Incidence of and Risk Factors for Contrast-Induced Nephropathy After Cardiac Catheterization in Japanese Patients

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Background: Contrast-induced nephropathy (CIN) is the third leading cause of all hospital-acquired renal insufficiency, accounting for 10%, and is associated with increased long-term mortality. The incidence of and risk factors for CIN after cardiac catheterization in Japanese patients are, however, unknown at present.

Methods and Results: The 1,157 consecutive patients who underwent cardiac catheterization at Kyoto University Hospital from January 2003 to December 2004 were retrospectively examined. The incidence of CIN defined as an absolute increase in serum creatinine (SCr) ≥ 0.5 mg/dl, a relative $\geq 25\%$ increase in SCr, and either an absolute or relative increase after cardiac catheterization were 4.0%, 13.8%, and 13.9%, respectively. Multivariate logistic models revealed that preexisting renal insufficiency and the use of high-volume contrast were independently associated with an absolute increase in SCr ≥ 0.5 mg/dl. Female gender, underweight, and high-volume contrast usage were independently associated with a relative $\geq 25\%$ increase and either an absolute or relative increase in SCr.

Conclusions: Although the incidence of and risk factors for CIN after cardiac catheterization varied in the study population according to the definition of CIN, careful attention should be paid to patients who have risk factors identified by each definition of CIN. (Circ J 2009; 73: 1518–1522)

Key Words: Cardiac catheterization; Contrast-induced nephropathy; Risk factors

Iodinated contrast medium used in diagnostic and therapeutic cardiac catheterization can cause renal damage, which ranges from a transient elevation of the serum creatinine (SCr) concentration to permanent renal failure necessitating dialysis.^{1,2} Recent studies have shown that contrast-induced nephropathy (CIN) is the third leading cause of all hospital-acquired renal insufficiency, accounting for 10%,³ and is associated with increased long-term mortality.⁴ CIN is defined as an increase in SCr ≥ 0.5 mg/dl or $\geq 25\%$ of the baseline level reaching a peak between 2 and 5 days after administration of the contrast medium.^{5–7} The incidence of CIN in previous reports varies among studies because of differences in the definition of CIN, background risk, type and dose of contrast medium, and the frequency of other potential causes of CIN.⁶ The most important risk factor for CIN is preexisting renal insufficiency.^{8,9} Older age, female gender, anemia, high-dose usage of contrast medium, heart failure, diabetes mellitus and peripheral vascular disease (PVD) are also reported as risk factors that increase the likelihood of CIN.^{9–12} It is still uncertain to what

extent these factors independently worsen renal function.

The incidence of and risk factors for CIN in Japanese patients are unknown at present, so we retrospectively analyzed a Japanese cohort.

Methods

Study Design and Patients

We retrospectively examined all Japanese patients who underwent cardiac catheterization in the Department of Cardiovascular Medicine at Kyoto University Hospital from January 2003 to December 2004. Patients on hemodialysis before catheterization and patients without laboratory data were excluded. Patients were administered iomeprol 350 (Iomeron; Bracco Eisai Co, Ltd, Tokyo, Japan; 350 mg iodine/ml) or iopamidol 370 (Iopamiron; Bayer, Osaka, Japan; 370 mg iodine/ml) during cardiac catheterization, and were admitted for intravenous hydration before and after the procedure at the discretion of their physicians.

This study was approved by the Ethics Committee of Kyoto University Graduate School of Medicine and the informed consent was waived because it was conducted in historical cohort fashion without any intervention and individual identification information was not used.

Definitions

In the present study, CIN was defined as an elevation in SCr concentration ≥ 0.5 mg/dl or 25% within 5 days after cardiac catheterization.^{4,13–16} Older age (elderly), underweight, anemia, and preexisting renal insufficiency were defined as ≥ 70 years old, body mass index (BMI) < 18.5 ,¹⁷ hemoglobin (Hb) concentration < 13 g/dl for men and < 12 g/dl

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Table 1. Baseline Clinical Characteristics

	All patients (n=1,157)
Age	68.4±11.5
Elderly (age ≥70 years)	626 (54.1%)
Female gender	329 (28.4%)
Body weight (kg)	59.8±12.2
BMI (kg/m ²)	23.3±3.7
Underweight (BMI <18.5)	104 (9.1%)
Hb (g/dl)	12.7±2.1
Anemia (M: Hb <13; F: Hb <12)	503 (44.3%)
SCr (mg/dl)	0.97±0.39
Renal insufficiency (SCr ≥1.2)	254 (22.0%)
DM	418 (36.1%)
Previous myocardial infarction	227 (19.6%)
CHF (NYHA ≥II)	219 (18.9%)
NYHA (II/III/IV)	121 (10.5%)/62 (5.4%)/36 (3.1%)
PVD	262 (22.6%)
PCI	562 (48.6%)

Continuous variables are mean±standard deviation and the categorical variables are expressed as number and percentage.

BMI, body mass index; M, male; F, female; Hb, hemoglobin; SCr, serum creatinine; DM, diabetes mellitus; CHF, congestive heart failure; NYHA, New York Heart Association functional class; PVD, peripheral vascular disease; PCI, percutaneous coronary intervention.

for women¹⁸ and a baseline SCr ≥1.2 mg/dl^{9–21} Patients with New York Heart Association class ≥II were regarded as suffering from congestive heart failure (CHF). PVDs included arterial sclerosis obliterans, and renal and carotid artery stenosis. The volume of administered contrast medium is linked to the development of CIN, although the volume of the medium to induce CIN varies and was not definitive in the previous studies.⁸ Some studies report that the tolerated dose of contrast medium depends on kidney function⁹ but we opted for the simple definition of high volume of contrast medium ≥200 ml for practical and easier application.^{8,12}

Statistical Analysis

Continuous variables of each group are presented as mean±standard deviation and the categorical variables are expressed as number and percentage. The potential risk factors for CIN examined in the present study were elderly, female gender, underweight, anemia, preexisting renal insufficiency, high-dose contrast medium, diabetes mellitus (DM), CHF, and PVD.^{9,10} Age was dichotomized to elderly or not (≥70 years old vs <70 years), BMI dichotomized to underweight or not (BMI <18.5 vs ≥18.5), Hb concentration dichotomized to anemia or not (Hb concentration <13 g/dl vs ≥13 g/dl for men and <12 g/dl vs ≥12 g/dl for women), renal function dichotomized to insufficiency or not (baseline SCr ≥1.2 mg/dl vs <1.2 mg/dl), and the volume of contrast medium dichotomized to high or not (≥200 ml vs <200 ml). The univariate relationships between CIN and these variables were evaluated using the chi-square test, followed by multiple logistic regression models with all potential risk factors with a P value <0.20 by univariate analysis. The results of analysis are shown as odds ratio (OR) given with 95% confidence interval (CI) and P values. Results were considered as significant with a P value of <0.05. We used JMP 8 (SAS Institute Inc, Cary, NC) for all analyses.

Results

Baseline Clinical Characteristics

The baseline clinical characteristics of the 1,157 patients in

Table 2. Procedural and Renal Outcomes

	All patients (n=1,157)
Contrast agent volume (ml)	185.5±103.5
High volume (≥200 ml)	426 (36.8%)
SCr concentration	
Baseline (mg/dl)	0.97±0.39
Follow-up peak (mg/dl)	1.05±0.47
Change from baseline (mg/dl)	0.08±0.22
Iomeprol/iopamidol	647 (55.9%)/510 (44.1%)
Occurrence of CIN	
SCr increase ≥0.5 mg/dl	46 (4.0%)
SCr increase ≥25%	160 (13.8%)
SCr increase ≥0.5 mg/dl or 25%	161 (13.9%)

Continuous variables are mean±standard deviation and the categorical variables are expressed as number and percentage.

CIN, contrast-induced nephropathy. Other abbreviation see in Table 1.

the present study are listed in **Table 1**. Mean age, percentage of elderly, and female gender were 68.4±11.5 years old, 54.1%, and 28.4%, respectively. The mean BMI and the percentage of underweight, and the mean Hb concentration and the percentage of anemia were 23.3±3.7, 9.1%, 12.7±2.1 g/dl, and 44.3%, respectively. The prevalence of pre-existing renal insufficiency, DM, CHF, and PVD were 22.0%, 36.1%, 18.9% and 22.6%, respectively. Percutaneous coronary intervention was performed in a total of 48.6% of patients.

Procedural and Renal Outcomes

The mean dose of contrast agent was 185.5±103.5 ml (**Table 2**). The percentage of patients administered with a high volume of the contrast media was 36.8%. The mean baseline SCr and the absolute change in SCr after administration of the contrast media were 0.97±0.39 mg/dl and 0.08±0.22 mg/dl. In our study population, an absolute increase in SCr ≥0.5 mg/dl occurred in 46 patients (4.0%) and a relative 25% increase in SCr was observed in 160 patients (13.8%). The incidence of either an absolute increase or a relative increase was 13.9% (161/1,157).

Contrast Volume and the Incidence of CIN

Those patients who received the highest quartile of contrast volume were 3-fold more likely to develop CIN defined as an absolute increase in SCr ≥0.5 mg/dl (8.3% vs 2.6%, P=0.002) (**Figure 1**), 2-fold more likely to develop CIN defined as a relative ≥25% increase (22.4% vs 9.7%, P<0.0001) (**Figure 2**) and either the absolute increase or the relative increase (22.4% vs 10.1%, P<0.0001) compared with those with the lowest quartile of contrast volume.

Univariate and Multivariate Analyses

Univariate factors correlated with the absolute increase in SCr ≥0.5 mg/dl after cardiac catheterization included elderly, anemia, preexisting renal insufficiency, the use of a high volume of contrast media, and PVD (**Table 3**). In contrast, univariate correlates of the relative 25% increase in SCr included female gender, underweight, anemia, and the use of a high volume of contrast media (**Table 4**), and univariate correlates of either an absolute increase or relative increase were female gender (P=0.002), underweight (P=0.001), anemia (P=0.02), and the use of a high volume of contrast media (P<0.0001).

Multivariate analysis revealed that the use of high-volume contrast was independently associated with both the abso-

Figure 1. Association of quartiles of administered contrast volume with the incidences of contrast-induced nephropathy defined as an absolute increase in serum creatinine ≥ 0.5 mg/dl ($P=0.0003$ by chi-square test for trend). Mean $\pm$ standard deviation of an administered contrast volume for each quartile shown in parentheses.

Figure 2. Association of quartiles of administered contrast volume with the incidences of contrast-induced nephropathy defined as a relative $\geq 25\%$ increase in serum creatinine ($P<0.0001$ by chi-square test for trend). Mean $\pm$ standard deviation of an administered contrast volume for each quartile shown in parentheses.

Table 3. Incidence of CIN (SCr Increase ≥ 0.5 mg/dl) After Cardiac Catheterization

	CIN (n=46)	No. of patients at risk (n=1,157)	P value
Age ≥ 70 years (elderly)	34 (5.4%)	626	0.005
Age <70 years	12 (2.3%)	531	
Male gender	31 (3.7%)	828	0.5
Female gender	15 (4.6%)	329	
Underweight	8 (7.7%)	104	0.06
Non underweight	37 (3.6%)	1,033	
Anemia	31 (6.2%)	503	0.0007
Non anemia	14 (2.2%)	632	
SCr ≥ 1.2 mg/dl (renal insufficiency)	24 (9.5%)	254	<0.0001
SCr <1.2 mg/dl	22 (2.4%)	903	
Contrast ≥ 200 ml	29 (6.8%)	426	0.0002
Contrast <200 ml	17 (2.3%)	731	
DM	22 (5.3%)	418	0.10
Non DM	24 (3.3%)	739	
CHF	9 (4.1%)	219	0.9
Non CHF	37 (3.9%)	938	
PVD	20 (7.6%)	262	0.001
Non PVD	26 (2.9%)	895	
Iomeprol	28 (4.3%)	647	0.5
Iopamidol	18 (3.5%)	510	

Abbreviations see in Tables 1,2.

Table 4. Incidence of CIN (SCr Increase $\geq 25\%$) After Cardiac Catheterization

	CIN (n=160)	No. of patients at risk (n=1,157)	P value
Age ≥ 70 years (elderly)	97 (15.5%)	626	0.07
Age <70 years	63 (11.9%)	531	
Male gender	97 (11.7%)	828	0.001
Female gender	63 (19.2%)	329	
Underweight	26 (25.0%)	104	0.001
Non underweight	129 (12.5%)	1,033	
Anemia	84 (16.7%)	503	0.02
Non anemia	75 (11.9%)	632	
SCr ≥ 1.2 mg/dl (renal insufficiency)	27 (10.6%)	254	0.09
SCr <1.2 mg/dl	133 (14.7%)	903	
Contrast ≥ 200 ml	83 (19.5%)	426	<0.0001
Contrast <200 ml	77 (10.5%)	731	
DM	55 (13.2%)	418	0.6
Non DM	105 (14.2%)	739	
CHF	28 (12.8%)	219	0.6
Non CHF	132 (14.1%)	938	
PVD	44 (16.8%)	262	0.12
Non PVD	116 (13.0%)	895	
Iomeprol	99 (15.3%)	647	0.10
Iopamidol	61 (12.0%)	510	

Abbreviations see in Tables 1,2.

Table 5. Adjusted Multivariate Risk Factors for CIN (SCr Increase ≥ 0.5 mg/dl)

	OR	95%CI Lower Upper	P value
Elderly (age ≥ 70 years)	1.65	0.81–3.52	0.2
Underweight (BMI < 18.5)	1.58	0.59–3.79	0.3
Anemia	1.55	0.76–3.26	0.2
Renal insufficiency (SCr ≥ 1.2 mg/dl)	3.79	1.96–7.43	< 0.0001
Contrast ≥ 200 ml	3.81	2.01–7.49	< 0.0001
DM	1.42	0.73–2.74	0.3
PVD	1.93	0.995–3.69	0.052

CI, confidence interval; OR, odds ratio. Other abbreviations see in Tables 1, 2.

lute increase in SCr ≥ 0.5 mg/dl (OR 3.81; 95%CI 2.01–7.49; $P < 0.0001$) (Table 5) and the relative 25% increase in SCr (OR 2.12; 95%CI 1.49–3.02; $P < 0.0001$) after cardiac catheterization (Table 6). Female gender (OR 1.59; 95%CI 1.09–2.31; $P = 0.02$) and underweight (OR 1.80; 95%CI 1.06–2.99; $P = 0.03$) were independent risk factors for either an absolute increase or relative increase, similar to the relative 25% increase in SCr.

Discussion

The major findings of this study are as follows. (1) The incidence of an absolute increase in SCr ≥ 0.5 mg/dl, relative $\geq 25\%$ increase in SCr, and either an absolute or relative increase after cardiac catheterization was 4.0%, 13.8%, and 13.9%, respectively. (2) After adjusting for the risk factors for CIN previously reported,^{8–10} preexisting renal insufficiency and the use of high-volume contrast were independent risk factors for an absolute increase in SCr ≥ 0.5 mg/dl after cardiac catheterization, and female gender, underweight, and the use of high-volume contrast were independent risk factors for a relative $\geq 25\%$ increase in SCr and either an absolute increase or relative increase.

Incidence of CIN After Cardiac Catheterization in Japanese Patients

The rate of absolute increase in SCr ≥ 0.5 mg/dl, relative $\geq 25\%$ increase, and either an absolute or relative increase in SCr after cardiac catheterization was 4.0%, 13.8%, and 13.9%, respectively, in our study group. Although the incidence of CIN after cardiac catheterization in previous reports varied, 1 study reported that the incidence of an absolute increase in SCr ≥ 0.5 mg/dl was 3.3%⁴ and another reported that the relative $\geq 25\%$ increase in SCr was 14.5%.¹ In other studies with small samples of Japanese patients, the incidences of CIN defined as either an absolute increase of ≥ 0.5 mg/dl or a relative increase of $\geq 25\%$ in SCr were 20.3% (12/59)²² and 20.7% (18/87).²³ The incidence of CIN in those studies was relatively higher than in ours using the same definition, although baseline renal function was somewhat better in the patients in our study. Kawashima et al reported that 11% of 332 Japanese patients with mild renal dysfunction ($1.3 \leq \text{SCr} < 2.0$ mg/dl) developed CIN defined as either an absolute increase of ≥ 0.5 mg/dl or a relative increase of $\geq 25\%$ in SCr within 7 days of the procedure.¹²

Risk Factors for CIN After Cardiac Catheterization in Japanese Patients

The results of multivariate analysis in the present study

Table 6. Adjusted Multivariate Risk Factors for CIN (SCr Increase $\geq 25\%$)

	OR	95%CI Lower Upper	P value
Elderly (age ≥ 70 years)	1.19	0.83–1.72	0.4
Female gender	1.61	1.10–2.33	0.01
Underweight (BMI < 18.5)	1.82	1.07–3.03	0.03
Anemia	1.40	0.96–2.04	0.08
Renal insufficiency (SCr ≥ 1.2 mg/dl)	0.66	0.40–1.04	0.07
Contrast ≥ 200 ml	2.12	1.49–3.02	< 0.0001
PVD	1.26	0.84–1.88	0.3
Iomerol (vs Iopamidol)	1.26	0.89–1.81	0.2

Abbreviations see in Tables 1, 2, 5.

revealed that preexisting renal insufficiency and the use of high-volume contrast were independently associated with an absolute increase in SCr ≥ 0.5 mg/dl after cardiac catheterization. On the other hand, female gender, underweight, and the use of high-volume contrast were independent risk factors for a relative $\geq 25\%$ increase and either an absolute increase or relative increase in SCr. Risk factors for CIN varied among previous studies because of differences in the definition of CIN, background risk, type and dose of contrast medium, and the frequency of other potential causes of CIN.⁶ Therefore, preexisting renal insufficiency, the use of high-volume contrast, female gender, and underweight are all considered as risk factors for CIN in Japanese patients. Of these, women have a higher prevalence of DM, hypertension, and being elderly.²⁴ Because the association of high BMI with better survival in chronic kidney disease is considered a “risk factor paradox” or “reverse epidemiology,”^{25,26} we examined and found that underweight was an independent risk factor for CIN. In contrast to previous reports, DM, anemia, and CHF did not correlate with CIN in the present study. Although PVD (OR 1.93; 95%CI 0.995–3.69; $P = 0.052$) and DM (OR 1.42; 95%CI 0.73–2.74; $P = 0.3$) had a tendency to increase CIN as an absolute increase in SCr ≥ 0.5 mg/dl, and anemia (OR 1.40; 95%CI 0.96–2.04; $P = 0.08$) had a tendency to increase CIN as a relative $\geq 25\%$ increase in SCr, our sample size might be too small to detect the significance of these factors. Because volume depletion is considered to be a risk factor for CIN,^{7,27} and intravenous hydration has been shown to reduce the frequency of CIN,²⁸ CHF as a consequence of volume excess might not be associated with CIN in our study population. Although the differences in the incidence of CIN among individual contrast media have been previously reported,²⁹ we could not find any significant difference between iomeprol and iopamidol.

Study Limitations

First, our study included a relatively small population, admitted to a single center. Therefore, the total number of CIN cases defined as an absolute increase in SCr ≥ 0.5 mg/dl, a relative $\geq 25\%$ increase, and either an absolute increase or relative increase in SCr that we observed was only 46, 160, and 161, respectively. Although our sample size was the largest among the previous studies, the number of patients might not be enough to precisely represent Japanese patients. Because the statistical power was insufficient, several risk factors that were shown significant in the previous reports were not statistically associated with CIN in the present study.

Second, we included patients in a retrospective fashion. Therefore, all patients underwent cardiac catheterization according to the doctors' judgment. Some patients did not undergo cardiac catheterization because of preexisting conditions, which undoubtedly resulted in selection bias.

Third, data on hydration status and potential nephrotoxic drugs, such as NSAIDs, were unavailable because this study was retrospective.

Fourth, our study was conducted in a single center in Japan and all enrolled patients were Japanese, thus, the muscular volume or other factors associated with renal function may differ from other populations. Therefore, the generalization of our findings is uncertain. These issues should be attested in future prospective studies.

Clinical Implications

We have investigated the incidence of CIN after cardiac catheterization in Japanese patients. CIN is not only the third leading cause of hospital-acquired renal insufficiency but is also associated with increased long-term mortality. Because percutaneous coronary intervention is reported to have no effects on reducing major cardiovascular events,³⁰ we should endeavor to avoid the development of CIN after cardiac catheterization.

We should also pay careful attention to patients who have risk factors, such as preexisting renal insufficiency, the use of high-volume contrast, female gender, and underweight.

Conclusions

In our study population, the incidence of CIN defined as an absolute increase in SCr ≥ 0.5 mg/dl, a relative $\geq 25\%$ increase, and either an absolute increase or relative increase in SCr after cardiac catheterization in Japanese patients was 4.0%, 13.8%, and 13.9%, respectively. After adjustment for risk factors for CIN previously reported, preexisting renal insufficiency, the use of high-volume contrast, female gender, and underweight were shown to be independent risk factors for CIN. To validate our results, a large multicenter study is needed.

Disclosure

None.

References

- McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: Incidence, risk factors, and relationship to mortality. *Am J Med* 1997; **103**: 368–375.
- Freeman RV, O'Donnell M, Share D, Meengs WL, Kline-Rogers E, Clark VL, et al. Nephropathy requiring dialysis after percutaneous coronary intervention and the critical role of an adjusted contrast dose. *Am J Cardiol* 2002; **90**: 1068–1073.
- Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. *Am J Kidney Dis* 2002; **39**: 930–936.
- Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002; **105**: 2259–2264.
- Spargias K, Alexopoulos E, Kyrzopoulos S, Iacovis P, Greenwood DC, Manginas A, et al. Ascorbic acid prevents contrast-mediated nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. *Circulation* 2004; **110**: 2837–2842.
- Barrett BJ, Parfrey PS. Clinical practice: Preventing nephropathy induced by contrast medium. *N Engl J Med* 2006; **354**: 379–386.
- McCullough PA. Contrast-induced acute kidney injury. *J Am Coll Cardiol* 2008; **51**: 1419–1428.
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: Development and initial validation. *J Am Coll Cardiol* 2004; **44**: 1393–1399.
- Maeder M, Klein M, Fehr T, Rickli H. Contrast nephropathy: Review focusing on prevention. *J Am Coll Cardiol* 2004; **44**: 1763–1771.
- McCullough P. Outcomes of contrast-induced nephropathy: Experience in patients undergoing cardiovascular intervention. *Catheter Cardiovasc Interv* 2006; **67**: 335–343.
- Pannu N, Wiebe N, Tonelli M. Prophylaxis strategies for contrast-induced nephropathy. *JAMA* 2006; **295**: 2765–2779.
- Kawashima S, Takano H, Iino Y, Takayama M, Takano T. Prophylactic hemodialysis does not prevent contrast-induced nephropathy after cardiac catheterization in patients with chronic renal insufficiency. *Circ J* 2006; **70**: 553–558.
- Solomon R, Werner C, Mann D, D'Elia J, Silva P. Effects of saline, mannitol, and furosemide to prevent acute decreases in renal function induced by radiocontrast agents. *N Engl J Med* 1994; **331**: 1416–1420.
- Recio-Mayoral A, Chaparro M, Prado B, Cozar R, Mendez I, Banerjee D, et al. The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcysteine in patients undergoing emergency percutaneous coronary intervention: The RENO Study. *J Am Coll Cardiol* 2007; **49**: 1283–1288.
- Briguori C, Airolidi F, D'Andrea D, Bonizzoni E, Morici N, Focaccio A, et al. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): A randomized comparison of 3 preventive strategies. *Circulation* 2007; **115**: 1211–1217.
- Solomon RJ, Natarajan MK, Doucet S, Sharma SK, Staniloae CS, Katholi RE, et al. Cardiac Angiography in Renally Impaired Patients (CARE) study: A randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. *Circulation* 2007; **115**: 3189–3196.
- Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. *JAMA* 2007; **298**: 2028–2037.
- Nutritional anaemias: Report of a WHO scientific group. *World Health Organ Tech Rep Ser* 1968; **405**: 5–37.
- Teipel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000; **343**: 180–184.
- Artunc FH, Fischer IU, Risler T, Erley CM. Improved estimation of GFR by serum cystatin C in patients undergoing cardiac catheterization. *Int J Cardiol* 2005; **102**: 173–178.
- Shiragami K, Fujii Z, Sakumura T, Shibuya M, Takahashi N, Yano M, et al. Effect of a contrast agent on long-term renal function and the efficacy of prophylactic hemodiafiltration. *Circ J* 2008; **72**: 427–433.
- Masuda M, Yamada T, Mine T, Morita T, Tamaki S, Tsukamoto Y, et al. Comparison of usefulness of sodium bicarbonate versus sodium chloride to prevent contrast-induced nephropathy in patients undergoing an emergent coronary procedure. *Am J Cardiol* 2007; **100**: 781–786.
- Kato K, Sato N, Yamamoto T, Iwasaki YK, Tanaka K, Mizuno K. Valuable markers for contrast-induced nephropathy in patients undergoing cardiac catheterization. *Circ J* 2008; **72**: 1499–1505.
- Ashby DT, Mehran R, Aymong EA, Lansky AJ, Iakovou I, Weisz G, et al. Comparison of outcomes in men versus women having percutaneous coronary interventions in small coronary arteries. *Am J Cardiol* 2003; **91**: 979–981, A974, A977.
- Beddhu S. The body mass index paradox and an obesity, inflammation, and atherosclerosis syndrome in chronic kidney disease. *Semin Dial* 2004; **17**: 229–232.
- Obermayr RP, Temml C, Gutjahr G, Kainz A, Klauser-Braun R, Függer R, et al. Body mass index modifies the risk of cardiovascular death in proteinuric chronic kidney disease. *Nephrol Dial Transplant* 2009 [E-pub ahead of print].
- Huber W, Jeschke B, Kreymann B, Hennig M, Page M, Salmhofer H, et al. Haemodialysis for the prevention of contrast-induced nephropathy: Outcome of 31 patients with severely impaired renal function, comparison with patients at similar risk and review. *Invest Radiol* 2002; **37**: 471–481.
- Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, et al. Prevention of contrast media-associated nephropathy: Randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. *Arch Intern Med* 2002; **162**: 329–336.
- Solomon R. The role of osmolality in the incidence of contrast-induced nephropathy: A systematic review of angiographic contrast media in high risk patients. *Kidney Int* 2005; **68**: 2256–2263.
- Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007; **356**: 1503–1516.