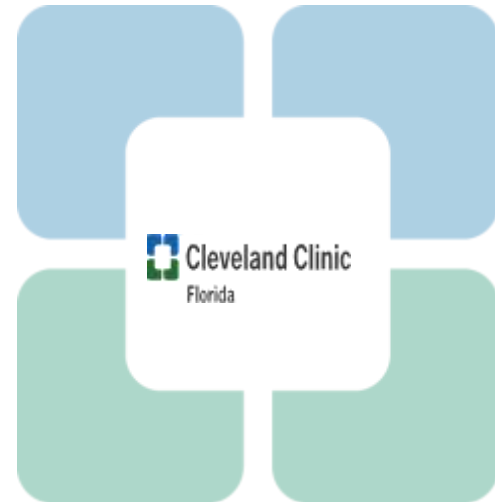


New Frontier : Obesity, Bariatric Surgery and Chronic Kidney Disease (CKD)

The Cleveland Clinic Florida Hypothesis

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Foregut Editor, SURGERY*



DISCLOSURES

- Consultant Diagnostic Green / Medtronic / Arthrex Honoraria
- Advisory Board Medica Simulation Stockholder
- CEO Dendrite Imaging Inc. Stockholder
- CEO Intelligent Surgical Eye Stockholder
- Educational Grants Medtronic / Stryker / Storz / Arthrex / Ethicon

NATIONWIDE IMPACT OF CKD

More than 1 in 7 adults
have CKD in America
and 90% are NOT
aware

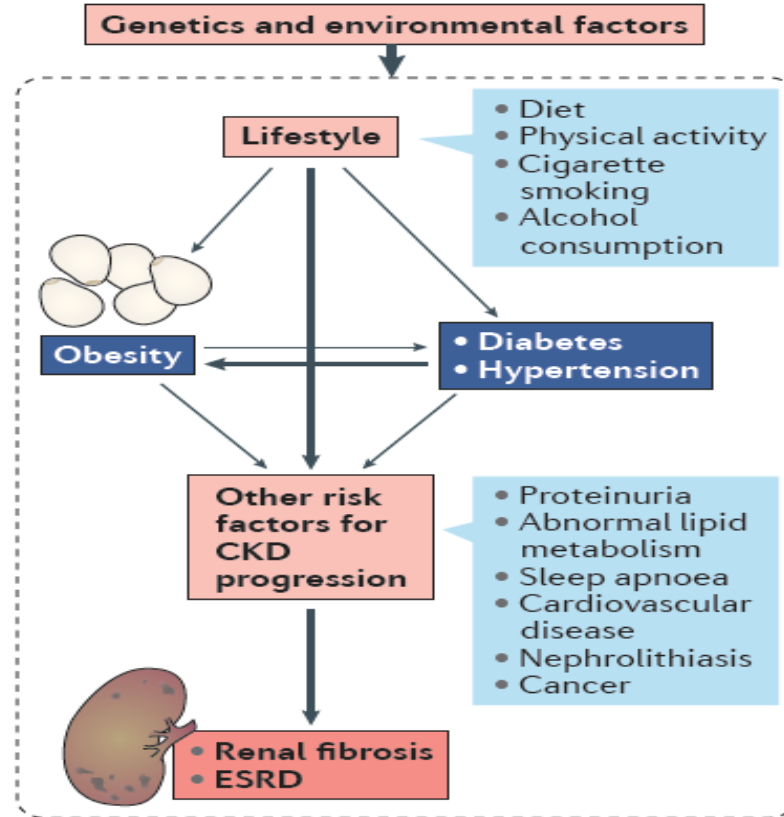
Total Medicare spending
CKD and ESRD excess of
\$120 Billion

TOP 10 leading
causes of death in
America

RISK FACTORS

National Kidney Foundation

- 2/3 (66%) **DM and HTN**
- Amongst the other 30%, metabolically healthy obesity related CKD
- In our experience 11%



Evidence of Bariatric Surgery as an alternative treatment for CKD?

MUCH HOPE in Bariatric Surgery?

Swedish obese subject
study $n=4047$

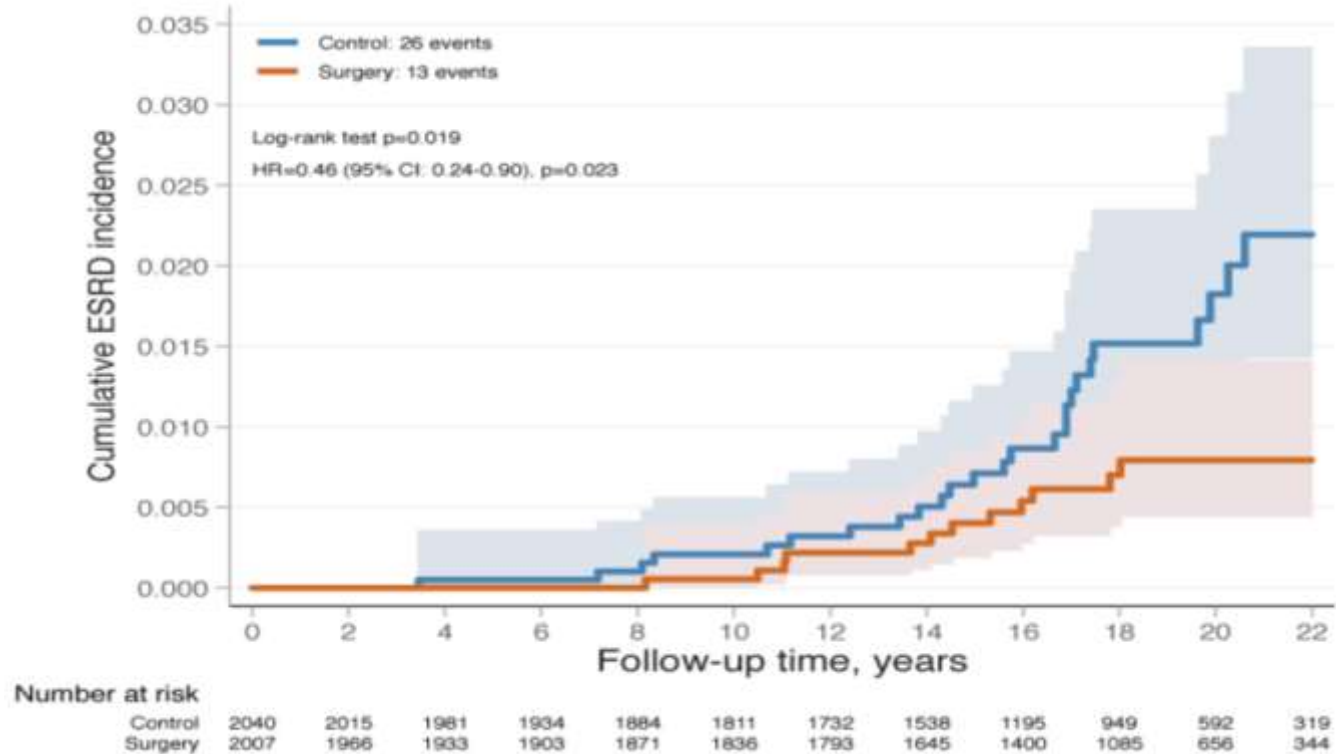
Trends in Bariatric
surgery procedures in
ESRD in US 100%
Medicare data SG 84%

Effects of bariatric
surgery on CKD Risk
 $n=2144$

Impact of renal function
on outcomes of bariatric
surgery $n=27,736$
<10% complication

1. *International Journal of Obesity*, 42(5), 964–973. doi:10.1038/s41366-018-0045-x
2. *Clinical Journal of the American Society of Nephrology*, CJN.01480219. doi:10.2215/cjn.01480219
3. *J Am Soc Nephrol* 29: 1289–1300, 2018. doi: <https://doi.org/10.1681/ASN.2017060707>
4. *J Am Soc Nephrol* 23: 885–894, 2012. doi: 10.1681/ASN.2011050476

Swedish obese subject study n=4047



RESEARCH ARTICLE

Effects of Bariatric Surgery on Renal Function in Obese Patients: A Systematic Review and Meta Analysis

Kun Li^{1✉*}, Jianan Zou^{2✉}, Zhibin Ye², Jianzhong Di³, Xiaodong Han³, Hongwei Zhang³, Weijie Liu³, Qinggui Ren³, Pin Zhang³

1 Department of General Surgery, Huadong Hospital Affiliated to Fudan University, Shanghai, China,
2 Department of Nephrology, Huadong Hospital Affiliated to Fudan University, Shanghai, China,
3 Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China

32 observational studies
30 included in the meta-analysis

Significant reduction in:

- Hyperfiltration
- Albuminuria



RCT Surgery VS. medical therapy

A RANDOMIZED CONTROLLED TRIAL OF GASTRIC BYPASS VERSUS BEST MEDICAL TREATMENT FOR EARLY STAGE CHRONIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES AND OBESITY
MOMS TRIAL

STUDY POPULATION

100 patients with

- Type 2 diabetes
- Chronic kidney disease
- BMI of 30-35kg/m²



INTERVENTION

Best Medical Therapy (BMT)

- ✓ Oral drugs including SGLT2i
- ✓ GLP1RA
- ✓ Insulin



X

Best Medical Therapy PLUS RYGB



OUTCOME

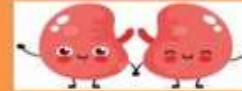


CKD Remission *
82%

*P<0.05

CKD Remission
48%

RYGB is as safe as BMT



Cohen RV et al. *JAMA Surg* 06/03/2020

JAMA Surgery

Beneficial effects of Bariatric Surgery 7 years Institutional and National Data Cleveland Clinic Florida Hypothesis

ASA PAPER

Metabolic Surgery Reduces the Risk of Progression From Chronic Kidney Disease to Kidney Failure

David Romero Funes, MD,* David Gutierrez Blanco, MD,* Camila Ortiz Gómez, MD,* Joel S. Frieder, MD,*
Emanuele Lo Menzo, MD, PhD, FACS, FASMBS,* Samuel Szomstein, MD, FACS, FASMBS,*
Kevin P. White, MD, PhD,† and Raul J. Rosenthal, MD, FACS, FASMBS*✉



Surgery for Obesity and Related Diseases 18 (2022) 281–287

Original article

Prevalence of chronic kidney disease and end-stage renal disease in a bariatric versus nonbariatric population: a retrospective analysis of the U.S. National Inpatient Sample database

David Romero Funes, M.D.^a, David Gutierrez Blanco, M.D.^a, Liang Hong, Ph.D.^b,
Emanuele Lo Menzo, M.D., Ph.D.^a, Samuel Szomstein, M.D.^a,
Raul J. Rosenthal, M.D., F.A.C.S., F.A.S.M.B.S., M.A.M.S.E.^{a,*,†}

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Received 24 September 2021; accepted 26 September 2021



Surgery for Obesity and Related Diseases 18 (2022) 772–778

SURGERY FOR OBESITY
AND RELATED DISEASES

Original article

Sleeve gastrectomy in patients with severe obesity and baseline chronic kidney disease improves kidney function independently of weight loss: a propensity score matched analysis

David Romero Funes, M.D.^a, Lisandro Montorfano, M.D.^a, David Gutierrez Blanco, M.D.^a,
Mauricio Sarmiento Cobos, M.D.^a, Emanuele Lo Menzo, M.D., Ph.D.^a,
Samuel Szomstein, M.D.^a, Neerja Agrawal, M.D.^a, Raul J. Rosenthal, M.D.^{a,*}

^aDepartment of General Surgery, Bariatric and Metabolic Institute, Cleveland Clinic Florida, Weston, Florida

SURGERY FOR OBESITY
AND RELATED DISEASES

Metabolic Surgery Reduces the Risk of Progression From Chronic Kidney Disease to Kidney Failure

David Romero Funes, MD,* David Gutierrez Blanco, MD,* Camila Ortiz Gómez, MD,* Joel S. Frieder, MD,*
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 Kevin P. White, MD, PhD,† and Raul J. Rosenthal, MD, FACS, FASMBS*✉

TABLE 2. uACR Differences at 12 mo Follow-up **uACR= GLOMERULAR INJURY**

uACR	% (n)	Preop		12-mo Follow-up		Δ		Pre- vs. Post- P Value*
		Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Mean	IQR	
uACR for all patients	100 (69)	172.1 ± 457.7	36 (9.9–92.2)	51.1 ± 78.3	25 (8–55.6)	121.0	34.7	<0.001‡
CKD stage 1	43.4 (30)	108 ± 14	11.35 (4.9–31.8)	104.54 ± 19.2	10.5 (5–26.25)	3.4	5.6	0.3261‡
CKD stage 2	27.5 (19)	113.2 ± 157.1	44.6 (15–187.3)	57.1 ± 70.6	30 (13–90.4)	56.1	94.9	0.0003‡
CKD stage ≥3	29.0 (20)	370.8 ± 778.5	66.5 (35.1–465.4)	66.4 ± 79.4	47 (25.13–66)	304.4	389.4	0.001‡

*Within-group comparison.

‡Paired t-test.

‡Wilcoxon Signed-rank test.

82.09% DIFFERENCE

BASELINE CKD

1st to adhere to KDOQI guidelines

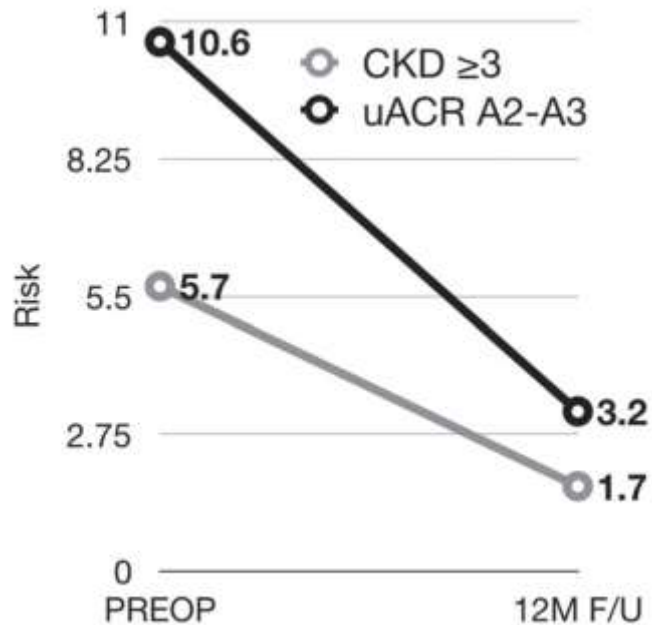


FIGURE 1. CKD risk of progression to kidney failure (2 yr risk). CKD indicates chronic kidney disease.

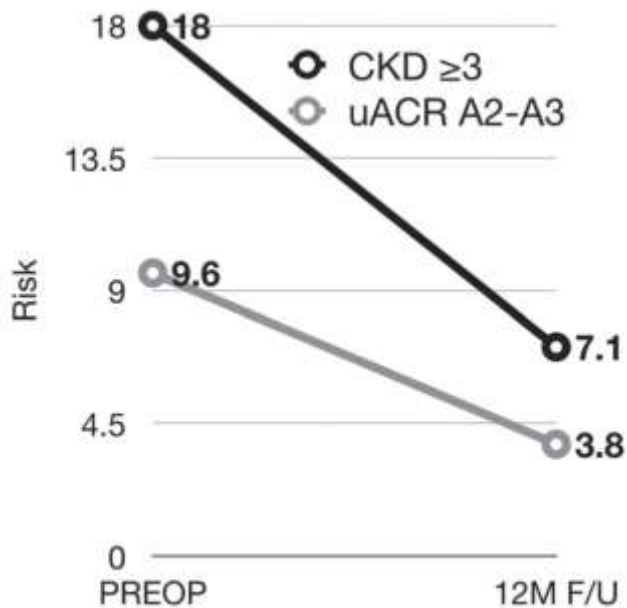


FIGURE 2. CKD risk of progression to kidney failure (5 yr risk).

Original article

Prevalence of chronic kidney disease and end-stage renal disease in a bariatric versus nonbariatric population: a retrospective analysis of the U.S. National Inpatient Sample database

David Romero Funes, M.D.^a, David Gutierrez Blanco, M.D.^a, Liang Hong, Ph.D.^b,
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Raul J. Rosenthal, M.D., F.A.C.S., F.A.S.M.B.S., M.A.M.S.E.^{a,†}

^aDepartment of General Surgery and the Bariatric and Metabolic Institute, Cleveland Clinic Florida, Weston, Florida

^bDepartment of Clinical Research, Cleveland Clinic Florida, Weston, Florida

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STAGES CKD Prevalence	Controls N=2,004,804	Surgery cases N=296,041	P-value
Stage II, n (%) INCREASED RISK	16,759 (0.84%)	1,097 (0.37%)	<0.0001
Stage III, n (%)	120,858 (6.05%)	6,612 (2.25%)	<0.0001
Stage IV, n(%)	37,513 (1.88%)	2,097 (0.71%)	<0.0001
ESRD	63,344 (3.15%)	5,502 (1.85%)	<0.0001

2 stage prospective trial

Cushing reflex = increased release of vasopressin, mediating oligoanuric response



Surgery

Volume 171, Issue 2, February 2022, Pages 399-404



Gastric

The role of Cushing's reflex and the vasopressin-mediated oligoanuric response to intracranial hypertension in patients with abdominal compartment syndrome

Lisandro Montorfano MD ^a, Fernando Dip MD ^{a, b}, Emanuele Lo Menzo MD, PhD ^a, Neerja Agrawal MD ^c, Edward H. Phillips MD ^d, Hong Liang PhD ^e, Kevin P. White MD, PhD ^f, Raul J. Rosenthal MD ^{a, g},

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SURGERY

BARIATRIC | VOLUME 167, ISSUE 2, P478-483, FEBRUARY 01, 2020

The Cushing reflex and the vasopressin-mediated hemodynamic response to increased intracranial pressure during acute elevations in intraabdominal pressure

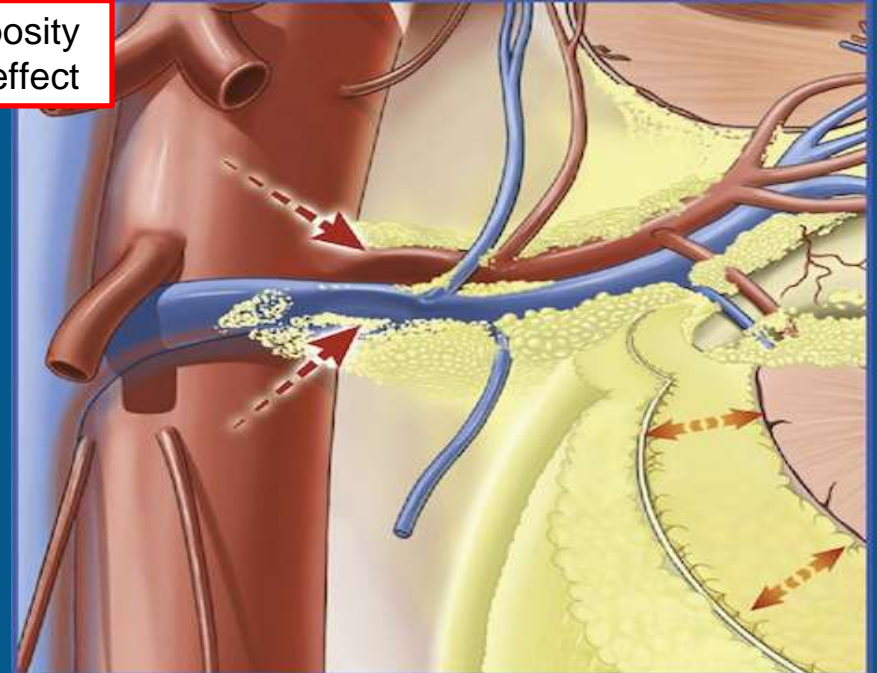
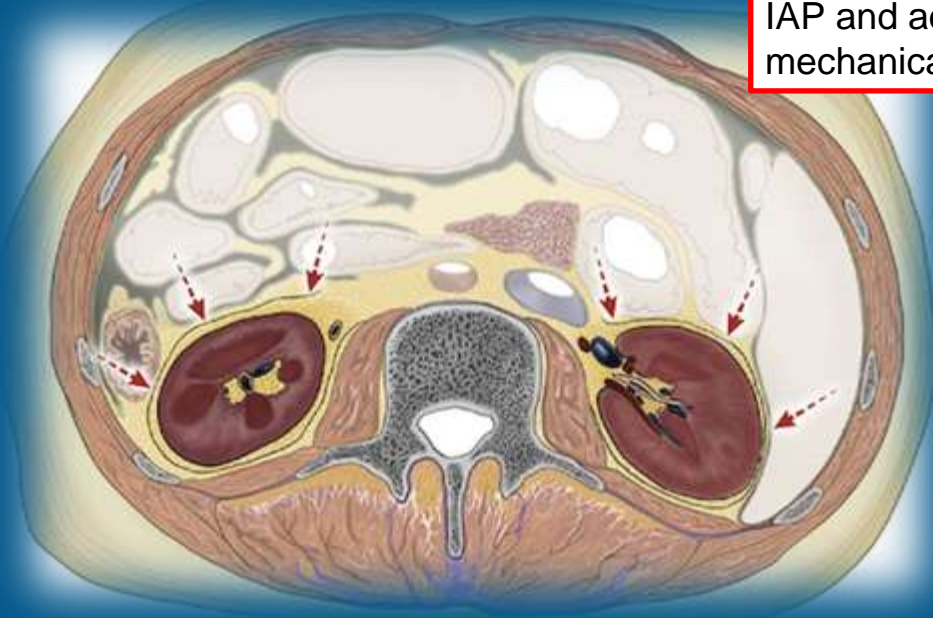
Lisandro Montorfano, MD • Giulio Giambartolomei, MD • David Romero Funes, MD • ... Fernando Dip, MD • Kevin P. White, MD, PhD • Raul J. Rosenthal, MD • [Show all authors](#)

Open Access • Published: December 05, 2019 • DOI: <https://doi.org/10.1016/j.surg.2019.10.005> • [Check for updates](#)

IAP, ICP, mechanical and hormonal (AVP) effects on the Kidney

HYPERFILTRATION
Vasopressin AVP

IAP and adiposity
mechanical effect





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SURGERY



Bariatric

The Cushing reflex and the vasopressin-mediated hemodynamic response to increased intracranial pressure during acute elevations in intraabdominal pressure



Lisandro Montorfano, MD^a, Giulio Giambartolomei, MD^a, David Romero Funes, MD^a, Emanuele Lo Menzo, MD, PhD^a, Fernando Dip, MD^{a,b}, Kevin P. White, MD, PhD^c, Raul J. Rosenthal, MD^{a,*}

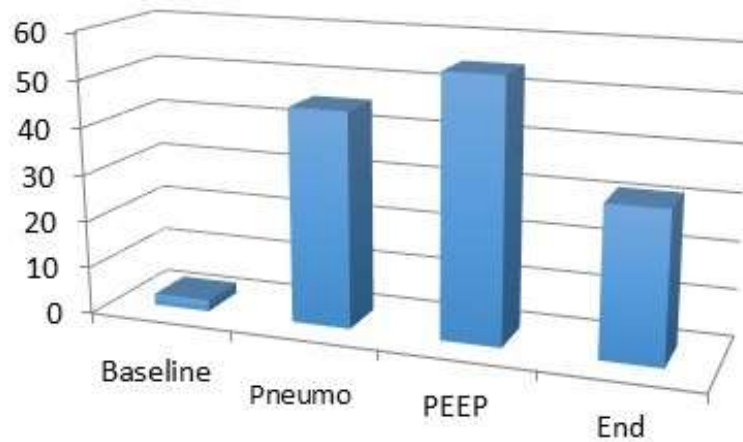
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^c ScienceRight Research Consultations, London, ON, Canada

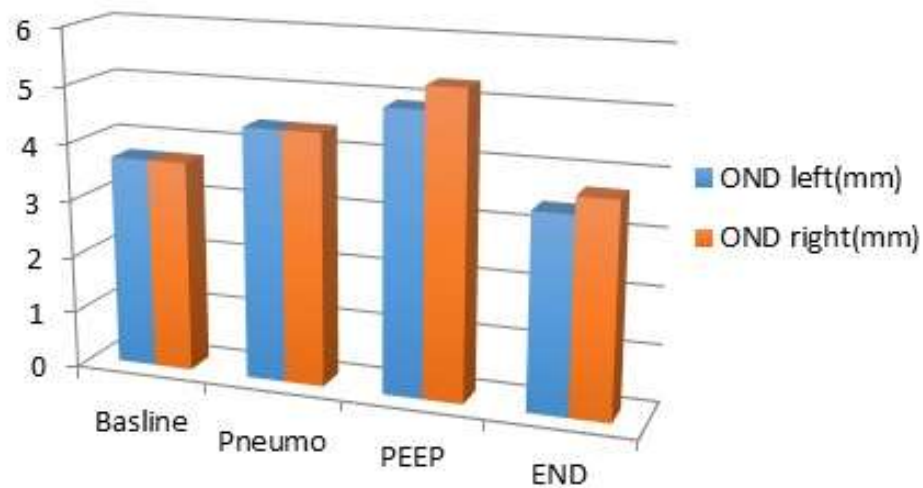
■ Vasopressin(pg/ml)

Serum Vasopressin

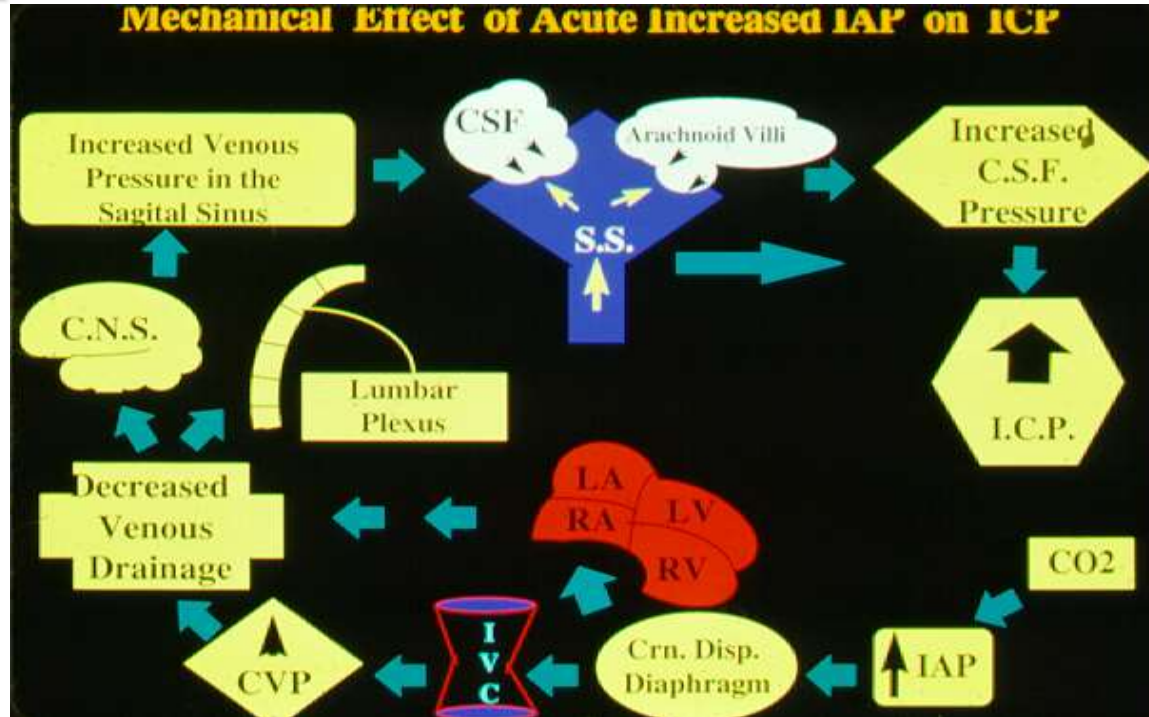


	Baseline	Pneumo	PEEP	End
Vasopressin(pg/ml)	2.37	45.48	54.75	31.57

Optic Nerve Diameter



	Baseline	Pneumo	PEEP	END
OND left(mm)	3.7	4.4	4.9	3.4
OND right(mm)	3.7	4.4	5.3	3.7

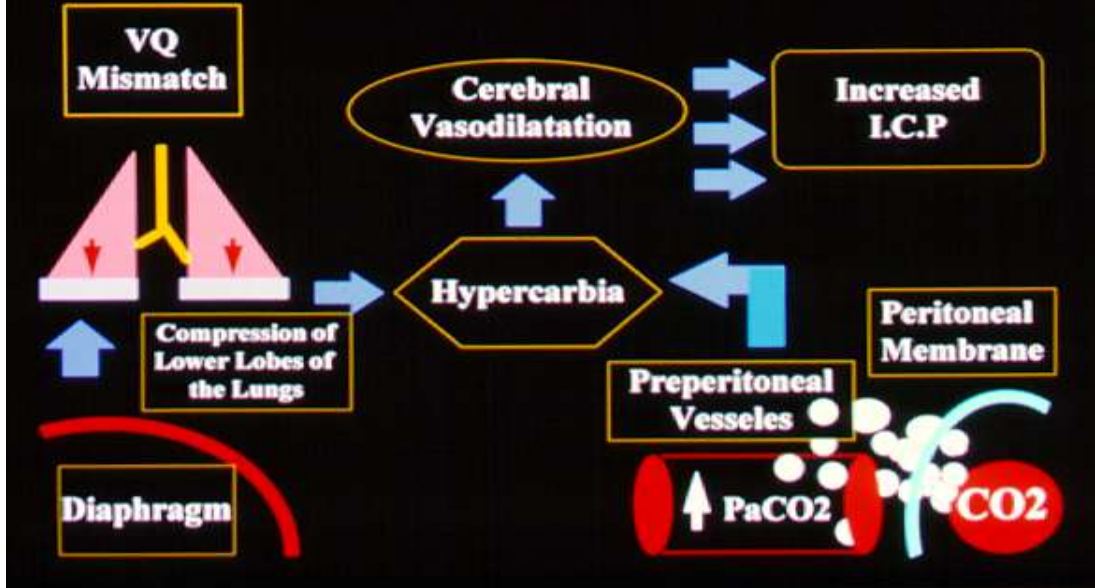


Abstract
 The Cushing reflex and the vasopressin-mediated hemodynamic response to increased intracranial pressure during acute elevations in intraabdominal pressure

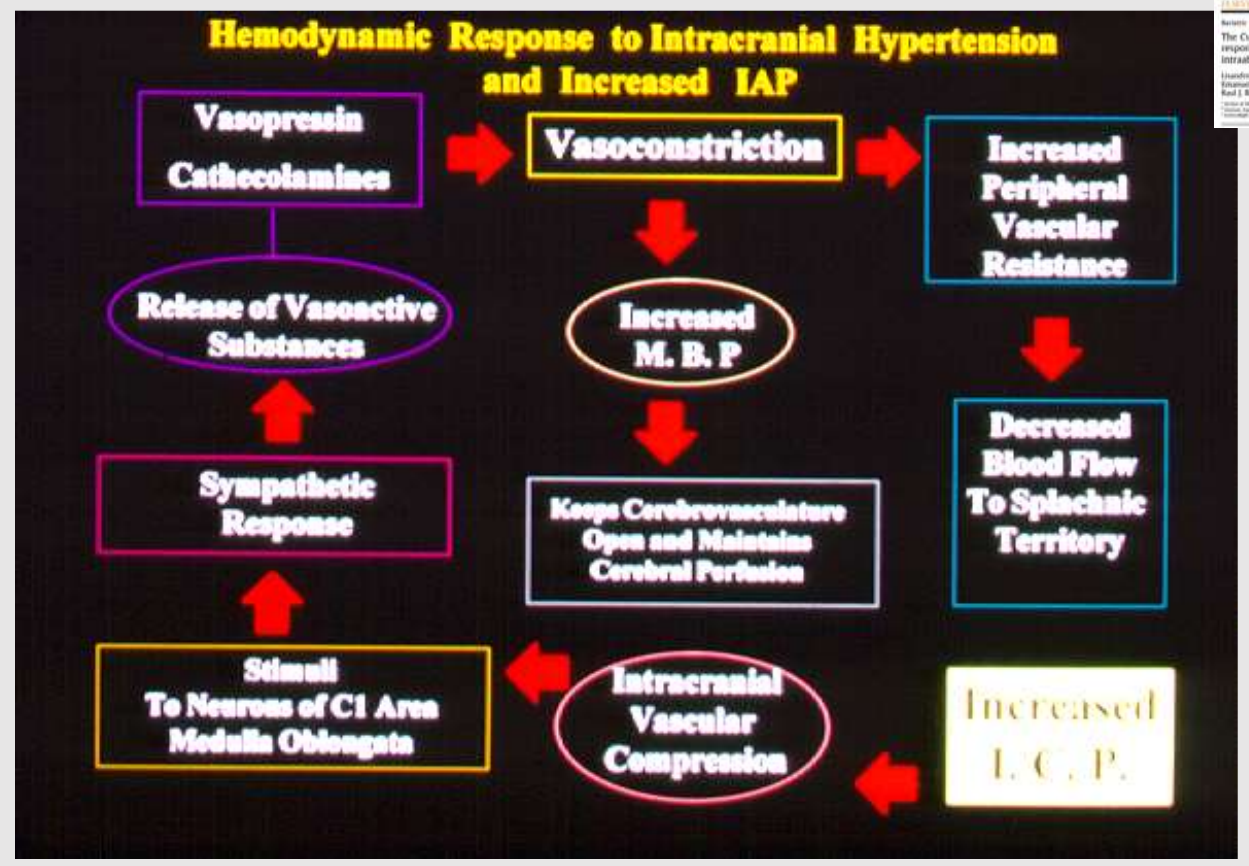
Francis Mooreaux, MD, Chitra Chandersekaran, MD, David Bennett Fung, MD, Giuseppe La Morte, MD, PhD, Fernando Dja, MD, Kevin P. Wilson, MD, PhD, and J. Rosenthal, MD*

*Division of Gastrointestinal Surgery, Department of Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, Ohio

Chemical Effect of Acute Increased IAP on ICP



Rosenthal RJ et al
 J Gastroint Surg 1994



Rosin et al, International Journal of Surgical Research, 2000



Vasopressin/Copeptin in CKD

Chronically high vasopressin 3 LARGE EUROPEAN COHORTS (copeptin Surroget marker)

(n = 5,047; France), MDCS-CC (n = 3,643; Sweden), and PREVEND (n = 7,684; the Netherlands)

High plasma copeptin at baseline= increased incidence of stage 3 CKD

- Kidney function decline assessed by the KDIGO criterion
- Microalbuminuria

A033 Changes in renal blood flow (RBF) in the severely obese a potentially reversible form of renal injury and a possible emerging mechanism for bariatric surgery on chronic kidney disease (CKD)

DOI: <https://doi.org/10.1016/j.soard.2023.04.033> •



- **Primary objective:** determine the prevalence of decreased RBF (dRBF) in severely obese patients with baseline CKD and risk of CKD at our institution.
- **Secondary objective:** we sought to establish the effects of bariatric surgery on the renal blood flow of patients with baseline CKD and at risk of CKD at baseline

A033 Changes in renal blood flow (RBF) in the severely obese a potentially reversible form of renal injury and a possible emerging mechanism for bariatric surgery on chronic kidney disease (CKD)

DOI: <https://doi.org/10.1016/j.soard.2023.04.033> •



N=2924

Bariatric Surgery 2003-2019

N=714 required data

N=228 CKD ≥ 2

PMH of **HTN or DM excluded.**

Pre and post-op BUN/Cr ratio

>20 pre-renal component; decreased RBF

<20 intrinsic component

CKD-EPI eGFR

Pre-op = 3 months average

**Post-op= 15-month
(1-time calculation)**

RESULTS (RBF)

Table 1. Improvement of kidney function and changes in BUN/Cr at 12 months follow-up for patient with Baseline CKD.

CKD stages	Pre eGFR	Post eGFR	Improvement mL/min/1.73 m ²	P value t-test	Pre-BUN/Cr	Post-BUN/Cr	P value T-test
CKD ≥ 2 N=228	67.37 ±18.17	79.89 ±21.81	12.57	0.0001	20.23 ±9.55	14.99 ±9.21	0.0001
Stage 2 N=165	76.66 ±8.18	86.88 ±14.99	10.22	0.0001	20.85 ±10.23	14.99 ±9.10	0.0001
Stage 3 N=53	47.27 ±8.56	69.99 ±16.90	22.72	0.0001	23.88 ±8.75	16.38 ±9.27	0.0001
Stage 4-5 N=10	18.78 ±7.78	17.66 ±8.78		0.8	21.71 ±9.28	19.29 ±14.58	0.6

RESULTS (Hyperfiltration)

N=2924 eGFR	Pre-op	Post-op	Difference eGFR ml/min/1.73m ²	BUN/Cr Pre-op	P-value
Hyperfiltration N=471 (16%) >120 eGFR	131.32±9.17	97.77± 20.12	33	14.26±6.71	0.001
120-149 eGFR N=459 97.45%	130.12±7.51	122±13.60	8 INTRINSIC	14.47±6.88	0.0001
150-179 eGFR N=12 2.55%	158.83±2.63	140.56±8.29	18	13.12 ±3.91	NS

CONCLUSIONS

Improvement in kidney-function in **CKD stages 2-3** could be attributed to **changes in RBF** following BaS

The prevalence of decreased renal blood flow and hyper-filtration in our bariatric population are **consistent with** the previously postulated **vasopressin/Copeptin hypothesis**

Hyper-filtration and the changes in RBF following bariatric surgery could be attributed to the **stabilization of the vasopressin release** resulting from the chronic iIAP and the Cushing reflex in the severely obese population.



Every life deserves world class care.