal bladder catheterization in severe obstructive uropathy before the 24th week of pregnancy.

[Szaflik K](#)¹, [Kozarzewski M](#), [Adamczewski D](#).

Early bladder drainage (before the 24th week of gestation) enables delivery of newborns with a good perinatal outcome, without pulmonary hypoplasia. This method of therapy limits renal damage and allows time for normal development of the fetal lungs.

Histology of the fetal prune belly syndrome with reference to the efficacy of prenatal decompression

International Journal of Urology (2000) **7**, 161–166

KENJI SHIMADA, SHYOZO HOSOKAWA, AKIRA TOHDA, FUMI MATSUMOTO AND KAZUYOSI JOHNIN

Conclusion: The clinical implication from the renal histology is that decompression of the urinary tract should be done before GA 20 weeks. However, the early fetal treatment appears to have no effect on the urodynamics in this disorder with deficient musculature.

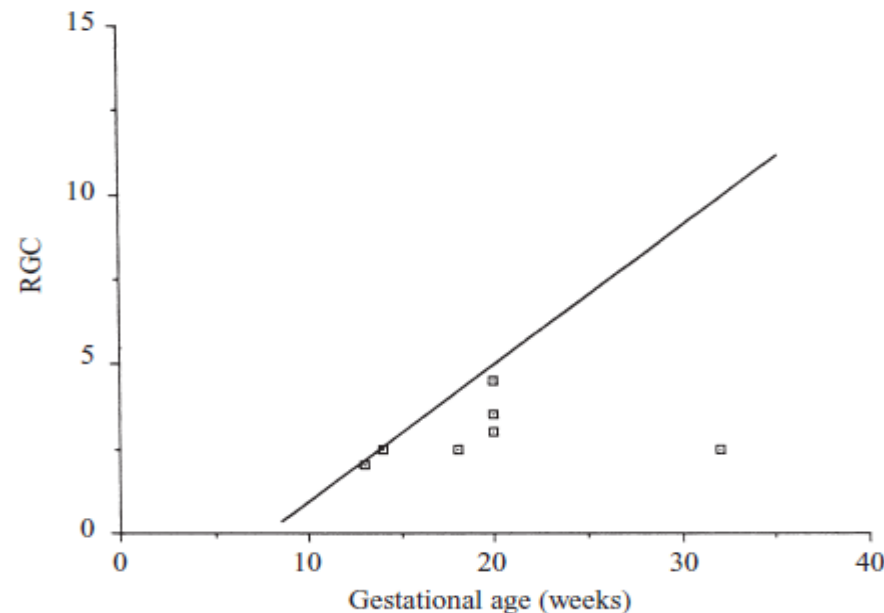


Fig. 3 Radial glomerular count (RGC) according to gestational age in fetal prune belly syndrome. The oblique line indicates a normal increase of RGC.

Wniosek I (TAK/NIE)
Conclusion I (YES/NO)

1. Interwencyjne zabiegi prenatalne powinny być ograniczone do cięższych przypadków nefropatii zaporowej, ale u dzieci nie obciążonych (innymi) nieuleczalnymi wadami, bo tylko w tych przypadkach duże ryzyko powikłań jest zbilansowane potencjalną korzyścią (dziecko przeżyje)
1. *Prenatal interventions should be limited to severe cases of obstructive uropathy, however in children with no other, not curative co-morbidities, as only in such cases the high risk of complications is balanced by potential benefit (child may survive)*

Wniosek II (TAK/NIE)
Conclusion II (YES/NO)

2. Przed podjęciem decyzji należy uprzedzić rodziców pacjenta, że o ile przeżyje pierwszy miesiąc po urodzeniu, istnieje duże ryzyko rozwoju przewlekłej choroby nerek, licznych zabiegów operacyjnych w przyszłości oraz konieczności leczenia nerkozastępczego

2. Before the decision is taken, the parents must be forwarned, that even if patient will survive the first month post-delivery, there is high risk of chronic renal disease, further multiple surgery and indication to renal replacement therapy

Wniosek III (TAK/NIE)
Conclusion III (YES/NO)

3. Optymalny okres czasu do prenatalnego odbarczenia wady zaporowej to.... tydzień życia płodowego

3. Optimal timing for prenatal procedure is...weeks of fetal life