Vasomotor nephropathy in the elderly

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Introduction

In a multicentre study carried out in Madrid, i.e. in a population of 4 million people, in 1995, 748 cases of acute renal failure (ARF) were treated in 13 hospitals in a 9 month period; 274 of these 748 cases occurred in subjects over 70 years old, which represents a prevalence of 36% (7% of the population and 10.5% of hospital admissions) [1]. This is one of the examples of the high incidence of ARF in the elderly that has even led to the suggestion to consider ARF as a typical geriatric disease [2].

Among the causes of ARF in the elderly, as compared with younger subjects, we may include important surgical procedures, such as aortic dissection and dissecting aneurysms, sepsis, intestinal haemorrhage, myocardial infarction, mesenteric ischaemia, occlusive diseases of large renal vessels and the aorta, atheroembolic renal disease and bladder outlet obstruction caused by benign prostatic hypertrophy or prostatic carcinoma [3–5]. However, vasomotor nephropathy is the most frequent cause of ARF in aged patients [6,7]; in recent studies, in fact, ischaemic ARF was not only the most frequent form of ARF (34%), but its incidence was greater than in younger subjects: 34 vs 18% in one study [6] and 23.4 vs 15.1% in another [7].

We may define ‘vasomotor nephropathy’ as the ARF due to an ischaemic insult, i.e. a rapid and severe deterioration of renal function associated with retention of nitrogenous wastes in the body, following haemorrhage, severe salt depletion, burns, shock, sepsis, trauma, rhabdomyolysis, haemolytic reactions or congestive heart failure. These conditions initially may cause a functional renal failure, that may be reversed if adequately treated [8,9].

Even though the relative role of haemodynamic factors, tubular obstruction and tubular leakage in the pathogenesis of vasomotor nephropathy is still a matter of debate, it is undoubtedly recognized that in humans this form of ARF is characterized by diffuse vasoconstriction of the renal cortex, as shown by a selective renal arteriogram in patients with vasomotor nephropathy in which the cortical vessels cannot be seen [3,8].

Pre-renal ARF

Pathophysiology of pre-renal ARF

Normal kidneys may withstand wide variations in renal perfusion pressure, maintaining unchanged renal blood flow (RBF) and glomerular filtration rate (GFR) (renal autoregulation). Should renal perfusion pressure fall (because of hypovolaemia) below the lower limit of the autoregulatory range (i.e. BP < 80 mmHg), RBF and/or glomerular capillary pressure are reduced, thereby leading to a fall in the GFR. The reduction in blood volume, on the other hand, will cause stimulation of the adrenergic nervous system and release of vasoconstrictor factors, both leading to renal vasoconstriction. This makes the renal hypoperfusion more severe and causes a greater decrease in glomerular capillary pressure; the immediate consequence is a fall in the GFR that is mirrored by the rise in serum creatinine [8].

We may define ‘pre-renal ARF’ as the abrupt impairment of renal function occurring in conditions of renal hypoperfusion that may be reversed by adequate fluid replacement (in the form of blood, plasma and/or saline solutions) or by reversion of the contraction of ‘effective’ circulating blood volume [8]. The ‘effective’ arterial blood volume may be defined as the relative fullness of the arterial tree as determined by cardiac output, peripheral vascular resistance and total blood volume; the ‘effective’ arterial blood volume is usually diminished in congestive heart failure (because of reduced cardiac output), in cirrhosis with ascites (because of reduced peripheral resistance) and in nephrotic syndrome (because of reduced blood volume secondary to protein losses). It is, in other words, a functional renal failure with no abnormalities in the kidneys. The renal hypoperfusion causes tubular over-reabsorption, mainly in the proximal tubules, with the aim of normalizing blood volume and, consequently, renal perfusion. This leads to oliguria with highly concentrated urine, very low urinary sodium concentration (since sodium is reabsorbed more avidly than water) and normal urinary sediment [8].

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Salt depletion and extracellular volume (ECV) contraction with severe true hypovolaemia (i.e. diminution of total intravascular volume) in the elderly, as in young subjects, may be due to non-renal or renal losses. Non-renal losses include vomiting, diarrhoea, gastric, enteric or biliary drainage, enterostomy, abuse of laxatives, skin burns and sweating. Internal redistribution from the intravascular to the interstitial space in states of hypoproteinaemia (nephrotic syndrome, malnutrition, hepatic cirrhosis) or during peritonitis or severe tissue injury (e.g. burns) may also cause hypovolaemia, particularly in geriatric patients [1]. Finally, true hypovolaemia may follow the sequestration of plasma in the ‘third space’, because of pancreatitis, traumatized muscles or intestinal obstruction [8]. Renal losses include abuse of diuretics (for treating hypertension or for control of oedema secondary to congestive heart failure), mineralocorticoid deficiency and salt-losing nephritis [10].

Contraction of the ‘effective’ circulating blood volume may follow a decrease in cardiac output after myocardial dysfunction or pericardial disease, which are particularly frequent in the elderly population [1].

Aged patients are at higher risk of volume depletion and the pre-renal type of ARF because of various age-related changes in renal physiological functions, such as a decrease in GFR, a tendency toward hypodipsia, reduced sodium intake, an impairment in the ability to concentrate urine, an inability to retain sodium under conditions of salt restriction (due to an inadequate secretion of aldosterone and an inadequate tubular responsiveness to this hormone, as well as to an intrinsic defect of tubular reabsorption of sodium in the loop of Henle) [7] and because of the tendency to use diuretics [4,10–12]. In a study on aged patients with ARF, volume depletion was responsible in 23.4% of 298 cases [7].

Because of the mentioned changes in renal physiological functions with age, the senescent kidney is unable to adapt to stress factors; minor insults for young subjects may therefore cause renal shutdown in the elderly. This tendency in old patients to conditions of ECV contraction can account for the higher frequency of non-oliguric ARF in the elderly and the tendency to reversion of ARF with vigorous fluid and electrolyte therapy [12].

Not infrequently, particularly in the elderly, ECV contraction is due to the incorrect use of diuretics for treating systolic hypertension or combined systolic and diastolic hypertension [13–15]. Actually the low values of plasma renin activity in hypertensive aged patients, suggesting an increase in plasma volume, represent a clear indication for diuretic treatment [16], and thiazide is the most used diuretic drug, usually in combination with amlodipine, a potassium-saving diuretic [16–18], or with angiotensin-converting enzyme inhibitors (ACEIs) [19], to avoid hypokalaemia. Not infrequently, loop diuretics are preferred or are even combined with a thiazide. However, the abuse of powerful loop diuretics may be particularly dangerous in the elderly population, since they may cause severe salt depletion, hypovolaemia, postural hypotension, reduction in central venous pressure and pre-renal azotaemia (Figure 1), or even shock. Thus diuretics should be used with caution in aged subjects, to avoid salt depletion, hypotension and renal function impairment [10].

As mentioned, the kidney responds to true blood volume depletion (secondary to haemorrhage, ECV contraction, etc.) and to the decrease in ‘effective’ circulating blood volume (as occurs in congestive heart failure) by avidly conserving sodium and water (through an increase in tubular reabsorption of sodium and concentration of urine) in an attempt to restore its ‘normal’ perfusion; if the stimulus is great, the kidney responds by decreasing the RBF and GFR [20]. Under such circumstances, even hyponatraemia may be observed (this was the case in our patient O.G. of Figure 1); because of ‘effective’ hypovolaemia, in fact, the initial priority of maintaining a normal osmolality in ECV is sacrificed in order to minimize the volume contraction; hence, the water-retaining forces are stimulated (rather than inhibited, as usually expected) and hyponatraemia occurs, reflecting severe hypovolaemia [8].

Older patients are particularly sensitive to changes in cardiac output and may exhibit a severe functional renal shutdown in a condition in which the kidney of a younger individual would show only a moderate renal insufficiency [3]. The renal mass in the aged kidney is, in fact, decreased with a reduction in GFR and RBF because of progressive increase with time in the number of sclerotic glomeruli and because of vascular atheromathosis and sclerosis and increased renal vascular resistance due to persistent arteriolar vasoconstriction [10]. It is therefore clear why the aged kidney may respond poorly to even modest changes of cardiac output and blood pressure, in a fashion similar to that of patients with already reduced renal function because of pre-existing renal disease [3].

Aged subjects are also particularly susceptible to the combined effects of pre-existing volume depletion and nephrotoxic drugs, such as aminoglycosides or contrast agents [4]. It has been stated that doses of aminoglycosides which are relatively innocuous in younger subjects are stimulated (rather than inhibited, as usually expected) and hyponatraemia occurs, reflecting severe hypovolaemia [8].

Pre-renal ARF may also result with increasing frequency in the elderly from the use of drugs that alter intrarenal haemodynamics, e.g. non-steroidal anti-inflammatory drugs (NSAIDs) and ACEIs [1,7], particularly when associated with salt depletion and hypovolaemia (Figure 1). Thus, the abuse of NSAIDs for relieving pain (particularly that due to rheumatoid arthritis), quite common in elderly people, may increase the already severe renal vasoconstriction occurring in hypovolaemic patients, because of their inhibition of vasodilator prostaglandins [8]. The release of these hormones, in fact, is enhanced when secretion of vasoconstrictors angiotensin II, norepinephrine and endothelins [8,21] is increased, as occurs both in ‘effective’ volume depletion (e.g. heart failure, hepatic cirrhosis) and in true volume depletion (e.g. following
Vasomotor nephropathy in the elderly

Pre-renal ARF is a well-known complication of ACEI treatment of hypertension and congestive heart failure, usually in cases of renal artery stenosis in a solitary kidney or in bilateral renal artery stenoses [30]. However, it has also been reported following the use of ACEIs even in the absence of renal artery stenosis [31–37].

In a recent retrospective study, 27 cases (14 older than 65 years, 20 older than 60 years) of pre-renal ARF occurred following treatment with an ACEI without documented renal artery stenosis; a concomitant condition functioning as a precipitating factor was volume depletion, linked to the combination of low-salt diet and use of diuretics [37]. A significant correlation has been reported between sodium depletion, due to excessive diuretic therapy, and the occurrence of ARF in patients with severe chronic heart failure receiving captopril or enalapril, hypovolaemia being attributed to excessive reduction in left ventricular filling pressure [34]. This functional ARF due to ACEIs is readily reversed by saline infusion as we demonstrated in 1987 [38]. Its (most accepted) pathophysiology is based on angiotensin II inhibition that, leading to a rapid fall of efferent arteriolar resistances (particularly raised in hypoperfused kidneys), will cause a decline in glomerular pressure and depression of glomerular filtration; the variable time necessary for the occurrence of ARF seems related to the extent of salt depletion [37].

Obviously the association of NSAIDs and ACEIs will disrupt the two main mechanisms of glomerular autoregulation, making the occurrence of pre-renal ARF more likely [37,39].

Clinical aspects of pre-renal ARF

Clinical signs of salt depletion and ECV contraction are postural hypotension and reduction in central venous pressure (CVP), whereas in the elderly, other physical findings, such as loss of skin turgor (because of the reduction of skin elastic tissue), dry mouth (because frequently the patient breathes through the mouth) and soft ocular globes may be confounding findings [10]. Recent (if available) and present body weights may be of help in the diagnosis, as the loss of two, three or more kilogrammes of body weight may indicate salt depletion; however, unchanged body weight may be observed in cases of abnormal distribution of extracellular fluids (because of sequestration of fluids as ascites or pleural effusions, or within the bowel for intestinal ileus, or because of concealed haemorrhage) [3].

It should be stressed, however, that aged patients, even when seriously hypovolaemic, can preserve normal blood pressure while lying in bed; a severe hypotension with tachycardia occurs only when they assume the upright position, because they cannot tolerate further shrinkage of the ‘effective’ arterial
blood volume induced by pooling of blood in the capacitance vessels of the lower extremities [3,5,10]. Thus it is important to measure blood pressure and pulse rate not only when the patient is lying in bed, but also while standing; if it is not the effect of antihypertensive drugs, orthostatic hypotension represents a physical sign of severe volume depletion. It is not observed, however, when ECV contraction is <10%, even though functional renal impairment has occurred; hence, the absence of orthostatic hypotension does not exclude volume depletion and the consequent hypovolaemic fall of GFR (Figure 1).

**Treatment of pre-renal ARF**

Pre-renal ARF is reversed when the initiating cause is removed. Thus true hypovolaemia due to haemorrhage should be reversed by blood transfusion, and the hypovolaemic hypotension due to salt depletion could be reversed by i.v. salt infusion; restoration of cardiac output will reverse ‘effective’ hypovolaemia in patients with heart failure.

Usually, physicians are reluctant to infuse saline in depleted aged subjects, because they are afraid to cause ECV expansion, thereby precipitating congestive heart failure [10,40]; a CVP catheter, however, is very helpful in monitoring fluid infusion.

Low-dose dopamine (1–3 μg/kg body weight/min) may be used to protect the kidney against ischaemic renal injury [8,9,41–44], even though it has been stated that there is a resistance to the actions of dopamine in the elderly [45].

Loop diuretics are indicated, preferably in combination with dopamine, in pre-renal ARF occurring in cardiogenic shock and left ventricular failure [8]. The association dopamine+frusemide (250–500 mg i.v.) may be used, once salt repletion has been performed, even in pre-renal ARF secondary to true volume depletion; quite frequently, urine output will increase even though renal function is not improved [8,46–48].

**Prevention of pre-renal ARF**

Considering the high incidence of pre-renal ARF in the elderly, preventive measures are very important. These should include the following: (i) Prevention of salt depletion: any condition leading to loss of salt should be treated immediately by salt replacement; under such circumstances, it is important to avoid electrolyte-free solutions (e.g. glucose or levulose in water) and to choose rather isotonic saline [7]. (ii) In patients with heart problems, a CVP catheter should be used to monitor the CVP (maintaining it at 8–10 cm H2O) [7] (in the case of low CVP, more fluid should be given; in the case of high CVP, frusemide i.v. may help). (iii) When using drugs altering intrarenal haemodynamics (NSAIDs or ACEIs), renal function should be carefully monitored. Among the NSAIDs, sulindac is to be preferred, because of its unusual metabolism that makes it less nephrotoxic than other NSAIDs [49]. The association of an ACEI with diuretics should be used with caution in the elderly, particularly in athromatous or diabetic patients, since small vessel disease seems an important facilitating condition for the development of ACEI-induced ARF in patients without stenosis of the main renal arteries [31–33,37].

(iv) Avoid the use of nephrotoxic drugs or, if necessary, use them at low dosage while frequently monitoring renal function.

**Acute tubular necrosis (ATN)**

**Pathophysiology of ATN**

Acute tubular necrosis (ATN) may represent an evolution of untreated pre-renal ARF. Under such conditions, the renal pathology can appear quite peculiar on renal biopsy. Interstitial oedema, attributed to altered capillary permeability, is usually responsible for the enlarged kidneys; in the medulla, by contrast, the vasa recta are engorged; patches of leukocyte infiltrate are observed in the cortical interstitium. Glomeruli and blood vessels are usually normal on both light and electron microscopy. Tubular lesions are variable in severity and extension; large areas exhibit little or no change in tubular structure on light microscopy, revealing degeneration of nuclei and swelling of mitochondria, with distortion of the cristae and, in some cells, disintegration of mitochondrial outer membranes on electron microscopy. Small areas may exhibit tubular necrosis, with cellular disruption and shedding of cellular debris in the tubular lumens together with proteinaceous material; however, there is usually no correlation between severity of histological lesions and severity of the clinical condition of the patient [3]. During recovery, the increasing number of mitoses indicates tissue repair, that usually leads to full healing [3].

**Clinical aspects of ATN**

The first signs and symptoms of ATN are related to the cause of the syndrome. The usual hallmark is oliguria, even though quite frequently the ARF may be non-oliguric [8]. Other symptoms may include the following: (i) Hyponatraemia: this may be a hypovolaemic hyponatraemia (as in our patient O.G. of Figure 1), usually when ECV contraction is >10%, as already mentioned. Under such circumstances, the need to normalize the ECV leads to water retention, despite the low tonicity of extracellular fluids. However, after prolonged ATN, hyponatraemia may be due to water overload easily occurring because of anuria [10]. (ii) Metabolic acidosis and, in the elderly, lactic acidosis: the kidney and liver are major sites of lactate metabolism, but the capacity of the liver for lactate extraction is much greater; this explains why the loss of renal function alone is insufficient to cause lactic acidosis. The fall of the left ventricular ejection fraction, as may easily occur in the elderly, may worsen tissue perfusion, enhancing lactate production and causing lactic acidosis. In aged patients with ARF who
died, blood lactate was significantly higher than in survivors [50]. (iii) Hyperkalaemia: this is particularly frequent in cases of necrotic tissue, sequestered blood, haemolysis, hypercatabolism, or following blood transfusion or i.v. infusion of potassium-containing fluids [8,10]. (iv) Hypocalcaemia, hyperphosphataemia and hypermagnesaemia. (v) Anaemia, particularly in cases of overt intestinal bleeding or marked haemolysis [3]. Sometimes, other symptoms may appear, such as anorexia, nausea, vomiting, stomatitis or gastrointestinal bleeding due to stress ulcers, gastritis or enterocolitis [3]. The cause of death is usually the infection, the occurrence of which is made easier by the use of central venous catheters or of an unnecessary indwelling bladder catheter. Heart failure, hypertension and arrhythmias are unusual if adequate dialysis therapy is performed thereby preventing volume overload and hyperkalaemia.

Treatment of ATN

The prevalence of dialysis-requiring cases of ARF in the aged is not different from younger patients [6]. Should fluid replacement therapy and subsequent therapy with high doses of frusemide (with dopamine) be ineffective, dialysis treatment becomes necessary in most cases, being the best way to correct the electrolyte disturbances (hyponatraemia, hyperkalaemia, acidosis, etc.).

Acetate-based dialysis solutions and cuprophane membranes should possibly be avoided, especially in haemodynamically unstable patients (persistent systolic BP < 100 mmHg); in such patients, haemodialfiltration instead of haemodialysis is recommended [5,7].

An aggressive renal replacement approach by continuous haemodialfiltration may improve the prognosis of elderly patients with ARF [51].

Diagnosis of pre-renal ARF and ATN

The differential diagnosis between pre-renal ARF and ATN frequently is difficult. In pre-renal ARF, the preserved capacity to retain sodium and concentrate urine is consistent with the integrity of tubular function; on the contrary, in ATN, sodium is usually lost and urine is not concentrated even when the patient is hypovolaemic, indicating an impairment of tubular function [8].

However, this general rule may not be valid when pre-renal ARF occurs in aged patients [52], in patients with pre-existing chronic renal failure, in patients under the effect of loop diuretics or in patients treated with mannitol or radiocontrast media, conditions in which the renal capacity to retain sodium is impaired. Finally, high urinary sodium concentration and isosthenuria may occur in other forms of ARF (post-renal ARF, renal cortical necrosis, acute interstitial nephritis and glomerular diseases) [8].

To help in distinguishing pre-renal ARF from ATN, several diagnostic indices have been suggested (Table 1) [8]: (i) urine specific gravity that is usually > 1013 in pre-renal ARF; (ii) urinary concentration of sodium (U\textsubscript{Na}+/P\textsubscript{Na}) that is usually < 20 mEq/l in pre-renal ARF (> 40 mEq/l in ATN); (iii) fractional excretion of filtered sodium (FE\textsubscript{Na}+ = [U\textsubscript{Na}+ × P\textsubscript{Cr}]/[P\textsubscript{Na} × U\textsubscript{Cr}] × 100) that is usually < 1% in pre-renal ARF (> 3% in ATN); (iv) the ratio between blood urea nitrogen and serum creatinine (BUN/S\textsubscript{Cr}) that is usually > 20 in pre-renal ARF; (v) the urine to plasma urea nitrogen ratio (U\textsubscript{UN}/P\textsubscript{UN}) that is usually > 8 in pre-renal ARF (< 3 in ATN); (vi) the urine to plasma creatinine ratio (U\textsubscript{Cr}/P\textsubscript{Cr}) that is usually > 40 in pre-renal ARF (< 20 in ATN) [5,8]; (vii) renal failure index (RFI = U\textsubscript{Na}+/[U\textsubscript{Cr}/P\textsubscript{Cr}] or [U\textsubscript{Na}+ × P\textsubscript{Cr}] U\textsubscript{Cr} is actually dependent on FE\textsubscript{Na}+; since P\textsubscript{Na}+ varies within fairly narrow limits, in fact, it may be disregarded in the FE\textsubscript{Na}+ formula) that is usually < 1 (> 4 in ATN) [8].

Thus in a patient (S.L., a 62-year-old male) with pre-renal ARF secondary to diarrhoea, vomiting and fever associated with no food intake (Figure 2), diagnostic indices gave the results shown in Table 2, that were fairly consistent with those expected for pre-renal ARF. Similarly, in a patient (B.M., a 73-year-old male) with ATN secondary to intestinal haemorrhage and septic fever followed by therapy with aminoglycosides (Figure 3), diagnostic indices gave the results shown in Table 3, that were consistent with those expected for ATN.

These indices, however, cannot be regarded as inviolate: the farther a value of an index strays from the stated limits, the less likely the corresponding diagnosis is to be correct [8,52].

A recent treatment with a loop diuretic or with radiocontrast media may alter the diagnostic indices, making the diagnosis of pre-renal ARF difficult. Thus, in a patient (C.M., a 65-year-old male) with pre-renal ARF secondary to heart failure, treated with frusemide, urine output was 900 ml/24 h, while diagnostic indices are not consistent with the diagnosis of pre-renal ARF (Table 4).

A positive response to fluid challenge, as mirrored by an increase in urine output and urinary sodium excretion, and a decrease in blood urea nitrogen represent strong evidence for pre-renal ARF [5], bearing in mind, however, that aged patients may have a delayed response to volume expansion (after prolonged salt loading).

<table>
<thead>
<tr>
<th>Table 1. Pre-renal ARF vs ATN</th>
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<tbody>
<tr>
<td>Indices</td>
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<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Urine specific gravity</td>
</tr>
<tr>
<td>U\textsubscript{Na}+ (mEq/l)</td>
</tr>
<tr>
<td>FE\textsubscript{Na}+</td>
</tr>
<tr>
<td>BUN/S\textsubscript{Cr}</td>
</tr>
<tr>
<td>U\textsubscript{UN}/P\textsubscript{UN}</td>
</tr>
<tr>
<td>U\textsubscript{Cr}/P\textsubscript{Cr}</td>
</tr>
<tr>
<td>RFI</td>
</tr>
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</table>
Fig. 2. (Pre-renal ARF) S.L., a 62-year-old male patient, was admitted, on October 3, to our unit because of severe oliguria (urine output of 200 ml/day). Past medical history included, 3 months earlier, a serum creatinine 1.8 mg/dl and plasma urea 50 mg/dl; a few days before admission, diarrhoea and vomiting occurred; the patient felt sick, had fever and refused any food. On admission, BP was low, but within the normal range; serum creatinine was 4.8 mg/dl, plasma urea 140 mg/dl; urinalysis showed a specific gravity of 1025, Na+ concentration 37 mEq/l, fractional excretion of sodium (FE Na+) 0.6%. The patient was treated immediately with i.v. infusion of NaHCO3 (500 ml/day) and NaCl 0.9% (1000 ml/day): urine output increased immediately while serum creatinine and plasma urea returned to baseline values in few days.

Table 2. Pre-renal hypovolaemic ARF: behaviour of the indices in the same patient as shown in Figure 2

<table>
<thead>
<tr>
<th>Indices</th>
<th>Pre-renal</th>
<th>S.L. 62-year-old male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine specific gravity</td>
<td>&gt;1013</td>
<td>1025</td>
</tr>
<tr>
<td>UNa+ (mEq/l)</td>
<td>&lt;20</td>
<td>37</td>
</tr>
<tr>
<td>FE Na+</td>
<td>&lt;1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>BUN/SCr</td>
<td>&gt;20</td>
<td>15</td>
</tr>
<tr>
<td>UN/UN</td>
<td>&gt;8</td>
<td>13</td>
</tr>
<tr>
<td>UCr/Pcr</td>
<td>&gt;40</td>
<td>43</td>
</tr>
<tr>
<td>RFI</td>
<td>&lt;1</td>
<td>0.85</td>
</tr>
</tbody>
</table>

depletion they may remain oliguric for up to 24 h [1,8,53].

In all cases of ARF, but particularly in the elderly, urinary tract obstruction should be suspected and checked first; ultrasound sonography of kidneys and the bladder is the simplest, non-invasive method to be used for ruling out obstructive ARF [5].

Prognosis

It is commonly believed that ARF in the elderly is associated with high mortality. Several retrospective studies have, in fact, shown a greater mortality in the

Table 3. ATN: behaviour of the indices in the same patient as shown in Figure 3.

<table>
<thead>
<tr>
<th>Indices</th>
<th>Pre-renal</th>
<th>B.M. 73-year-old male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine specific gravity</td>
<td>&lt;1013</td>
<td>1008</td>
</tr>
<tr>
<td>UNa+ (mEq/l)</td>
<td>&gt;40</td>
<td>107</td>
</tr>
<tr>
<td>FE Na+</td>
<td>&gt;3%</td>
<td>23%</td>
</tr>
<tr>
<td>BUN/SCr</td>
<td>&lt;20</td>
<td>7</td>
</tr>
<tr>
<td>UN/UN</td>
<td>&lt;3</td>
<td>0.7</td>
</tr>
<tr>
<td>UCr/Pcr</td>
<td>&lt;20</td>
<td>3</td>
</tr>
<tr>
<td>RFI</td>
<td>&gt;4</td>
<td>31</td>
</tr>
</tbody>
</table>

Table 4. The effects of a diuretic on the indices of pre-renal ARF

<table>
<thead>
<tr>
<th>Indices</th>
<th>Pre-renal</th>
<th>C.M. 65-year-old male</th>
</tr>
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<tbody>
<tr>
<td>Urine specific gravity</td>
<td>&gt;1013</td>
<td>1010</td>
</tr>
<tr>
<td>UNa+ (mEq/l)</td>
<td>&lt;20</td>
<td>63</td>
</tr>
<tr>
<td>FE Na+</td>
<td>&lt;1%</td>
<td>6%</td>
</tr>
<tr>
<td>BUN/SCr</td>
<td>&gt;20</td>
<td>55</td>
</tr>
<tr>
<td>UN/UN</td>
<td>&gt;8</td>
<td>1.1</td>
</tr>
<tr>
<td>UCr/Pcr</td>
<td>&gt;40</td>
<td>8</td>
</tr>
<tr>
<td>RFI</td>
<td>&lt;1</td>
<td>7.7</td>
</tr>
</tbody>
</table>

This patient was taking frusemide because of heart failure. Serum creatinine reached 4.4 mg/dl, BUN 259 mg/dl. Urine volume was 900 ml/day.
elderly than in young patients with ARF. A retrospective study on 101 aged patients has shown a mortality of 27% vs 12% observed in a group of younger subjects, sepsis being the main cause of death [6]. Another retrospective study on 88 patients older than 65 (mean age: 73.5 years) produced worse figures: the overall mortality was as high as 68% and was similar in men and in women, the leading cause of death being sepsis [54]. In another study on 55 patients aged >60 years with ARF, the mortality was 53%; it was 35% in pre-renal ARF and 64% in ATN (being 76% in oliguric ATN, 50% in non-oliguric ATN); again the main cause was sepsis (62%) [55]. In a further retrospective study on 68 patients over 65 admitted to the same intensive care unit (ICU), the mortality rate was 63.3% (the main causes of death being septic shock and multiple organ failure) [50]. The different figures are related to many factors, such as type of population study, definition of ARF or type of unit where the study was performed (results are obviously different if we consider patients admitted to divisions of Medicine, or to Nephrology Units or to ICUs).

Mortality in aged patients with ARF has been associated with five clinical or biological parameters: (i) organ system failure index (more than two organs involved) [7,50,56]; (ii) oliguria [50,57–59]; (iii) high urea appearance rate [Δ blood urea x body weight x 60%/urinary urea nitrogen] (a more precise index of protein catabolism than plasma urea), usually secondary to sepsis [50,57]; (iv) hypotension [50]; and (v) elevated blood lactate [50,60].

In contrast to these studies supporting an adverse effect of increasing age on prognosis in ARF patients, there are many investigations which have reported that age per se is not a determinant of survival [1,12,58,59,61,62]. Thus, a retrospective analysis in 242 elderly intensive care patients with ARF failed to demonstrate an excess mortality in subjects aged >65 years. The mortality rate in these patients was 61%, which was comparable with other age groups in the same institution, i.e. 57% in subjects aged <18 years and 59% in patients aged 19–64 years. Furthermore even in patients aged >65 years, there was no age dependency of survival, i.e. mortality in aged >80 years was not greater than in those aged 65–68 years; mortality in those requiring renal replacement therapy was twice as high as in non-dialysed patients, but comparable with that observed in other age groups [12]. Similarly, in another study, the difference in mortality rate (45% in elderly vs 41% in younger subjects) did not reach statistical significance [1].

Few data are available on the long-term prognosis in surviving ARF patients; it has been observed, however, that aged patients who survived after ARF needed more time for total recovery than younger survivors [1], nevertheless frequently attaining normal renal function [63].

References