Investigation of Changes in Oxidative Stress Before and After Nasal Packing Following Nasal Septoplasty

Septoplasti Operasyonunu Takiben Uygulanan Burun Tamponu Öncesi ve Sonrası Oksidatif Stresteki Değişimin Araştırılması

Tevfik NOYAN, MD,[a]
A. Faruk KIROĞLU, MD,[b]
Tolga KARA, MD,[b]
Sıddık KESKİN, MD[c]

[a]Department of Biochemistry,
[b]Department of Otorhinolarygology,
[c]Department of Biostatistics,
Yüzüncü Yıl School of Medicine University, Van

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Yazışma Adresi/*Correspondence:*
Tevfik NOYAN, MD
Yüzüncü Yıl School of Medicine University, Department of Biochemistry, Van
TÜRKİYE/TURKEY
tevfiknoyan@hotmail.com

ABSTRACT Objective: The aim of the study was to investigate the changes of the oxidant and antioxidant system in blood samples before and after nasal packing following nasal septoplasty. **Material and Methods:** A total of 23 patients, 7 females and 16 males, who were planned to undergo nasal septoplasty were included in the study. Nasal packing was removed at postoperative 48 hours in all patients. Blood gases, serum advanced oxidation protein products (AOPP), serum and erythrocyte malondialdehyde (MDA) levels, and catalase (CAT) activity were measured at preoperative 24 hours (period 1), postoperative 24 hours (period 2) and on postoperative day 15 (period 3) in all subjects. **Results:** pO2, pCO2, O2 saturation and HCO_3 values were similar at all three periods. MDA level was lower and CAT activity in erythrocyte was higher at period 3 compared to periods 1 and 2. Serum CAT activity was also increased at period 3 compared to period 1. Serum MDA and AOPP levels did not change among the periods. **Conclusion:** The findings suggest that a decrease in oxidative stress as indicated by the decrease in lipid peroxidation and increased CAT activity may have a protective role via free radical-scavenging properties 15 days after the operation.

Key Words: Antioxidants; nasal obstruction; oxidative stress

ÖZET Amaç: Bu çalışmada septoplasti operasyonunu takiben uygulanan burun tamponu öncesi ve sonrası, oksidan ve antioksidan sistemdeki değişiklerin araştırılması amaçlanmıştır. **Gereç ve Yöntemler:** 7'si kadın, 16'sı erkek olmak üzere toplam 23 hasta çalışmaya katılmıştır. Bütün hastalarda burun tamponu operasyondan 48 saat sonra çıkarılmıştır. Kan gazları analizi, serum ileri protein oksidasyon ürünü (AOPP), serum ve eritrosit malondialdehit (MDA) düzeyi ve katalaz (KAT) aktivitesi operasyondan 24 saat önce (dönem 1) ve operasyon sonrası 24. saat (dönem 2) ve 15. günde (dönem 3) ölçülmüştür. **Bulgular:** Dönemler arasında; pO_2, pCO_2, O_2 doygunluğu ve HCO_3 değerleri anlamlı farklılık göstermemiştir. Dönem 1 ve 2 ile karşılaştırıldığında dönem 3'te; eritrosit MDA düzeyi anlamlı olarak azalma gösterirken, KAT aktivitesi ise anlamlı olarak artış göstermiştir. Serum KAT aktivitesi ise dönem 3'te, yalnızca dönem 1'e göre anlamlı artış göstermiştir. Serum MDA ve AOPP düzeyleri açısından ise dönemler arasında anlamlı değişme gözlemlenmemiştir. **Sonuç:** Bu çalışmanın sonuçları, burun tamponu uygulaması ve burun tıkanıklığının oksidatif streste artışa yol açabileceğini ve operasyondan 15 gün sonra KAT aktivitesindeki artışın serbest radikal oluşumunu azaltarak lipid oksidasyonunu azaltabileceğini göstermektedir.

Anahtar Kelimeler: Antioksidanlar; burun tıkanıklığı; oksadatif stress

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Free radicals are defined as molecules having an unpaired electron on the outer orbit. They are generally unstable and very reactive. Examples of oxygen (O_2) free radicals are superoxide, hydroxyl, peroxyl,

alkoxyl, and hydroperoxyl radicals.[1,2] Free radicals are formed in the energy/respiratory pathways of the body as inflammatory mediators in the immune system and in other biochemical pathways that are essential aspects of cellular metabolism. Free radicals may play an important role in the origin of life and biological evolution, implicating their beneficial effects on the organisms.[3]

Oxidative stress is defined as an imbalance between the cellular generation of reactive oxygen species (ROS) and the capacity of anti-oxidants to prevent oxidative damage. Throughout the life cycle, any person may be at a risk of oxidative stress induced by high rates of O_2 use (e.g., strenuous work and competitive sports), the autoimmune activation of immune system cells (e.g., respiratory burst of polymorphonuclear and mononuclear cells), and environmental factors (e.g., pollutants containing nitric oxide, nitrogen dioxide, and hydroxyl radicals). Prolonged exposure to free radicals, even at low concentrations, may result in the damage of biologically important molecules and potentially lead to DNA mutation, tissue injury, and disease.[3,4] Thus, although molecular O_2 is essential for aerobic life, it may be toxic under certain conditions. This phenomenon has been termed the O_2 paradox.[1,5] Enzymatic antioxidants such as glutathione peroxidase (GSH-Px), CAT, superoxide dismutase (SOD) and non-enzymatic antioxidants such as uric acid, bilurubin, vitamin A, E and ascorbic acid limit tissue concentrations of free radicals and free radical scavengers that have been produced and conserved during the evolution of aerobic life.[6]

Previous clinical studies pertaining to changes in blood gases following nasal packing although agreed that packing was frequently followed by hypoxia, observed differing responses in arterial pCO_2 to nasal packing.[7] Under hypoxic conditions, the decrease in partial pressure of O_2 causes less availability of O_2 inside the cell, which is the ultimate electron acceptor in the electron transport chain. Superoxide ion-radical (O2.-), the one-electron reduction product of molecular oxygen, is a long-suspected first intermediate in chemical reactions using oxygen as the ultimate electron acceptor. SOD converts O2.- to hydrogen peroxide (H2O2). A reduction in O_2 availability under hypoxia which acts as an electron sink may result in the accumulation of reducing equivalents in the mitochondrial electron transport chain, thereby leading to enhanced production of ROS.[8,9] In this way, increased level of ROS in hypoxia causes oxidative stress.[10] Under hypoxic stress, the cellular defense systems get disturbed and their activity decreases.[11,12]

This is the first study to our knowledge, which compares the changes in oxidant and antioxidant system in blood samples after nasal packing following nasal septoplasty.

MATERIAL AND METHODS

"World medical association decleration of Helsinski Ethical Principles for medical research involving human subjects" was accepted in the present study, and all subjects provided informed consent. The study was also approved by the ethical committee. The study group consisted of 23 patients, 7 females (mean age and standard deviation (SD), 32.40 ± 6.28 years) and 16 males (mean age and SD, 33.73 ± 3.04 years), who were planned to undergo nasal septoplasty. Nasal packing was removed at postoperative 48 hours in all patients.

Three 10 mL venous blood samples were obtained at different time points-preoperative 24 hours (period 1), postoperative 24 hours (period 2) and on postoperative day 15 (period 3). Blood samples were placed in three different test tubes, one including no anticoagulant substance for measuring MDA, AOPP levels and CAT activity. A second tube that included heparin was used for measuring blood gases. Measurements of blood gases were performed immediately by using ABL-5 (Radiometer, Denmark) blood gas analyzer. The last blood sample was collected into tubes containing EDTA for erythrocyte measurements. All blood samples were centrifuged at 2000 rpm for 10 min in a refrigerated centrifuge to separate serum and plasma samples. Plasma and buffy coat were discarded. The cells were washed with cold 0.15 mol/L sodium

chloride (NaCl) solution three times. Washed erythrocytes were prepared immediately after blood collection from subjects. All samples were stored at -70°C until they were analyzed. MDA and CAT values for erythrocytes were expressed as per gram of hemoglobin (Hb).

The serum levels of thiobarbituric acid-reacting substances (TBARS), an end product of lipid peroxidation, were measured fluorometrically at wavelengths of 525 nm for excitation and 547 nm for emission.13 Serum and erythrocyte MDA concentration was expressed as nmol/mL and nmol/gHb respectively.

Determination of AOPP was based on a spectrophometric assay according to Witko-Sarsat et al AOPP levels were expressed in μmol of chloramine-T equivalents per litre of serum (μmol/L).[14]

The serum CAT activity was determined by Goth's colorimetric method, in which a homogenate was incubated with H_2O_2 substrate and the enzyme reactions were stopped by the addition of ammonium molybd ate.[15] Serum and erythrocyte CAT activity (kU) was expressed as kU/L and kU/gHb respectively.

Statistical analysis

The results were expressed as mean ($\bar{X}$) ± SD, median, minimum and maximum values. In order to use parametric statistical methods, data were controlled for assumptions. For some variables, departure from the assumptions of parametric tests was determined. Thus Friedman test which is used for comparing k dependent samples was used. Pairwise comparisons were run when the Friedman test statistics were significant. For pairwise comparisons, minimum required difference (CD) was computed as CD = Z_{adj} (Adjusted Z value is a function of the maximum familywise Type I error rate, n is the number of observations and k is the comparisons number). In addition, Spearman's rank (order) correlation coefficient was used to determine relationships among the variables within each period.

RESULTS

Descriptive statistics for levels of MDA, AOPP and CAT activities and results of blood gases at all periods are presented in Table 1. Lower erythrocyte MDA levels and higher erythrocyte CAT activity were obtained at period 3 as compared to periods 1 and 2 ($p< 0.05$). The serum CAT activity was also higher at period 3 as compared to period 1 ($p< 0.05$). However, there was no significant difference regarding serum and erythrocyte MDA levels and CAT activity between periods 1 and 2. The results for the remaining parameters were similar at all periods. Table 2 depicts the correlation between the parameters. In general, there were significant positive and negative correlations between the variables.

DISCUSSION

Most surgeons still routinely perform nasal packing after septal surgery since this is generally recommended. The aims of packing are numerous: homeostasis, prevention of haematoma, increasing septal flap apposition, closure of dead space and prevention of displacement of the replaced cartilage. However, nasal packing is an injurious procedure and may lead to cardiovascular changes, continued bleeding, nasal injury, hypoxia, foreign body reaction or infection. The major disadvantage of nasal packing is patient discomfort and the need to administer antibiotics.[16] In adults, obstruction of the nose by nasal packing has been shown to cause hypercapnia and sudden death.[17]

Previous clinical studies pertaining to changes in blood gases following nasal packing agreed that the packing was frequently followed by hypoxia but detected differing responses in arterial pCO_2 to nasal packing. In accordance with other studies; pO_2, pCO_2, O_2 saturation and HCO_3 levels did not change at any time point in the present study.[18,19] Based on these observations, it was suggested that nasal packing is not a important cause for hypoxia and hypercapnia in the present study. However, Hady et al have reported significantly increased pCO_2 and HCO_3 and decreased pO_2 after nasal packing.[20] Slocum et al have reported decreased

TABLE 1: Descriptive statistics and comparison results for the variables MDA, AOPP, CAT, pO2, pCO2, O2 saturation and HCO3. (MDA; malondialdehyde, AOPP; advanced oxidation protein products, CAT; catalase, pCO2;partial carbondioxide pressure, pO2; partial oxygen pressure, O2; oxygen, HCO3; bicarbonate)

Parameters	n = 23	$\bar{X}$ ± SD	Median	Min.	Max.	Friedman test
Serum MDA	Period 1	2.30 ± 1.06	1.87	1.26	4.06	χ^2 = 3.231
(nmol/mL)	Period 2	1.67 ± .72	1.65	1.02	3.52	DF = 2
	Period 3	1.95 ± .91	2.04	1.24	5.38	p = 0.199
Erythrocyte MDA	Period 1	0.31 ± .14	0.33	0.13	0.52	χ^2 = 8.714
(nmol/gHb)	Period 2	0.34 ± .24	0.25	0.10	0.92	DF = 2
	Period 3	0.12 ± .05	0.14*a,b	0.05	0.22	p = 0.013
Serum AOPP	Period 1	84.63 ± 41.24	77.01	27.60	185.74	χ^2 = 3.323
(μmol/L)	Period 2	104.70 ± 44.17	95.55	53.58	193.20	Ser. Der. = 2
	Period 3	92.39 ± 34.48	89.57	48.51	173.31	p = 0.190
Serum CAT	Period 1	44.50 ± 30.98	41.26	21.20	111.30	χ^2 = 6.020
(kU/L)	Period 2	54.96 ± 34.29	49.18	23.17	170.00	DF = 2
	Period 3	84.59 ± 71.79	64.00*a	25.40	270.30	p = 0.049
Erythrocyte CAT	Period 1	173.49 ± 294.37	163.02	124.40	495.71	χ^2 = 8.23
(kU/gHb)	Period 2	177.33 ± 241.52	183.70	33.052	454.21	DF = 2
	Period 3	319.45 ± 442.90	270.01*a,b	17.70	825.60	p = 0.016
pCO_2	Period 1	47.43 ± 4.12	49.00	40.00	52.00	χ^2 = 0.543
(mmHg)	Period 2	47.47 ± 6.43	46.70	38.00	63.40	DF = 2
	Period 3	46.42 ± 4.65	46.00	39.00	56.00	p = 0.762
pO_2	Period 1	31.94 ± 19.42	28.50	18.00	104.00	χ^2 = 1.900
(mmHg)	Period 2	28.47 ± 17.94	25.00	16.20	96.00	DF = 2
	Period 3	29.09 ± 6.81	28.70	17.00	43.00	p = 0.387
O_2 saturation	Period 1	50.54 ± 22.16	54.35	11.00	97.00	χ^2 = 0.494
(%)	Period 2	46.36 ± 18.51	43.50	20.00	90.00	DF = 2
	Period 3	47.34 ± 17.26	46.50	25.00	76.00	p = 0.781
HCO_3	Period 1	27.49 ± 2.78	28.00	23.00	34.20	χ^2 = 2.800
(mmol/L)	Period 2	28.83 ± 3.07	28.45	24.00	34.40	DF = 2
	Period 3	26.76 ± 2.93	26.00	22.00	33.00	p = 0.247

*p< 0.05, a; as compared to period 1, b; as compared to period 2. $\bar{X}$ Mean, SD: Standard deviation, Min: Minimum value, Max: Maximum value, DF: Degrees of freedom.

pO_2 and similar pCO_2 levels after nasal packing.[21] While the arterial blood samples were used for blood gas analyze by other investigators, we used venous blood samples in the present study. The differences in the results of blood gas analyses regarding pO_2, pCO_2, O_2 saturation and HCO_3 levels may be attributed to this.

Assessments of lipid peroxidation included the analysis of lipid peroxides, isoprostanes, diene conjugates, and breakdown products of lipids (e.g., MDA, ethane, pentane, and 4-hydroxynonenal). Among these products, MDA is often used as a reliable marker of lipid peroxidation.2 We found decreased erythrocyte MDA level and icreased erythrocyte CAT activity at period 3 as compared to periods 1 and 2. However serum CAT activity was also increased at period 3 as compared to only period 1. These results suggest that oxidative stress is decreased on postoperative day 15, which may be possibly due to increased CAT activity. It is known that CAT is located in peroxisomes and it decomposes hydrogen peroxide to water and O_2.[22] It is likely that increased CAT activity may be the first line defense mechanism against oxidative stress. Red blood cells are an important contributor to the blood's antioxidant capacity measured as the specific intracellular enzyme activities (SOD, CAT) and the state of glutathione system. Blood O_2-binding properties take part in the antioxidant system by establishing

TABLE 2: The Spearman's rank (order) correlation coefficients among the variables within each period (MDA; malondialdehyde, AOPP; advanced oxidation protein products, CAT; catalase, pCO2; partial carbondioxide pressure, pO2; partial oxygen pressure, O2; oxygen, HCO3; bicarbonate).

n= 23	Periods	Serum MDA	Erythrocyte MDA	Serum AOPP	Serum CAT	Erythrocyte CAT	pCO_2	pO_2	O_2 saturation
Erythrocyte MDA	1	.390							
	2	.469*							
	3	-.261							
Serum AOPP	1	.462*	.681**						
	2	.406	-.203						
	3	.152	.794**						
Serum CAT	1	-.291	.346	.137					
	2	.378	-.098	.399					
	3	.345	.515**	.564**					
Erythrocyte CAT	1	.016	-.593**	-.165	-.440*				
	2	.002	-.427*	-.154	.182				
	3	-.103	.345	.467*	.661**				
pCO_2	1	-.723**	-.377	-.131	.262	.460*			
	2	.133	.441*	.147	-.014	-.566**			
	3	-.178	.351	.462*	.191	.178			
pO_2	1	.406	.423*	.550**	-.348	-.227	-.396		
	2	-.130	-.336	.287	.200	.266	-.518**		
	3	.530**	-.518**	-.244	-.171	-.293	-.594**		
O_2 saturation	1	.421	.424*	.415*	-.421	-.250	-.524**	.934**	
	2	-.112	-.375	.249	.130	.252	-.592**	.975**	
	3	.207	-.310	-.316	-.079	-.012	-.914**	.709*	
HCO_3	1	-.612**	.134	.078	.273	-.284	.537	-.129	-.162
	2	.384	.327	.046	.176	-.338	.792**	-.707**	-.704**
	3	-.123	.455*	.505**	.295	.105	.931**	-.607**	-.874**

*: p< 0.05, **: p< 0.01.

tissue O_2 transport conditions and tissue pO2 values.[23,24] The higher CAT activity in serum and red blood cells at period 3 may obviously be the result of endogenous H_2O_2 accumulation. The O_2-dependent nature of free radical generation suggests that blood O_2 transport influences the lipid peroxidation activity in biological systems. Although, we did not observe any changes in the pO_2, pCO_2 and O_2 saturation values at any time point, it is well known that the shift of the oxyhemoglobin dissociation curve correlates with the free radical oxidation indices, which allows considering Hb-O_2 affinity a factor participating in the maintenance of the body's prooxidant-antioxidant balance.[25] In the present study, while the serum MDA levels were similiar at all periods, erythrocyte MDA levels significantly decreased at period 3. This observation suggests that in response to oxidative stress, antioxidant enzymes in the erythrocyte may protect the cellular functions with compensatory increases in activity. We did not find any argument that indicate hypoxia according to blood gas analyze. However, we think that it is necessary to investigate the changes in oxidative and antioxidant systems in tissue samples. Therefore, we suggest an experimental animal study that investigates the changes in oxidant and antioxidant systems in the nasal tissue before and after nasal packing.

Plasma AOPP concentration may be a useful marker in protein oxidative damage, measuring highly oxidized proteins and especially albumin.26 AOPP concentration did not change at any period in this study. While a significant correlation was

present between AOPP and MDA at period 1, the correlation at periods 2 and 3 was not significant. AOPP levels are reported to be correlated with plasma concentrations of dityrosine and advanced glycation end products-pentosidine as indices of oxidant-mediated protein damage, but not with thiobarbituric reactive substances as lipid peroxidation markers.[14]

In conclusion, as mentioned above, similar studies that investigate the effect of oxidative stress on nasal packing are lacking. This is the first study reporting the changes in the oxidant and antioxidant system before and after nasal packing. Results of our study indicate that oxidative stress may decrease and the antioxidant enzyme CAT may increase on day 15 after nasal packing. However, further studies are necessary that investigate changes in oxidant and antioxidant systems following nasal packing.

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REFERENCES

1. Gilbert DL. Fifty years of radical ideas. Ann N Y Acad Sci 2000;899:1-14.
2. Fang YZ, Yang S, Wu G. Free radicals, antioxidants, and nutrition. Nutrition 2002;18:872-9.
3. McCord JM. The evolution of free radicals and oxidative stress. Am J Med 2000;108:652-9.
4. Fridovich I. Fundamental aspects of reactive oxygen species, or what's the matter with oxygen? Ann N Y Acad Sci 1999;893:13-8.
5. Maiti P, Singh SB, Sharma AK, Muthuraju S, Banerjee PK, Ilavazhagan G. Hypobaric hypoxia induces oxidative stress in rat brain. Neurochem Int 2006;49:709-16.
6. Noyan T, Güler A, Sekeroğlu MR, Kamaci M. Serum advanced oxidation protein products, myeloperoxidase and ascorbic acid in preeclampsia and eclampsia. Aust N Z J Obstet Gynaecol 2006;46:486-91.
7. Cavo JW, Kawamoto S, Berlin BP, Zollinger W, Ogura JH. Arterial blood gas changes following nasal packing in dogs. Laryngoscope 1975;85(12 pt 1):2055-68.
8. Magalhaes J, Ascensao A, Soares JM, Neuparth MJ, Ferreira R, Oliveira J et al. Skeletal muscle ultrastructural and plasma biochemical signs of endothelium dysfunction induced by a high-altitude expedition (Pumori, 7161m). Basic Appl Myol 2005;91:185-91.
9. Chandel NS, Maltepe E, Goldwasser E, Mathieu CE, Simon MC, Schumacker PT. Mitochondrial reactive oxygen species trigger hypoxia-induced transcription. Proc Natl Acad Sci U S A 1998;95:11715-20.
10. Jayalakshmi K, Sairam M, Singh SB, Sharma SK, Ilavazhagan G, Banerjee PK. Neuroprotective effect of N-acetyl cysteine on hypoxia-induced oxidative stress in primary hippocampal culture. Brain Res 2005;1046:97-104.
11. Nakanishi K, Tajima F, Nakamura A, Yagura S, Ookawara T, Yamashita H, et al. Effects of hypobaric hypoxia on antioxidant enzymes in rats. J Physiol 1995;489(Pt 3):869-76.
12. Ramanathan L, Gozal D, Siegel JM. Antioxidant responses to chronic hypoxia in the rat cerebellum and pons. J Neurochem 2005;93:47-52.
13. Wasowicz W, Nève J, Peretz A. Optimized steps in fluorometric determination of thiobarbituric acid-reactive substances in serum: importance of extraction pH and influence of sample preservation and storage. Clin Chem 1993;39:2522-6.
14. Witko-Sarsat V, Friedlander M, Capeillère-Blandin C, Nguyen-Khoa T, Nguyen AT, Zingraff J, et al. Advanced oxidation protein products as a novel marker of oxidative stress in uremia. Kidney Int 1996;49:1304-13.
15. Góth L. A simple method for determination of serum catalase activity and revision of reference range. Clin Chim Acta 1991;196:143-51.
16. Lemmens W, Lemkens P. Septal suturing following nasal septoplasty, a valid alternative for nasal packing? Acta Otorhinolaryngol Belg 2001;55:215-21.
17. Taasan V, Wynne JW, Cassisi N, Block AJ. The effect of nasal packing on sleep-disordered breathing and nocturnal oxygen desaturation. Laryngoscope 1981;91:1163-72.
18. Yiğit O, Cinar U, Uslu B, Akgül G, Topuz E, Dadaş B. The effect of nasal packing with or without an airway on arterial blood gases during sleep. Kulak Burun Bogaz Ihtis Derg 2002;9:347-50.
19. Ogretmenoglu O, Yilmaz T, Rahimi K, Aksöyek S. The effect on arterial blood gases and heart rate of bilateral nasal packing. Eur Arch Otorhinolaryngol 2002;259:63-6.
20. Hady MR, Kodeira KZ, Nasef AH. The effect of nasal packing on arterial blood gases and acid-base balance and its clinical importance. J Laryngol Otol 1983;97:599-604.
21. Slocum CW, Maisel RH, Cantrell RW. Arterial blood gas determination in patients with anterior packing. Laryngoscope 1976;86:869-73.
22. Winterbourn CC. Superoxide as an intracellular radical sink. Free Radic Biol Med 1993;14:85-90.
23. Zinchuk V, Borisiuk M. The effect of NO synthase inhibition on blood oxygen-carrying function during hyperthermia in rats. Respir Physiol 1998;113: 39-45.
24. Zinchuk VV, Khodosovsky MN, Maslakov DA. Influence of different oxygen modes on the blood oxygen transport and prooxidant-antioxidant status during hepatic ischemia/reperfusion. Physiol Res 2003;52:533-44.
25. Zinchuk V. High hemoglobin affinity to oxygen and its relationships with lipid peroxidation during fever. J Physiol Biochem 1999;55:301-8.
26. Witko-Sarsat V, Gausson V, Nguyen AT, Touam M, Drüeke T, Santangelo F, et al. AOPP-induced activation of human neutrophil and monocyte oxidative metabolism: a potential target for N-acetylcysteine treatment in dialysis patients. Kidney Int 2003;64:82-91.