

Utility of Urinary Biomarkers to Predict Delayed Graft Function After Kidney Transplantation

Richard J. Marcus¹, Jonathan M. Duran¹, Samuel C. Barood¹, Dana E. Brandys¹, Joshua C. Sysak¹, Ifeatu U. Oti¹, Kalathil K. Sureshkumar¹, Sabiha M Hussain¹, WK Han², Barbara J. Carpenter¹, Dai D. Nghiem⁴, Stephen E. Sandroni¹

¹Division of Nephrology, Allegheny General Hospital, Pittsburgh, PA; ²Renal Division, Brigham and Women's Hospital, Boston, MA; ³Department of Medicine, and ⁴Department of Transplant Surgery, Allegheny General Hospital, Pittsburgh, PA.



Introduction – Delayed Graft Function

- Ischemia-reperfusion injury occurs during renal transplant and can cause delayed graft function (DGF)
 - Reported incidence of DGF is between 10 and 50% worldwide
- After renal transplant, allograft function is monitored by daily urine output and serum creatinine levels
 - Both parameters have limitations



Introduction – Urinary Biomarkers

- **N-acetyl β -(D) glucosaminidase (NAG)** → lysosomal brush border enzyme of proximal renal tubular cells
 - Elevated in patients with ischemia-reperfusion injury but also in patients with proteinuria, on calcineurin inhibitors, and in episodes of acute rejection
- **Matrix Metalloproteinase-9 (MMP-9)** → gelatinase with proteolytic activities towards basement membrane components
 - Elevated in ischemia-reperfusion injury and in situations where TNF α levels are increased
- **Kidney Injury Molecule-1 (KIM-1)** → trans membrane glycoprotein that is increased in the proximal tubule after ischemia-reperfusion injury
 - Levels increase with dedifferentiation and remodeling of tubule cells after ischemic damage



Study Objectives

- To determine if urinary biomarkers can predict DGF following renal transplant
- To explore the utility of urinary biomarkers in predicting DGF earlier than the traditional methods (urine output and serum creatinine)



Delayed Graft Function

- DGF is defined as the requirement for dialysis in the first seven days post transplant or a reduction by less than 10% in the serum creatinine by POD #2 compared to the pre-operative value



Study Design

- Prospective pilot study of consecutive renal transplant patients from August 2006 to September 2006 at Allegheny General Hospital in Pittsburgh, PA

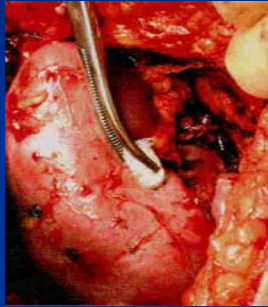


Inclusion Criteria

- History of chronic kidney disease (CKD) Stage IV, V, or VI
- Undergoing a deceased or living donor renal transplant
- Age > 18



Study Course



Informed consent obtained



Pre transplant blood work done



Renal transplantation



t=0, 6, 12, and 24 hours - 10 mL urine sample obtained



POD # 2 and 3 - 10 mL urine sample obtained



POD # 1-4 – Daily blood work

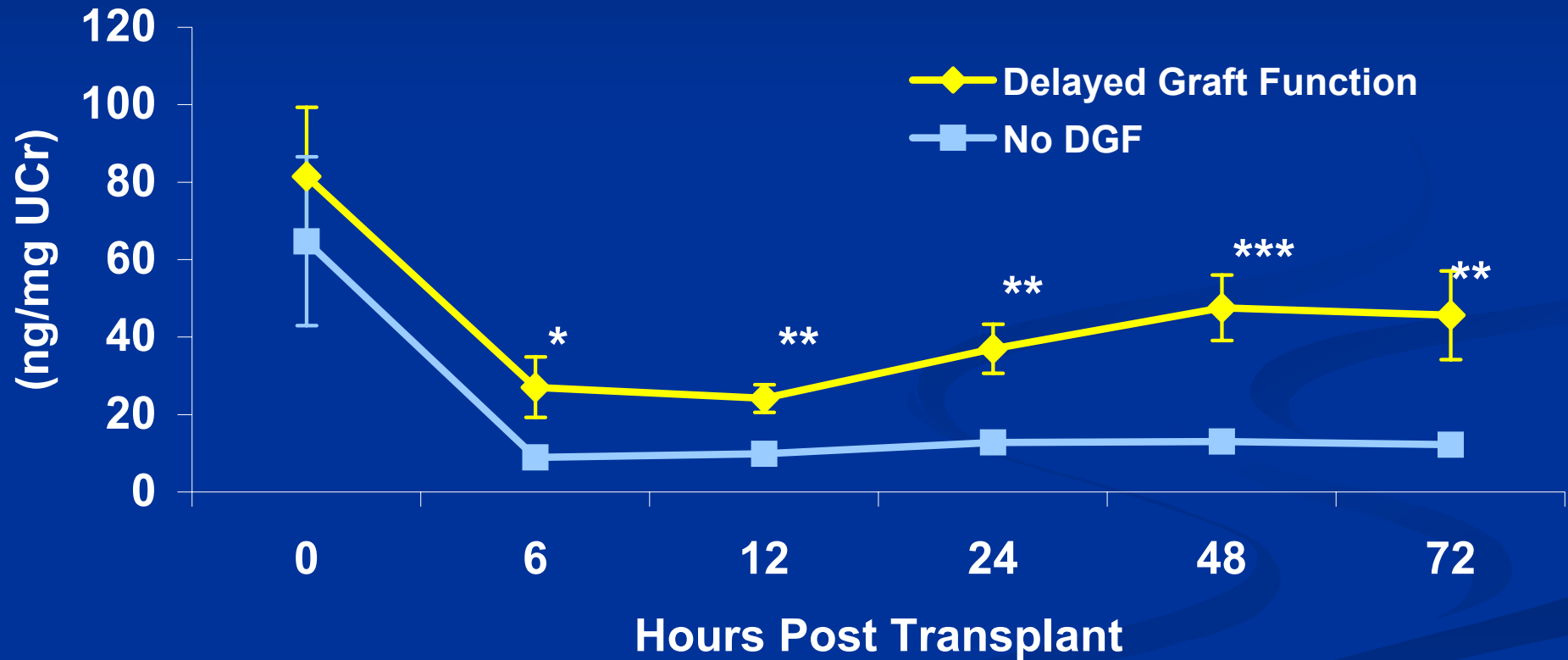


Demographic and Clinical Information

Characteristic	DGF	No DGF
Number of Patients (M/F)	10(6/4)	10(4/6)
Age (yrs)	53 ± 8	47 ± 11
Etiology of kidney disease		
Glomerulonephritis	3	2
Diabetes	3	2
Hypertension	2	0
Other	2	6
Pre-transplant mode of dialysis		
Hemodialysis	8	6
Peritoneal Dialysis	1	3
None	1	1
No. of pts with prior transplant	3	3
Cold Ischemia Time (hrs)	35 ± 13	24 ± 13
Lowest Intra-Operative SBP	102 ± 10	97 ± 12
No. of pts with rejection in 30 days	4	1



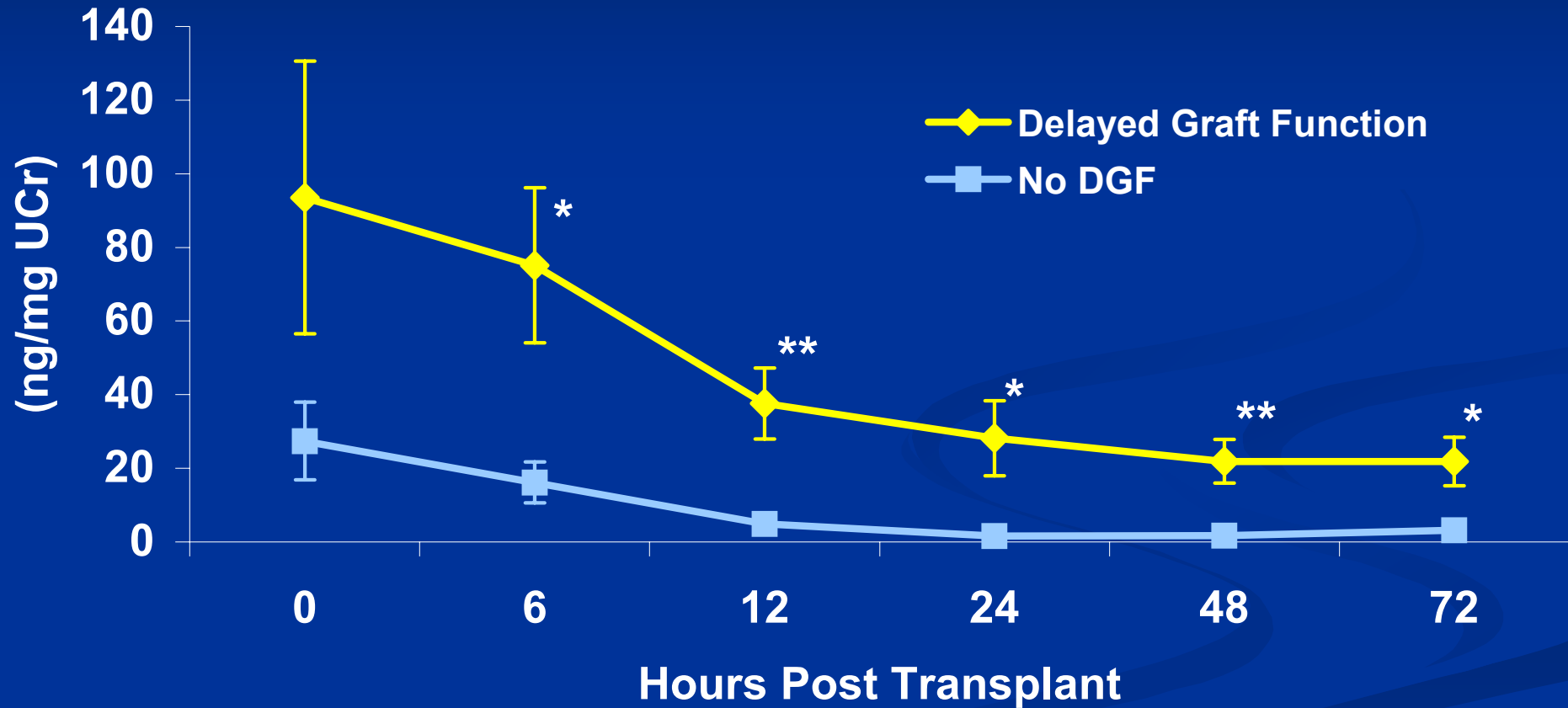
N-acetyl β -(D) glucosaminidase (NAG) Levels Post Transplantation in DGF and Non DGF Patients



*p < 0.05, **p < 0.01, ***p < 0.001



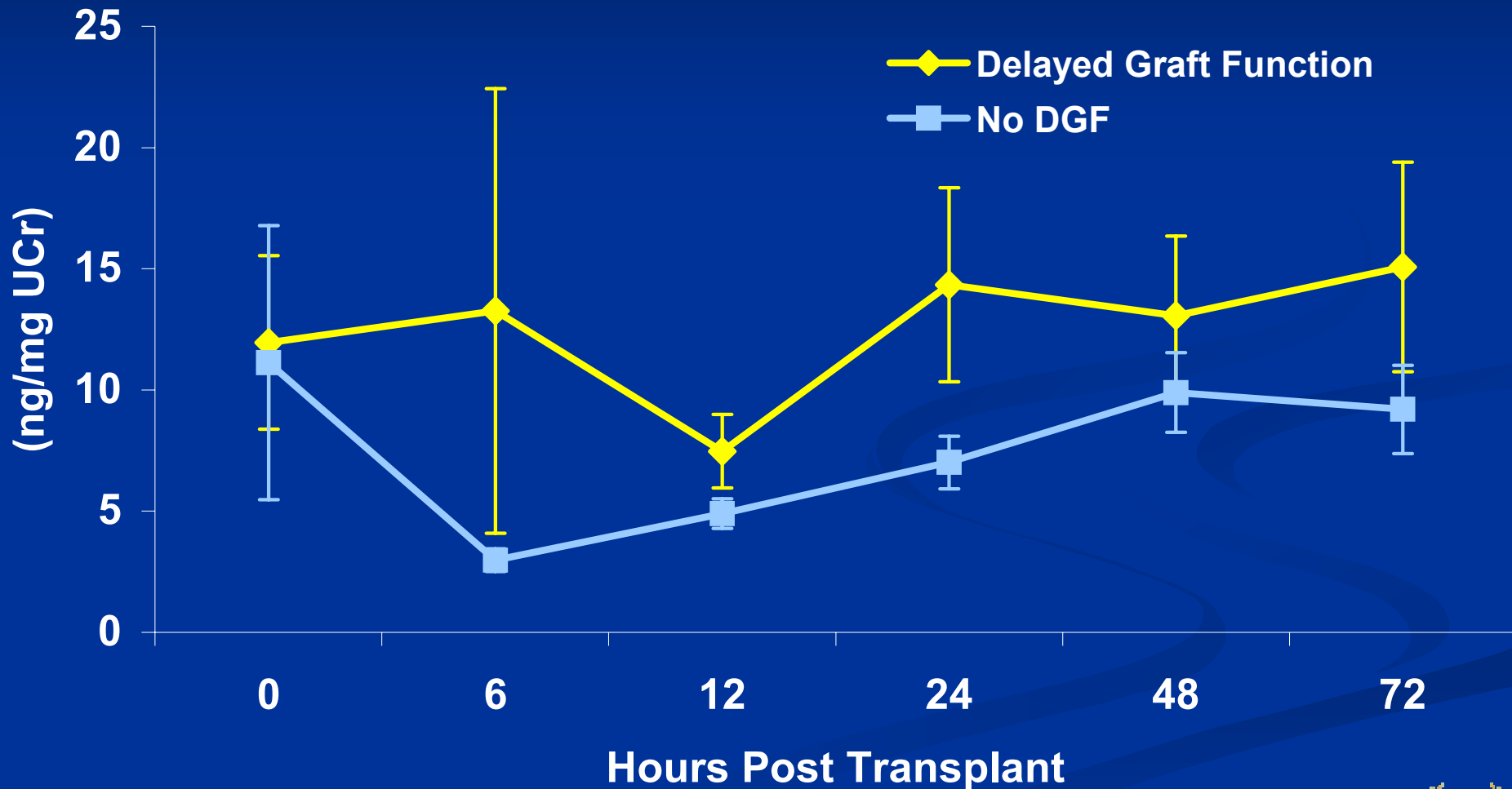
Matrix Metalloproteinase-9 (MMP-9) Levels Post Transplantation in DGF and Non DGF Patients



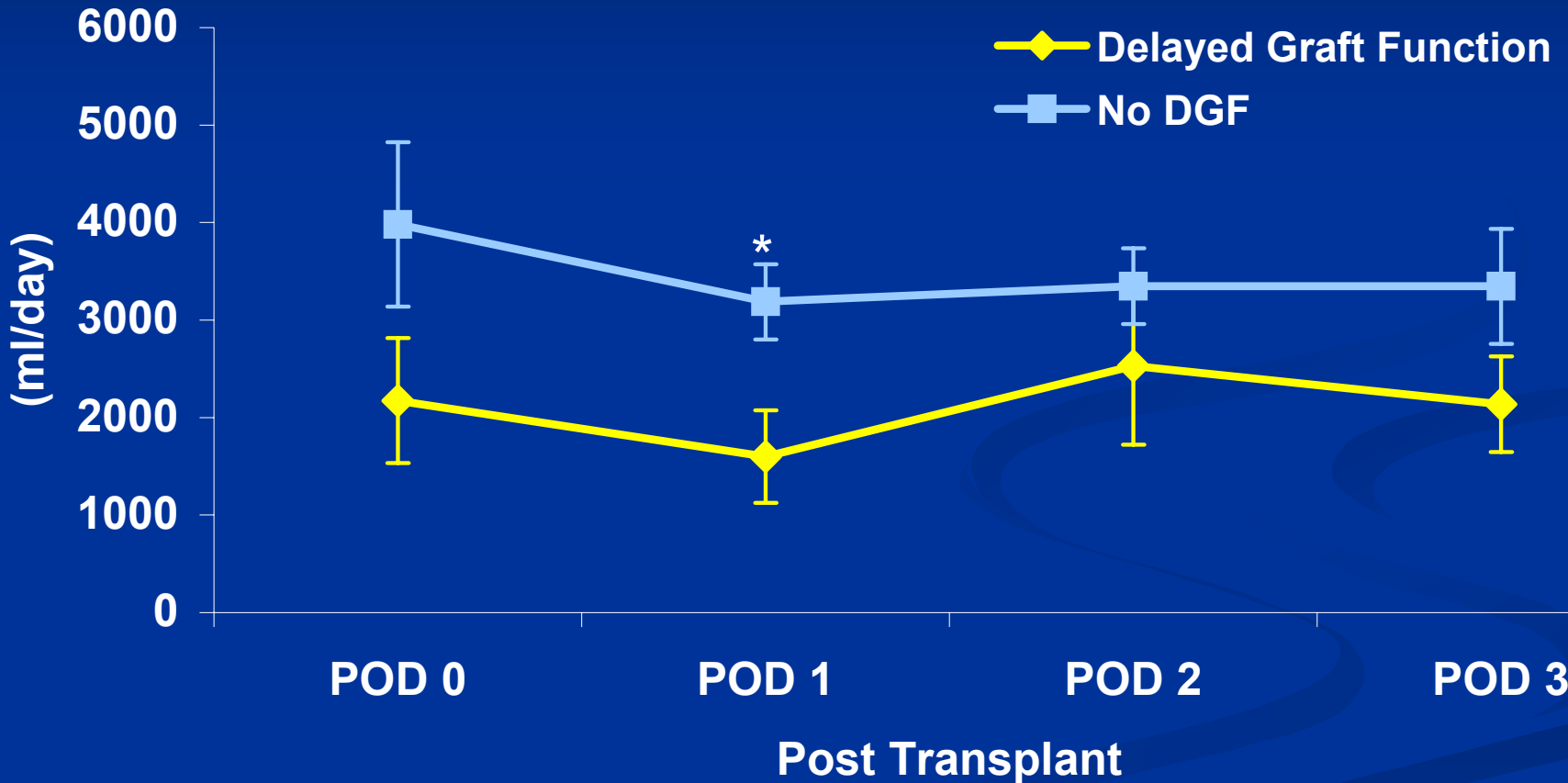
*p < 0.05, **p < 0.01



Kidney Injury Molecule-1 (KIM-1) Levels Post Transplantation in DGF and Non DGF Patients



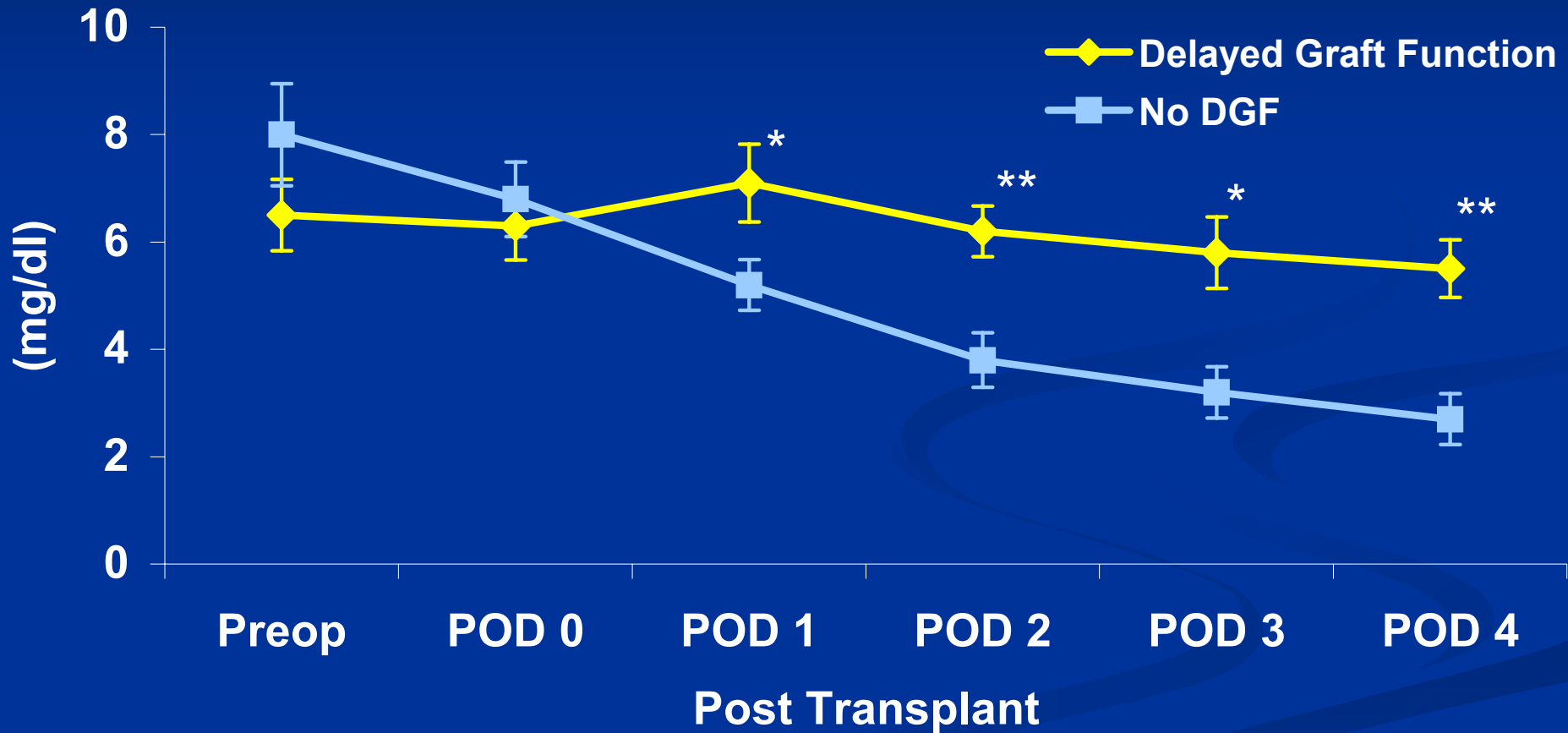
Urine Output Post Transplantation in DGF and Non DGF Patients



*p < 0.05



Serum Creatinine Levels Post Transplantation in DGF and Non DGF Patients



*p < 0.05, **p < 0.01



Summary

- MMP-9 and NAG were significantly elevated as early as 6 hours post operatively in patients with DGF
- KIM-1 levels did not peak until 72 hours after renal transplant whereas the other urinary markers peaked at time 0
- Serum creatinine was significantly increased and the urine output was significantly decreased in DGF patients when compared to non DGF patients on POD #1



Conclusions

- Urinary biomarkers show promise in predicting DGF
- Urinary biomarkers may be able to detect DGF earlier than traditional markers
- Urinary biomarkers may provide insight into the pathophysiology of DGF



Acknowledgements

- Brigham and Women's Hospital, Boston, MA
 - Won Han, MD
- Allegheny General Hospital, Pittsburgh, PA
 - Richard J. Marcus, MD
 - Barbara J. Carpenter, MD
 - Dai D. Nghiem, MD
 - Jonathan M. Duran, MD
 - Samuel C. Barody, DO
 - Dana E. Brandys, DO
 - Ifeatu U. Oti, MD
 - Kalathil K. Sureshkumar, MD
 - Sabiha M. Hussain, MD
 - Stephen E. Sandroni, MD

