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CURRENT OPINION

Flash pulmonary oedema and bilateral renal artery stenosis: the Pickering Syndrome†

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Introduction

In 1988 Pickering *et al*. reported in the Lancet a series of 11 hypertensive patients with bilateral atheromatous renovascular disease who presented with a history of multiple episodes of pulmonary oedema.[1] Seven of these patients had stenosis of both renal arteries and in a subsequent series of 90 patients, pulmonary oedema was significantly more common in patients with bilateral than in those with unilateral renal artery stenosis (RAS).[2] Successful revascularization of one or both renal arteries eliminated pulmonary oedema in 77% of patients with bilateral RAS.[2] The authors concluded that 'bilateral RAS may be a specific and treatable predisposing factor to pulmonary oedema in azotemic hypertensive patients'.[1] Since the initial observation of this clinical entity 29 case reports,[3–31] 9 case series,[1,32–39] and 10 clinical studies[1–2,40–47] of flash pulmonary oedema (FPO) and RAS (both unilateral and bilateral) have been published of which 16 case reports, 2 case series, and 7 clinical studies comprising a total of 87 patients relate to bilateral RAS and FPO. The underlying pathophysiological mechanisms responsible for triggering FPO in patients with bilateral RAS have been delineated in several clinical and experimental studies. Since FPO and bilateral RAS seem to be a unique entity with distinct pathophysiological, clinical, and therapeutic features, we propose to name it Pickering Syndrome. In the following, we review incidence, pathophysiology, clinical findings, and treatment of the Pickering Syndrome.

Definition

Flash pulmonary oedema is a general term used to describe a particularly dramatic form of acute decompensated heart failure. Regardless of its aetiology, an acute increase of left ventricular (LV) end diastolic pressure is the conditio sine qua non for the development of FPO and remains the common denominator of all clinical situations associated with it. However, what distinguishes FPO from other forms of decompensated heart failure is that because of unique underlying pathophysiological mechanisms, flooding of the alveolar space can occur within minutes resulting in an acute life-threatening emergency.[48]

Prevalence

Atherosclerotic renal artery disease is increasingly diagnosed and strongly associated with atherosclerotic disease in other vascular beds such as the coronary, carotid, and iliofemoral circulation.[49] Renovascular hypertension is the most common secondary cause of hypertension. In 26 studies comprising a total patient population of 30 092 undergoing diagnostic coronary angiography for suspected coronary artery disease the prevalence of RAS >50% averaged 8.0% with a range from 3.1 to 22.9% (*Table 1*).[43,50–74] Of all patients with atherosclerotic RAS, 20.3% had significant bilateral RAS. The prevalence of FPO varies a great deal and seems to depend on the pressure load as well as on the degree of renal impairment. In a series of 56 patients with bilateral RAS, Bloch *et al*.[2] reported a history of FPO before revascularization in 23 (41%) patients. Messina *et al*.[35] reported 17 patients with RAS treated at the University of Michigan Hospital, 16 of who had bilateral disease. Mean blood pressure was 207/110 mmHg and serum creatinine was 3.5 mg/dL. Two-thirds of these patients had FPO despite evidence of normal ventricular function. Overall the weighted prevalence of FPO in patients with RAS was 15.3%. In patients with bilateral RAS the weighted prevalence of FPO was 14.3% compared with 3.5% in those with unilateral RAS.

Pathophysiology

Bilateral RAS predisposes patients to develop FPO by three main pathophysiological mechanisms: (i) defective natriuresis;

† Thomas G. Pickering passed away on 14 May 2009 after a short battle with a brain tumour.

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Table 1 Prevalence of RAS >50% in patients undergoing cardiac catheterization

Study	Year	Number of patients	Prevalence of RAS (%)	Prevalence of bilateral RAS[a] (%)
Alhaddad *et al.*[50]	2001	171	7.60	38.5
Aqel *et al.*[51]	2003	90	27.8	36
Buller *et al.*[52]	2004	851	14.1	—
Cohen *et al.*[53]	2005	843	18.3	—
Conlon *et al.*[54]	2001	3987	9.10	—
Crowley *et al.*[55]	1998	14 152	6.20	20.2
Dzielińska *et al.*[56]	2007	333	12.0	20
Ghaffari *et al.*[43]	2009	732	11.9	42.5
Harding *et al.*[57]	1992	1235	15.2	27.7
Jean *et al.*[58]	1994	196	18.4	—
Leandri *et al.*[59]	2004	467	9.00	31
Ollivier *et al.*[60]	2009	650	14.5	21.3
Ramirez *et al.*[61]	1987	102	4.90	—
Ravichandran *et al.*[62]	2003	614	8.47	9.6
Rigatelli *et al.*[63]	2005	205	19.5	37.5
Rihal *et al.*[64]	2002	297	19.2	19.3
Rimoldi *et al.*[65]	2010	1403	8.00	25
Saleh and Bustami[66]	2004	354	3.10	18.2
Sani *et al.*[67]	2008	260	14.2	—
Shen *et al.*[68]	2001	280	15.4	32.6
Song *et al.*[69]	2000	427	5.60	25
Tumelero *et al.*[70]	2005	1656	13.7	11
Vetrovec *et al.*[71]	1989	118	23	37
Wang *et al.*[72]	2003	203	14.8	16.7
Weber *et al.*[73]	2002	177	10.7	26.3
Yamashita *et al.*[74]	2002	289	7.3	14.3
Total		30 092	8.0	20.3

[a]Prevalence of bilateral RAS as % of all RAS patients. RAS, renal artery stenosis.

(ii) increased haemodynamic burden and exacerbation of diastolic dysfunction;[75] and (iii) failure of the pulmonary capillary blood–gas barrier (*Figure 1*).

Experimental studies allow us to clearly delineate differences in pathophysiology between unilateral and bilateral RAS. In patients with unilateral RAS corresponding to the 2-kidney-1-clip hypertension model, stenosis of one renal artery decrease ipsilateral renal perfusion thereby activating the renin–angiotensin–aldosterone cascade and causing sodium and fluid retention.[76] Concomitantly, stimulation of the sympathetic nervous system occurs, triggered directly by renal ischaemia[77] as well as by the activation of the renin–angiotensin system.[78] Since the contralateral kidney is functioning normally, it compensates for the increase in blood pressure by suppressing renin secretion and augmenting sodium excretion; so-called pressure natriuresis occurs. However, this escape mechanism is defective in patients with bilateral RAS which corresponds to the1-kidney-1-clip hypertension model. Since now perfusion to both kidneys is hampered, pressure natriuresis cannot take place and intravascular volume expansion secondary to sodium and water retention persists.[79] Indeed, Hall *et al.*[80] experimentally showed that high circulating angiotensin levels caused a marked increase in blood pressure and sodium retention, rapidly resulting in FPO when renal artery perfusion pressure was kept low, as is the case with bilateral RAS. In contrast, no sodium retention was observed when renal artery pressure was allowed to increase, suggesting that this increase is seminal in helping the kidneys to escape from the sodium retaining effect of angiotensin.

Sustained blood pressure elevation in patients with RAS may give rise to left ventricular hypertrophy (LVH) most often of the concentric type and to diastolic LV dysfunction.[81] Concomitant arterial stiffening increases pulse wave velocity so that the reflected pulse wave returns during systole instead of during diastole[82–83] thereby further augmenting systolic ventricular pressure load.[84] Normally, the LV compensates for an increase in afterload by increasing end-diastolic volume (preload reserve). However, in patients with a stiff LV, this safety mechanism is rapidly exhausted and even small increases in LV end-diastolic volume may give rise to a marked elevation in end-diastolic pressure, left atrial, and pulmonary venous pressure.[78] Moreover, in patients with diastolic dysfunction and stiff LV, excessive sympathetic activation may also precipitate the development of FPO. The tachycardia-induced decrease of diastole duration further impairs the ability of the stiff LV to fill and results in retrograde elevation of pulmonary venous pressure. Hence, patients with LV and vascular stiffening

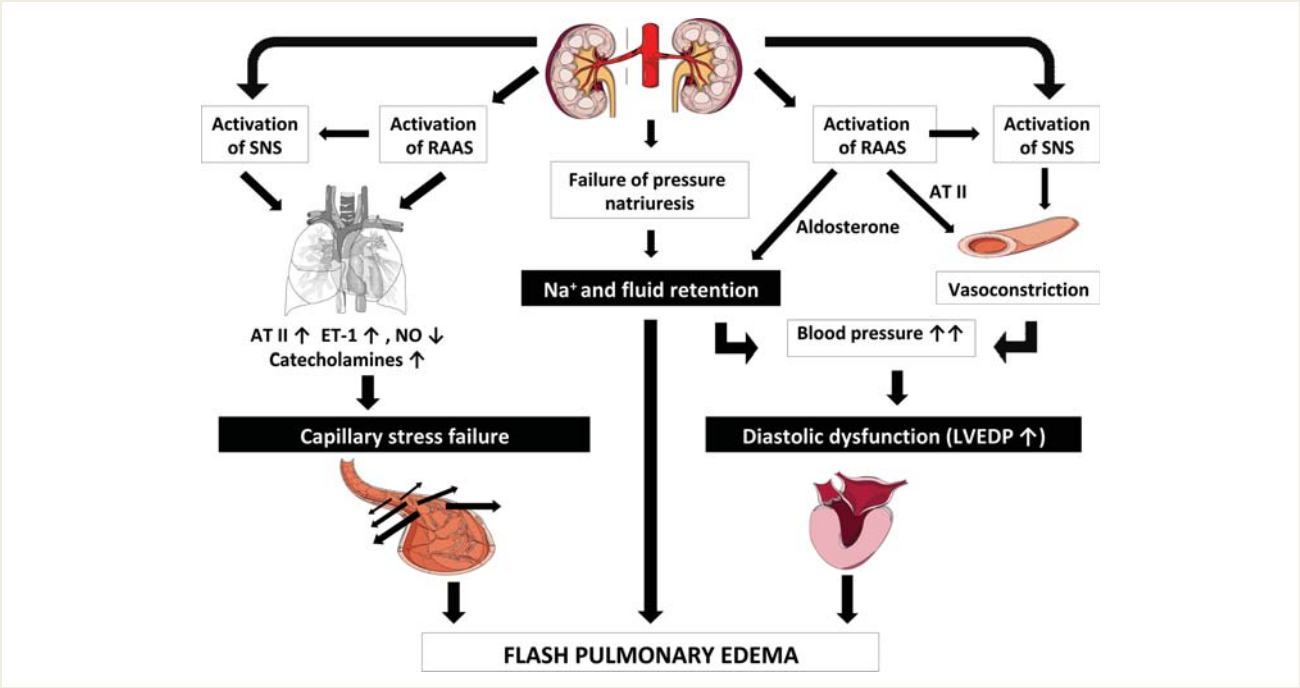

Figure 1 The Pickering Syndrome. Three main pathophysiological mechanisms contribute to the development of flash pulmonary oedema: defective pressure natriuresis with sodium and fluid retention, increased left ventricular end-diastolic pressure associated with left ventricular hypertrophy and stiffening, and failure of the pulmonary capillary blood–gas barrier. RAAS, renin–angiotensin–aldosterone system; SNS, sympathetic nervous system; Na^+, sodium; AII, angiotensin II; ET-1, endothelin-1; NO, nitric oxide.

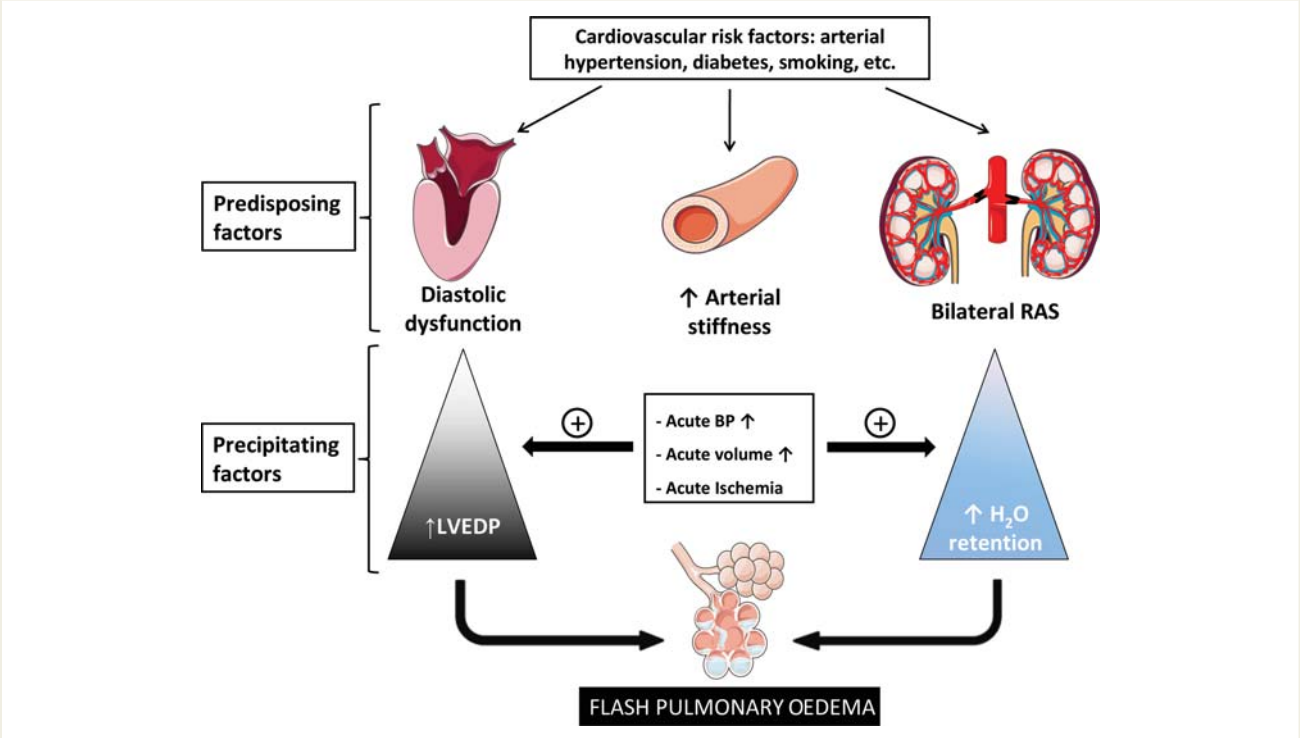

Figure 2 Key predisposing (left ventricular diastolic dysfunction, increased arterial stiffness, bilateral renal artery stenosis) and precipitating (acute increase in blood pressure and/or intravascular volume, acute myocardial ischaemia) factors of the Pickering Syndrome. RAS, renal artery stenosis. LVEDP, left ventricular end-diastolic pressure.

have an exaggerated response to changes in intravascular volume and sympathetic activity.[85] Furthermore, the increased systemic vascular resistance secondary to activation of renin angiotensin aldosterone cascade and sympathetic nervous system increases LV wall stress and causes a mismatch between increased oxygen demand and delivery to the myocardium. This, in turn, aggravates LV diastolic dysfunction resulting in a further increase in LV end-diastolic pressure (*Figure 1*).

Pulmonary capillary stress failure and increased pulmonary vascular permeability are important but often overlooked pathogenetic mechanism of FPO.[48] The rapid and exaggerated increase in LV pressure transmits to left atrium, pulmonary veins and to the unprotected pulmonary capillaries. Once intracapillary pressure exceeds 20–25 mmHg the oedema fluid leaks through the endothelial barrier and floods the interstitial and, subsequently, alveolar space.[48] Excessive plasma and tissue levels of neurohumoral mediators, such as angiotensin II, catecholamines, and endothelin-1, may increase permeability of the alveolo-capillary barrier.[48]

In the case of decompensated bilateral RAS all of the above-mentioned predisposing factors reunite and overcome the protective mechanisms against alveolar fluid accumulation. In this precarious situation even small fluctuations in blood pressure, intravascular volume or renal perfusion and/or myocardial ischaemia may act as precipitating factors that can trigger FPO (*Figure 2*).[48] Once FPO ensues, LV pump function is prone to decline which, in turn, will further hamper perfusion of the kidneys, thereby giving rise to a vicious circle.

Clinical findings

The Pickering Syndrome can present a diagnostic conundrum and the clinical findings of bilateral RAS must be differentiated from unilateral RAS (*Table 2*). In the series described by Pickering, FPO occurred on average 2.3 times before a diagnosis of RAS was established. In our literature review of 87 patients with the Pickering Syndrome mean age was 63 years, 47% were male and 73% were smokers. Of these patients 58% had coronary artery disease and 40% had heart failure diagnosed in the past. Average ejection fraction was 49% and 50% had LVH. Renal failure was evident in 94% of patients and the mean creatinine was 3.8 mg/dL (336 μmol/L). As to FPO, only 7% had a single episode of FPO before the diagnosis and 93% had recurrent episodes of FPO. Classically, patients present with sudden onset of severe, unprovoked dyspnoea ('flash' pulmonary oedema) although the LV systolic function is usually normal. The occasional presence of coronary artery disease may result in misinterpretation of FPO as being caused by coronary ischaemia. However, in many patients, coronary angiography reveals no flow limiting stenosis. This finding coupled with normal LV systolic function can lead to a false sense of security or give rise to evaluation for non-cardiac causes for dyspnoea. The frequent nocturnal appearance of FPO may be due to reverse nocturnal dipping which has been well documented in patients with RAS.[86,87]

Table 2 Differences in clinical findings before unilateral and bilateral renal artery stenosis

	Renal artery stenosis	
	Unilateral	**Bilateral**
RAAS activation	↑↑	↑
Na/Fluid volume state	Pressure natriuresis	Sodium retention
Cardiac output	Normal	↑
Total peripheral resistance	↑↑	↑
BP response to RAS blockade	↑↑	↑
Flash pulmonary oedema	Rare	Common
Natriuresis post angioplasty of RAS	No	Yes

BP, blood pressure; RAAS, renin–angiotensin–aldosterone system; RAS, renal artery stenosis.

Therapy

The therapeutic approach to the Pickering Syndrome can be divided into two distinct phases.

Phase 1 is characterized by the occurrence of FPO which represents a hypertensive emergency requiring immediate therapeutic intervention. Haemodynamic unloading by antihypertensive drugs usually result in prompt resolution of FPO but may further compromise renal blood flow and function. This is particularly true with inhibitors of the renin–angiotensin–aldosterone system. Although empirically, renin–angiotensin–system inhibitors should prove to be very useful for emergency treatment of FPO, they may precipitate acute renal failure and their continued use becomes relatively contraindicated once the patient has been stabilized. In the acute phase, a loop diuretic should be added to initiate natriuresis and overcome sodium retention. Of note, there is no iron clad evidence to exactly guide us, how to optimally proceed in a patient presenting with the acute phase of the Pickering Syndrome. In *Phase 2*, once the patient is out of pulmonary oedema and has been stabilized, renal revascularization is the treatment of choice, since the pathophysiology of the Pickering Syndrome is characterized by the inability to generate a pressure natriuresis due to renal hypoperfusion.[2,47] Both surgical and percutaneous revascularization techniques have been successful in treating RAS and its clinical manifestations such as FPO (*Table 3*).[1–2,32,35–36,38,44–45,88–90] Renal revascularization decreases circulating angiotensin and aldosterone levels resulting in a fall in blood pressure, and since revascularization improves renal perfusion, in an increase in glomerular filtration rate and natriuresis.

Renal artery surgery is an effective method for revascularization but is associated with greater morbidity and mortality than percutaneous endovascular techniques. The ACC/AHA guidelines endorse percutaneous revascularization as a class I recommendation for patients with haemodynamically significant RAS and recurrent, unexplained congestive heart failure, or pulmonary oedema.[91] The efficacy of successful renal artery revascularization in resolving FPO can be dramatic (*Table 3*). Evidence is compelling that stenting is superior over balloon angioplasty.[91–93] This is particularly true for atherosclerotic aorta-ostial RAS.[94–96] In patients with severe/acute heart failure and combined renovascular and coronary artery disease, renal revascularization with stents

Table 3 Responders to revascularization as reported in various studies

Study	Patients	Bilateral RAS	Unilateral RAS	Surgery	Balloon	Stent	Responders (%)
Bloch *et al.*[2]	25	22	3	0	0	25	72.0
Diamond[32]	3	3	0	3	0	0	66.0
Gray[88] 2002	39	39	0	0	0	39	77.0
Kane[89] 2010	50	27	23	0	0	50	88.0
Khosla[44] 1997	28	20	8	0	0	28	85.7
Messina *et al.*[35]	17	16	1	16	1	0	100.0
Missouris[90]	9	5	4	1	8	0	100.0
Pelta *et al.*[45]	8	4	4	0	0	8	88.0
Pickering[1]	11	9	2	3	8	0	90.9
Planken and Rietveld[36]	2	2	0	0	2	0	100.0
Weatherford[38]	5	5	0	5	0	0	100.0

RAS, renal artery stenosis.

achieves similar outcomes and improved functional status independent of coronary revascularization.[47] A recent cohort-controlled study demonstrated a significant benefit for renal stent revascularization compared with continued medical therapy in 50 patients presenting with heart failure who had bilateral RAS or RAS and a solitary kidney being treated for uncontrolled hypertension or ischaemic nephropathy.[89] Patients who received renal stents improved their New York Heart Association Functional Class (1.9 ± 0.8 vs. 2.6 ± 1.0, $P < 0.04$) compared with those treated conservatively. Although there was no mortality benefit, there was a significant reduction in recurrent heart failure events and the need for rehospitalization was reduced five-fold in the renal stent group. Renal stenting has a remarkably low failure rate with primary patency rates of 79–84% and secondary patency rates of 92–98% after 5 years of follow-up.[97,98]

In our literature review of 87 reported cases of bilateral RAS and FPO, 35% were treated with unilateral and 22% with bilateral angioplasty. In 43% of patients, mostly in earlier reports, surgical revascularization was performed. Stenting was unsuccessful in two patients, one of whom improved with carvedilol and the other after resuming ACE-Inhibitor therapy. Renal function improved in 81% of patients and the mean creatinine on follow-up was 1.6 mg/dL (141 μmol/L) after the procedure. Renal function was normal at baseline and after angioplasty in two patients only. Importantly, in 92% of all patients there was no further episode of FPO after revascularization.

The acute phase the Pickering Syndrome can be treated effectively by haemodynamic unloading and diuresis. In the subacute phase renal stenting is treatment of choice. However, long-term prognosis in patients with bilateral RAS remains guarded. Conlon *et al.*[54] reported a 4-year survival rate of <50% in a series of 33 patients.

Comments

The Pickering Syndrome must be considered a unique pebble in the mosaic of the so-called cardiorenal syndrome, a pathophysiological condition in which impairment of cardiac and renal function mutually accelerates each other. However, in contrast to the cardiorenal syndrome which is ill defined and has a somewhat nebulous pathophysiology, the Pickering Syndrome is clearly defined and its pathophysiological mechanisms have been precisely delineated. As such it is prone to serve as an illuminating teaching model shedding light on one straight forward aspect of the complex interaction between heart and kidney. This brings us back to Thomas Pickering who dedicated his career in cardiovascular medicine to research, teaching, and patient care. His original paper in Lancet[1] is a prime example of keen observation and crystal clear thinking attesting to his preeminence as an astute teacher and clinician.

A personal memoir

Tom Pickering was one of my first D.Phil students in Oxford in the late 1960s, following Harley Smyth in the early studies of the cardiovascular effects of sleep in man. He was quietly modest, but an outstandingly able and intelligent person, a pleasure to work with—even during the middle of the night! His Oxford thesis on 'Baroreceptor reflexes in man in health and disease' was published in 1970 and resulted in a series of publications in high-impact journals. I tried hard to get him to stay in Oxford, but could understand his wish not to stay there—where his famous father was Regius Professor of Medicine. He made his name in New York with seminal work describing the psychological influences on cardiovascular disease, with thoroughly controlled studies of the effects of different kinds of job stress on blood pressure. The importance of psycho-social influences on cardiovascular disease is now well recognized and has become academically respectable—in large part due his work. I was immensely impressed with the way Tom managed himself when knowing he had limited time left. Supported bravely by his wife Janet, he came to several European meetings in his final year, giving papers and joining discussions as if nothing was amiss (P.S.).

Conflict of interest: none declared.

References

1. Pickering TG, Herman L, Devereux RB, Sotelo JE, James GD, Sos TA, Silane MF, Laragh JH. Recurrent pulmonary oedema in hypertension due to bilateral renal

artery stenosis: treatment by angioplasty or surgical revascularisation. *Lancet* 1988;**2**:551–552.
2. Bloch MJ, Trost DW, Pickering TG, Sos TA, August P. Prevention of recurrent pulmonary edema in patients with bilateral renovascular disease through renal artery stent placement. *Am J Hypertens* 1999;**12**:1–7.
3. Aslam MS, Balasubramanian J, Greenspahn BR. Brachytherapy for renal artery in-stent restenosis. *Catheter Cardiovasc Interv* 2003;**58**:151–154.
4. Bali HK, Jha V. Nephrotic syndrome and recurrent pulmonary oedema in bilateral atherosclerotic renal artery stenosis: resolution following renal angioplasty and stenting. *Natl Med J India* 2006;**19**:253–254.
5. Basaria S, Fred HL. Images in cardiovascular medicine. Flash pulmonary edema heralding renal artery stenosis. *Circulation* 2002;**105**:899.
6. Chrysochou C, Sinha S, Chalmers N, Kalra PR, Kalra PA. Anuric acute renal failure and pulmonary oedema: a case for urgent action. *Int J Cardiol* 2009;**132**:e31–e33.
7. Ducloux D, Jamali M, Chalopin JM. Chronic congestive heart failure associated with bilateral renal artery stenosis. *Clin Nephrol* 1997;**48**:54–55.
8. Farmer CK, Reidy J, Scoble JE. 'Flash pulmonary oedema' in a patient 24 years after aorto-renal vein graft. *Nephrol Dial Transplant* 1999;**14**:1310–1312.
9. Feinstein EI, Weissman M, Gadallah MF, Finck E. Anuria in a patient with pulmonary edema. *Am J Nephrol* 1989;**9**:222–229.
10. Fujigaki Y, Togawa A, Miyaji T, Suzuki H, Ohashi N, Fukasawa H, Yasuda H, Yamamoto T, Hishida A, Yonemura K. Rapid improvement of acute pulmonary edema with angiotensin converting enzyme inhibitor under hemodialysis in a patient with renovascular disease. *Ther Apher Dial* 2004;**8**:148–152.
11. Halma C, Leemans R. [Anuria and recurrent pulmonary edema due to ischemic nephropathy successfully treated with surgical renal revascularization]. *Ned Tijdschr Geneeskd* 1994;**138**:1230–1233.
12. Hoieggen A, Draganov B, Os I. [Bilateral renal artery stenosis—a cause of acute pulmonary edema]. *Tidsskr Nor Laegeforen* 2001;**121**:1789–1790.
13. Islam MA, Rosenfield K, Maree AO, Patel PM, Jaff MR. Percutaneous revascularization of occluded renal arteries in the setting of acute renal failure. *Vasc Med* 2009; **14**:365–369.
14. Kalimanovska-Ostric DV, Simic-Ogrizovic SP, Bonaci-Nikolic BM, Bozic VD, Ostric VZ, Davidovic LB. Heart and renal failure in renovascular hypertension caused by giant cell arteritis—case report. *Clin Nephrol* 2007;**67**:58–60.
15. Kanamori H, Toma M, Fukatsu A. Improvement of renal function after opening occluded atherosclerotic renal arteries. *J Invasive Cardiol* 2009;**21**:E171–E174.
16. Kiykim AA, Boz M, Ozer C, Camsari A, Yildiz A. Two episodes of anuria and acute pulmonary edema in a losartan-treated patient with solitary kidney. *Heart Vessels* 2004;**19**:52–54.
17. Koduganti SC, Kumar R. Bilateral Renal Artery Stenosis Presenting as Flash Pulmonary Edema. *J Assoc Physicians India* 2006;**54**:651–654.
18. Krzesinski JM. [Renal artery stenosis: acute congestive heart failure as a possible cause]. *Rev Med Liege* 2002;**57**:253–257.
19. Kwan T, Feit A, Alam M, Mandawat MK, Clark LT. Pulsus alternans in diastolic left ventricular dysfunction—a case report. *Angiology* 1997;**48**:1079–1085.
20. Maillard JO, Descombes E, Fellay G, Regamey C. Repeated transient anuria following losartan administration in a patient with a solitary kidney. *Ren Fail* 2001; **23**:143–147.
21. Mansoor S, Shah A, Scoble JE. 'Flash pulmonary oedema'—a diagnosis for both the cardiologist and the nephrologist? *Nephrol Dial Transplant* 2001;**16**: 1311–1313.
22. Massing JL, Baille N, Raddad M, Gangloff C, Lecourtois P. [Benefits of a beta-blocking agent (carvedilol) on bilateral atherosclerotic renal artery stenosis. A case report]. *Ann Cardiol Angeiol (Paris)* 2004;**53**:114–117.
23. Noh HJ, Jo HC, Yang JH, Kim SM, Lee HJ, Choi JH, Choi SH, Song BG, Choe YH, Choi SH, Kim DK, Cho DK. Flash pulmonary edema in a patient with unilateral renal artery stenosis and bilateral functioning kidneys. *Korean Circ J* 2010;**40**: 42–45.
24. Nunez E, White CJ. Renal artery stent implantation in a patient with bilateral renal artery stenoses presenting with flash pulmonary edema. *Int J Cardiovasc Intervent* 1998;**1**:49–53.
25. Palmar AH, Defeyter IR, Vandenbogaerde JF. Renal arterial stenosis as a cause of high output cardiac failure. *Int J Cardiol* 1989;**22**:404–406.
26. Shinohara M, Washida N, Tanaka A, Ueda S, Kuwahara T, Kojima H. ACE inhibitor-induced acute renal failure in a patient with progressive systemic sclerosis: ischemic nephropathy mimicking PSS renal crisis. *Intern Med* 2007;**46**: 1605–1607.
27. Spratt JC, Leslie SJ, Verin V. A case of renal artery brachytherapy for in-stent restenosis: four-year follow-up. *J Invasive Cardiol* 2004;**16**:287–288.
28. Ungar A, Lambertucci L, Agresti C, Pini R, Boddi M, Valentini MC, Parati G, Modesti PA. Hypertension and reduced renal function in an 83-year-old patient. *Intern Emerg Med* 2006;**1**:40–48.
29. Walker F, Walker DA, Nielsen M. Flash pulmonary oedema. *Lancet* 2001;**358**:556.
30. Williams SG, Lindsay SJ, Tan LB. Recurrent pulmonary oedema in a 53 year old woman. *Postgrad Med J* 2001;**77**:408, 416–417.
31. Wykrzykowska JJ, Williams M, Laham RJ. Stabilization of renal function, improvement in blood pressure control and pulmonary edema symptoms after opening a totally occluded renal artery. *J Invasive Cardiol* 2008;**20**:E26–E29.
32. Diamond JR. Flash pulmonary edema and the diagnostic suspicion of occult renal artery stenosis. *Am J Kidney Dis* 1993;**21**:328–330.
33. Duclos J, Goecke H, Opazo M. [Flash pulmonary edema: when the kidney causes decompensation of the heart]. *Rev Med Chil* 2002;**130**:1033–1036.
34. Kalimonovska-Ostric D, Ivanovic B, Ostric V, Knezivic V, Stojanov V, Simic D. ["Flash" pulmonary edema as a clinical manifestation of renovascular hypertension]. *Srp Arh Celok Lek* 2003;**131**:208–210.
35. Messina LM, Zelenock GB, Yao KA, Stanley JC. Renal revascularization for recurrent pulmonary edema in patients with poorly controlled hypertension and renal insufficiency: a distinct subgroup of patients with arteriosclerotic renal artery occlusive disease. *J Vasc Surg* 1992;**15**:73–80; discussion 80–2.
36. Planken II, Rietveld AP. Rapid onset pulmonary edema (flash edema) in renal artery stenosis. *Neth J Med* 1998;**52**:116–119.
37. Pun E, Dowling RJ, Mitchell PJ. Acute presentations of renal artery stenosis in three patients with a solitary functioning kidney. *Australas Radiol* 2004;**48**: 523–527.
38. Weatherford DA, Freeman MB, Regester RF, Serrell PF, Stevens SL, Goldman MH. Surgical management of flash pulmonary edema secondary to renovascular hypertension. *Am J Surg* 1997;**174**:160–163.
39. Wengrovitz M, Healy DA, Diamond JR, Atnip RG. Renal revascularization in patients on dialysis. *J Cardiovasc Surg (Torino)* 1995;**36**:241–246.
40. Acher CW, Belzer FO, Grist TM, Turnipseed WD, Hoch JR, Archibald JE. Late renal function in patients undergoing renal revascularization for control of hypertension and/or renal preservation. *Cardiovasc Surg* 1996;**4**:602–606.
41. Bhandari S, Wilkinson A, Nicholson A, Farr MJ, Sellars L. Atherosclerotic renovascular disease in the elderly: angioplasty with stenting versus reconstructive surgery. *Geriatr Nephrol Urol* 1997;**7**:87–94.
42. Cambria RP, Kaufman JL, Brewster DC, Gertler JP, LaMuraglia GM, Bazari H, Abbott WM. Surgical renal artery reconstruction without contrast arteriography: the role of clinical profiling and magnetic resonance angiography. *J Vasc Surg* 1999; **29**:1012–1021.
43. Ghaffari S, Sohrabi B, Siahdasht RB, Pourafkari L. Prevalence and predictors of renal artery stenosis in hypertensive patients undergoing coronary angiography. *Hypertens Res* 2009;**32**:1009–1014.
44. Khosla S, White CJ, Collins TJ, Jenkins JS, Shaw D, Ramee SR. Effects of renal artery stent implantation in patients with renovascular hypertension presenting with unstable angina or congestive heart failure. *Am J Cardiol* 1997;**80**:363–366.
45. Pelta A, Andersen UB, Just S, Baekgaard N. Flash pulmonary edema in patients with renal artery stenosis - the Pickering Syndrome. *Blood Press* 2010;**20**:15–19.
46. Reilly JM, Rubin BG, Thompson RW, Allen BT, Flye MW, Anderson CB, Sicard GA. Revascularization of the solitary kidney: a challenging problem in a high risk population. *Surgery* 1996;**120**:732–736; discussion 736–7.
47. Wierema TK, Yaqoob MM. Renal artery stenosis in chronic renal failure: caution is advised for percutaneous revascularization. *Eur J Intern Med* 2008;**19**:276–279.
48. Rimoldi SF, Yuzefpolskaya M, Allemann Y, Messerli F. Flash pulmonary edema. *Prog Cardiovasc Dis* 2009;**52**:249–259.
49. Chrysochou C, Kalra PA. Epidemiology and natural history of atherosclerotic renovascular disease. *Prog Cardiovasc Dis* 2009;**52**:184–195.
50. Alhaddad IA, Blum S, Heller EN, Beato MA, Bhalodkar NC, Keriaky GE, Brown EJ Jr. Renal artery stenosis in minority patients undergoing diagnostic cardiac catheterization: prevalence and risk factors. *J Cardiovasc Pharmacol Ther* 2001;**6**: 147–153.
51. Aqel RA, Zoghbi GJ, Baldwin SA, Auda WS, Calhoun DA, Coffey CS, Perry GJ, Iskandrian AE. Prevalence of renal artery stenosis in high-risk veterans referred to cardiac catheterization. *J Hypertens* 2003;**21**:1157–1162.
52. Buller CE, Nogareda JG, Ramanathan K, Ricci DR, Djurdjev O, Tinckam KJ, Penn IM, Fox RS, Stevens LA, Duncan JA, Levin A. The profile of cardiac patients with renal artery stenosis. *J Am Coll Cardiol* 2004;**43**:1606–1613.
53. Cohen MG, Pascua JA, Garcia-Ben M, Rojas-Matas CA, Gabay JM, Berrocal DH, Tan WA, Stouffer GA, Montoya M, Fernandez AD, Halac ME, Grinfeld LR. A simple prediction rule for significant renal artery stenosis in patients undergoing cardiac catheterization. *Am Heart J* 2005;**150**:1204–1211.
54. Conlon PJ, Little MA, Pieper K, Mark DB. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. *Kidney Int* 2001;**60**: 1490–1497.
55. Crowley JJ, Santos RM, Peter RH, Puma JA, Schwab SJ, Phillips HR, Stack RS, Conlon PJ. Progression of renal artery stenosis in patients undergoing cardiac catheterization. *Am Heart J* 1998;**136**:913–918.
56. Dzielińska Z, Januszewicz A, Demkow M, Makowiecka-Cieśla M, Prejbisz A, Naruszewicz M, Nowicka G, Kadziela J, Zieliński T, Florczak E, Janas J,

Januszewicz M, Ruzyłło W. Cardiovascular risk factors in hypertensive patients with coronary artery disease and coexisting renal artery stenosis. *J Hypertens* 2007;**25**:663–670.
57. Harding MB, Smith LR, Himmelstein SI, Harrison K, Phillips HR, Schwab SJ, Hermiller JB, Davidson CJ, Bashore TM. Renal artery stenosis: prevalence and associated risk factors in patients undergoing routine cardiac catheterization. *J Am Soc Nephrol* 1992;**2**:1608–1616.
58. Jean WJ, al-Bitar I, Zwicke DL, Port SC, Schmidt DH, Bajwa TK. High incidence of renal artery stenosis in patients with coronary artery disease. *Cathet Cardiovasc Diagn* 1994;**32**:8–10.
59. Leandri M, Lipiecki J, Lipiecka E, Hamzaoui A, Amonchot A, Mansour M, Albuisson E, Citron B, Ponsonnaille J, Boyer L. [Prevalence of renal artery stenosis in patients undergoing cardiac catheterization: when should abdominal aortography be performed? Results in 467 patients]. *J Radiol* 2004;**85**:627–633.
60. Ollivier R, Boulmier D, Veillard D, Leurent G, Mock S, Bedossa M, Le Breton H. Frequency and predictors of renal artery stenosis in patients with coronary artery disease. *Cardiovasc Revasc Med* 2009;**10**:23–29.
61. Ramirez G, Bugni W, Farber SM, Curry AJ. Incidence of renal artery stenosis in a population having cardiac catheterization. *South Med J* 1987;**80**:734–737.
62. Ravichandran R, Rengarajan T, Reddy KN, Rao SM. Prevalence of renovascular abnormality in patients undergoing cardiac catheterization. *J Assoc Physicians India* 2003;**51**:175–177.
63. Rigatelli G, Roncon L, Rinuncini M, Giordan M, Bedendo E, Panin S, Rigatelli G, Zonzin P. Angiographic characteristics of renal arterial disease over the spectrum of coronary artery disease. *Am J Nephrol* 2005;**25**:116–120.
64. Rihal CS, Textor SC, Breen JF, McKusick MA, Grill DE, Hallett JW, Holmes DR Jr. Incidental renal artery stenosis among a prospective cohort of hypertensive patients undergoing coronary angiography. *Mayo Clin Proc* 2002;**77**:309–316.
65. Rimoldi SF, de Marchi SF, Windecker S, Meier B, Allemann Y. Screening renal artery angiography in hypertensive patients undergoing coronary angiography and 6-month follow-up after ad hoc percutaneous revascularization. *J Hypertens* 2010;**28**:842–847.
66. Saleh AA, Bustami BB. Prevalence of renal artery stenosis in patients undergoing routine cardiac catheterization. *Saudi Med J* 2004;**25**:52–54.
67. Sani SH, Hasanzadeh M, Gholoobi A, Alimi H, allah Esmaily H, Gifani M. Relationship between coronary and renal artery disease and associated risk factors in hypertensive and diabetic patients undergoing coronary angiography. *EuroIntervention* 2008;**4**:373–377.
68. Shen Z, Shang Y, Zhu W. [The prevalence of renal artery stenosis in patients with coronary artery disease]. *Zhonghua Nei Ke Za Zhi* 2001;**40**:521–524.
69. Song HY, Hwang JH, Noh H, Shin SK, Choi DH, Shim WH, Lee HY, Cho SY, Han DS, Choi KH. The prevalence and associated risk factors of renal artery stenosis in patients undergoing cardiac catheterization. *Yonsei Med J* 2000;**41**:219–225.
70. Tumelero RT, Duda NT, Tognon AP, Thiesen M. Prevalence of renal artery stenosis in 1,656 patients who have undergone cardiac catheterization. *Arq Bras Cardiol* 2006;**87**:248–253.
71. Vetrovec G, Landwehr D, Edwards V. Incidence of renal artery stenosis in hypertensive patients undergoing coronary angiography. *J Interv Cardiol* 1989;**2**:69–76.
72. Wang Y, Ho DS, Chen WH, Wang YQ, Lam WF, Shen ZJ, Lu CZ, Chui M. Prevalence and predictors of renal artery stenosis in Chinese patients with coronary artery disease. *Intern Med J* 2003;**33**:280–285.
73. Weber-Mzell D, Kotanko P, Schumacher M, Klein W, Skrabal F. Coronary anatomy predicts presence or absence of renal artery stenosis. A prospective study in patients undergoing cardiac catheterization for suspected coronary artery disease. *Eur Heart J* 2002;**23**:1684–1691.
74. Yamashita T, Ito F, Iwakiri N, Mitsuyama H, Fujii S, Kitabatake A. Prevalence and predictors of renal artery stenosis in patients undergoing cardiac catheterization. *Hypertens Res* 2002;**25**:553–557.
75. Gandhi SK, Powers JC, Nomeir AM, Fowle K, Kitzman DW, Rankin KM, Little WC. The pathogenesis of acute pulmonary edema associated with hypertension. *N Engl J Med* 2001;**344**:17–22.
76. Rundback JH, Murphy TP, Cooper C, Weintraub JL. Chronic renal ischemia: pathophysiologic mechanisms of cardiovascular and renal disease. *J Vasc Interv Radiol* 2002;**13**:1085–1092.
77. Ritz E, Amann K, Fliser D. The sympathetic nervous system and the kidney: its importance in renal diseases. *Blood Press* suppl. 1998;**3**:14–19.
78. Grisk O, Rettig R. Interactions between the sympathetic nervous system and the kidneys in arterial hypertension. *Cardiovasc Res* 2004;**61**:238–246.
79. Gavras H, Brunner HB, Vaughan ED, Laragh JH. Angiotensin-sodium interaction in blood pressure maintenance of renal hypertensive and normotensive rats. *Science* 1973;**180**:1369–1371.
80. Hall JE, Granger JP, Hester RL, Coleman TG, Smith MJ Jr, Cross RB. Mechanisms of escape from sodium retention during angiotensin II hypertension. *Am J Physiol* 1984;**246**:F627–F634.
81. Mandinov L, Eberli FR, Seiler C, Hess OM. Diastolic heart failure. *Cardiovasc Res* 2000;**45**:813–825.
82. Avolio AP, Deng FQ, Li WQ, Luo YF, Huang ZD, Xing LF, O'Rourke MF. Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation* 1985;**71**:202–210.
83. Laurent S. Arterial wall hypertrophy and stiffness in essential hypertensive patients. *Hypertension* 1995;**26**:355–362.
84. Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB. Relation of arterial structure and function to left ventricular geometric patterns in hypertensive adults. *J Am Coll Cardiol* 1996;**28**:751–756.
85. Kawaguchi M, Hay I, Fetics B, Kass DA. Combined ventricular systolic and arterial stiffening in patients with heart failure and preserved ejection fraction: implications for systolic and diastolic reserve limitations. *Circulation* 2003;**107**:714–720.
86. Schrader J, Schoel G, Lüders S, Ruschitzka F, Warneke G, Scheler F. [Diagnostic significance of absent nocturnal blood pressure decrease in 24-hour long-term blood pressure measurement]. *Z Kardiol* 1992;**81**(Suppl. 2):83–86. German.
87. Iantorno M, Pola R, Schinzari F, Filice G, Mettimano M, Cardillo C, Melina D. Association between altered circadian blood pressure profile and cardiac end-organ damage in patients with renovascular hypertension. *Cardiology* 2003;**100**:114–119.
88. Gray BH, Olin JW, Childs MB, Sullivan TM, Bacharach JM. Clinical benefit of renal artery angioplasty with stenting for the control of recurrent and refractory congestive heart failure. *Vasc Med* 2002;**7**:275–279.
89. Kane GC, Xu N, Mistrik E, Roubicek T, Stanson AW, Garovic VD. Renal artery revascularization improves heart failure control in patients with atherosclerotic renal artery stenosis. *Nephrol Dial Transplant* 2010;**25**:813–820.
90. Missouris CG, Belli AM, MacGregor GA. "Apparent" heart failure: a syndrome caused by renal artery stenoses. *Heart* 2000;**83**:152–155.
91. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B; American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol* 2006;**47**:1239–1312.
92. Gray BH. Intervention for renal artery stenosis: endovascular and surgical roles. *J Hypertens Suppl* 2005;**23**:S23–S29.
93. Mackrell PJ, Langan EM III, Sullivan TM, Gray BH, Taylor SM, Cull DL, Snyder BA, Youkey JR, Carsten CG III. Management of renal artery stenosis: effects of a shift from surgical to percutaneous therapy on indications and outcomes. *Ann Vasc Surg* 2003;**17**:54–59.
94. Isles CG, Robertson S, Hill D. Management of renovascular disease: a review of renal artery stenting in ten studies. *QJM* 1999;**92**:159–167.
95. Leertouwer TC, Gussenhoven EJ, Bosch JL, van Jaarsveld BC, van Dijk LC, Deinum J, Man In 't Veld AJ. Stent placement for renal arterial stenosis: where do we stand? A meta-analysis. *Radiology* 2000;**216**:78–85.
96. van de Ven PJ, Kaatee R, Beutler JJ, Beek FJ, Woittiez AJ, Buskens E, Koomans HA, Mali WP. Arterial stenting and balloon angioplasty in ostial atherosclerotic renovascular disease: a randomised trial. *Lancet* 1999;**353**:282–286.
97. Blum U, Krumme B, Flügel P, Gabelmann A, Lehnert T, Buitrago-Tellez C, Schollmeyer P, Langer M. Treatment of ostial renal-artery stenoses with vascular endoprostheses after unsuccessful balloon angioplasty. *N Engl J Med* 1997;**336**:459–465.
98. Henry M, Amor M, Henry I, Ethevenot G, Tzvetanov K, Courvoisier A, Mentre B, Chati Z. Stents in the treatment of renal artery stenosis: long-term follow-up. *J Endovasc Surg* 1999;**6**:42–51.